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PTO/SB/21 (07-09)
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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/151,436
Filing Date	May 20, 2002
First Named Inventor	Ellsworth, et al
Art Unit	1623
Examiner Name	Devesh Khare
Attorney Docket Number	102919-US CIP

Total Number of Pages in This Submission

ENCLOSURES *(Check all that apply)*

- [✓] Fee Transmittal Form
- [ ] Fee Attached
- [ ] Amendment/Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
- [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [✓] Other Enclosure(s) (please Identify below):

This is an application for Patent Term Extension

Remarks

Applicants authorizes the Commissioner to charge the $200 associated with the filing of this Patent Term Extension or to charge any deficiency or overpayment under 37 C.F.R. §1 to our Deposit Account Number 260166

RECEIVED
MAR 0 6 2014
PATENT EXTENSION
OPLA

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name			
Signature	/David M. Gryte/		
Printed name	David M. Gryte		
Date	March 6, 2014	Reg. No.	41,809

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name		Date	

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

PTO/SB/17 (03-13)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL

Complete if known	
Application Number	10/151,436
Filing Date	May 20, 2002
First Named Inventor	Ellsworth, et al
Examiner Name	Devesh Khare
Art Unit	1623
Practitioner Docket No.	102919-USCIP

☐ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($) 200

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____

☑ Deposit Account Deposit Account Number: 260166 Deposit Account Name: AstraZeneca, Inc.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

☐ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, **except for the filing fee**

☑ Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17 ☑ Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	U ($)	S ($)	M ($)	U ($)	S ($)	M ($)	U ($)	S ($)	M ($)	Fees Paid ($)
Utility	280	140*	70	600	300	150	720	360	180	
Design	180	90	45	120	60	30	460	230	115	
Plant	180	90	45	380	190	95	580	290	145	
Reissue	280	140	70	600	300	150	2,160	1,080	540	
Provisional	260	130	65	0	0	0	0	0	0	

* The $140 small entity status filing fee for a utility application is further reduced to $70 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	Undiscounted Fee ($)	Small Entity Fee ($)	Micro Entity Fee ($)
Each claim over 20 (including Reissues)	80	40	20
Each independent claim over 3 (including Reissues)	420	210	105
Multiple dependent claims	780	390	195

Total Claims		Extra Claims		Fee ($)		Fee Paid ($)
_____	-20 or HP =	_____	x	_____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims		Extra Claims		Fee ($)		Fee Paid ($)
_____	-3 or HP =	_____	x	_____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	Fee ($)	Fee Paid ($)
	_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $400 ($200 for small entity) ($100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		Extra Sheets		Number of each additional 50 or fraction thereof		Fee ($)		Fee Paid ($)
_____	- 100 =	_____	/ 50 =	_____ (round up to a whole number)	x	_____	=	_____

4. OTHER FEE(S) Fees Paid ($)

Non-English specification, $130 fee (no small or micro entity discount) _____

Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity) _____

Other (e.g., late filing surcharge): Filing of Patent Term Extension $200 _____

SUBMITTED BY

Signature	/David M. Gryte/	Registration No. (Attorney/Agent) 41,809	Telephone 302-885-6609
Name (Print/Type)	David M. Gryte		Date March 6, 2014

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

EK085035201US	BY "EXPRESS MAIL" UNDER 37 CFR 1.10
Express Mail Label Number	MARCH 6, 2014 Date of Deposit

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

U.S. Patent No.:	**6,515,117**	)
		)
Granted:	**February 4, 2003**	)
		)
Inventors:	**Ellsworth *et al.***	)
		)
Serial No.:	**10/151,436**	)
		)
Filed:	**May 20, 2002**	)
		)
For:	**C-Aryl Glucoside SGLT2 Inhibitors and Method**	)

Mail Stop Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22303-1450

APPLICATION FOR PATENT TERM EXTENSION
PURSUANT TO 35 U.S.C. §156

Dear Madam:

Applicant, AstraZeneca AB, the owner of record of U.S. Patent No. 6,515,117 ("the '117 patent"; *attached hereto* as **Exhibit A**) submits this Application for Patent Term Extension pursuant to the provisions of 35 U.S.C. § 156. In making this application for patent term extension, Applicant's predecessor-in-interest, Bristol-Myers

Squibb Company, has received regulatory approval of a new human anti-diabetic drug as disclosed below and claimed in the '117 patent.

I. Eligibility

Applicant is entitled to patent term extension for this patent on the grounds that the circumstances fulfill the requirements of 35 U.S.C. § 156. Specifically:

a) U.S. Patent 6,515,117 claims a product according to the provisions of § 156(a);

b) The term of this patent has not expired before submission of this application for patent term extension pursuant to § 156(a)(1);

c) The term of this patent has never been extended, pursuant to § 156(a)(2);

d) Applicant is the owner of record of the patent according to the assignment documents appended to this application, pursuant to § 156(a)(3);

e) The product has been subject to a regulatory review period before commercial marketing and use pursuant to § 156(a)(4); and

f) Permission for commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provisions of the law under which the regulatory review period was conducted pursuant to § 156(a)(5).

Applicant, AstraZeneca AB, is the owner of all right, title and interest in U.S. Patent 6,515,117, as recorded by assignment in the U.S. Patent and Trademark Office at reel 011206 and frame 0916 (from inventors to Bristol-Myers Squibb Company) and reel 032347 and frame 0115 (from Bristol-Myers Squibb Company to AstraZeneca AB) (USPTO assignment records attached hereto as **Exhibit B**).

Bristol-Myers Squibb Company, Applicant's predecessor-in-interest, received regulatory approval for the approved product on January 8, 2014.

The term of U.S. Patent No. 6,515,117 has not expired prior to submission of this application.

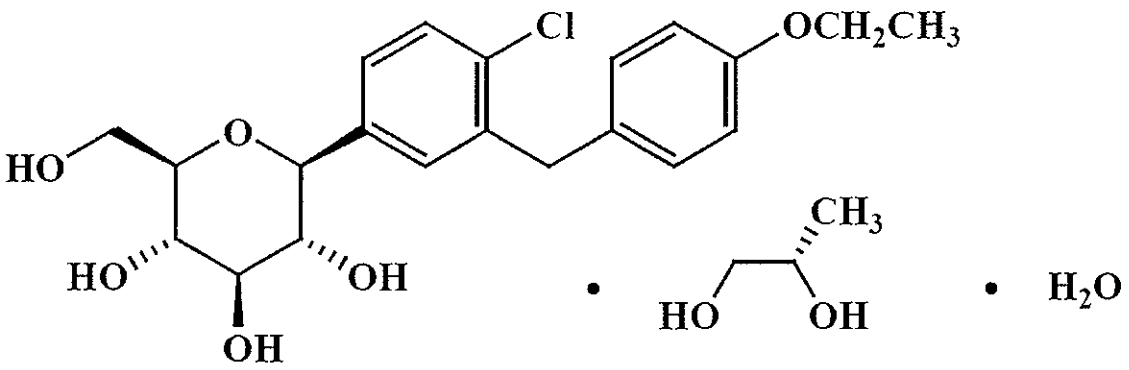
II. Requirements

Applicant provides the following information, pursuant to the requirements of 35 U.S.C. § 156(d) and 37 C.F.R. § 1.740 *et seq.*:

(a) An application for extension of patent term must be made in writing to the Commissioner. A formal application for the extension of patent term must include:

(1) A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics;

The approved product is FARXIGA® (generic name: dapagliflozin), an anti-diabetic drug described chemically as D-glucitol, 1,5-anhydro-1-*C*-[4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl]-, (1*S*)-, compounded with (2*S*)-1,2-propanediol, hydrate (1:1:1). The empirical formula is $C_{21}H_{25}ClO_6 \cdot C_3H_8O \cdot H_2O$ and the molecular weight is 502.98. The structural formula is



(2) A complete identification of the Federal statute including the applicable provision of law under which the regulatory review occurred;

The approved product was subject to regulatory review pursuant to 21 U.S.C. § 355(a) and Title 505(b)(1) of the Federal Food, Drug and Cosmetic Act, *codified at*

21 U.S.C. § 355(b)(1).

(3) An identification of the date on which the product received permission for commercial marketing or use under the provision of law under which the applicable regulatory review period occurred;

The product received permission for commercial marketing or use on January 8, 2014, pursuant to NDA 202293 by the letter of that date from Curtis J. Rosebraugh, M.D., M.P.H., Director, Office of Drug Evaluation II, Center for Drug Evaluation and Research, Food and Drug Administration, Public Health Services, Department of Health and Human Services (attached hereto as **Exhibit C**).

(4) In the case of a drug product, an identification of each active ingredient in the product and as to each active ingredient, a statement that it has not been previously approved for commercial marketing or use under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act, or a statement of when the active ingredient was approved for commercial marketing or use (either alone or in combination with other active ingredients), the use for which it was approved, and the provision of law under which it was approved.

The active ingredient of the approved drug product is D-glucitol, 1,5-anhydro-1-*C*-[4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl]-, (1*S*)-, generic name dapagliflozin. This active ingredient has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-Toxin Act.

The product has been approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

The product has been approved pursuant to 21 U.S.C. § 355(a) and Title 505(b)(1) of

the Federal Food, Drug and Cosmetic Act, *codified at* 21 U.S.C. § 355(b)(1).

(5) A statement that the application is being submitted within the sixty day period permitted for submission pursuant to 37 C.F.R. § 1.720(f) and an identification of the date of the last day on which the application could be submitted;

This application is submitted within 60 days of the date that the product first received permission for commercial marketing or use under the provisions of law under which the regulatory review period occurred, the last day for such submission being March 9, 2014.

(6) A complete identification of the patent for which an extension is being sought by the name of the inventor, the patent number, the date of issue, and the date of expiration;

This application is made for U.S. Patent No. 6,515,117, issued February 4, 2003 to Bruce Ellsworth, William N. Washburn, Philip M. Sher, Gang Wu and Wei Meng. The inventorship was corrected via a certificate of correction to list as inventors Bruce Ellsworth, William N. Washburn and Wei Meng. The '117 patent will expire on October 4, 2020.

(7) A copy of the patent for which an extension is being sought, including the entire specification (including claims) and drawings;

A copy of this patent is attached hereto as **Exhibit A**.

(8) A copy of any disclaimer, certificate of correction, receipt of maintenance fee payment, or reexamination certificate issued in the patent;

A copy of a receipt for payment of the first maintenance fee, paid July 7, 2006, is attached hereto as **Exhibit D**. A copy of a receipt for payment of the second maintenance fee, paid July 8, 2010, is attached hereto as **Exhibit E.**

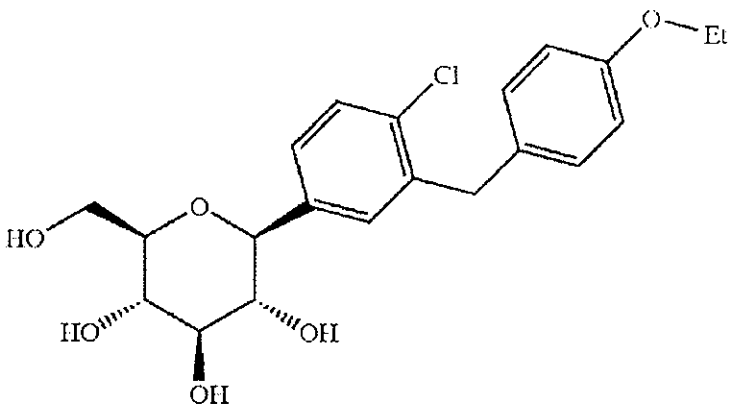
A copy of a Terminal Disclaimer, filed August 19, 2002, is attached hereto as **Exhibit F.**

A copy of a Certificate of Correction, issued October 23, 2008, is attached hereto as **Exhibit G.**

(9) A statement that the patent claims the approved product, or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which at least one such patent claim reads on:

This patent claims the approved product and methods for using the approved product. Specifically, the approved product and methods for using the approved product are claimed in the following claims of U.S. Patent No. 6,515,117:

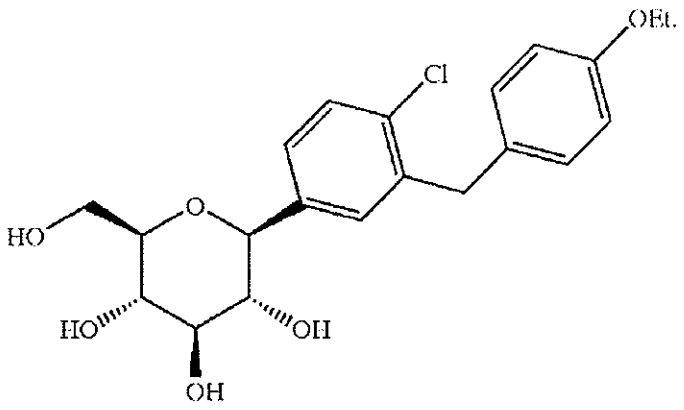
Claim 1. A compound having the structure



or a pharmaceutically acceptable salt, a stereoisomer thereof, or a prodrug ester thereof.

Claim 1 reads on the approved product.

Claim 2. The compound as defined in claim 1 having the structure:



Claim 2 reads on the approved product.

Claim 3. A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

Claim 3 reads on the approved product.

Claim 4. A pharmaceutical combination comprising an SGLT2 inhibitor compound as defined in claim 3 and an antidiabetic agent other than an SGLT2 inhibitor, an agent for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent, and/or a lipid-lowering agent.

Claim 4 reads on a combination comprising the approved product.

Claim 5. The pharmaceutical combination as defined in claim 4 comprising said SGLT2 inhibitor compound and an antidiabetic agent.

Claim 5 reads on a combination comprising the approved product.

Claim 6. The combination as defined in claim 5 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR γ agonist, a PPAR α/γ dual agonist, an aP2 inhibitor, a DP4 inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1), insulin, a meglitinide, a PTP1B inhibitor, a glycogen phosphorylase inhibitor, and/or a glucos-6-phosphatase inhibitor.

Claim 6 reads on a combination comprising the approved product.

Claim 7. The combination as defined in claim 6 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-

262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, and/or NVP-DPP-728A.

Claim 7 reads on a combination comprising the approved product.

Claim 8. The combination as defined in claim 5 wherein the SGLT2 inhibitor compound is present in a weight ratio to the antidiabetic agent within the range from about 0.01 to about 300:1.

Claim 8 reads on a combination comprising the approved product.

Claim 9. The combination as defined in claim 4 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta compound, and/or an anorectic agent.

Claim 9 reads on a combination comprising the approved product.

Claim 10. The combination as defined in claim 9 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, and/or mazindol.

Claim 10 reads on a combination comprising the approved product.

Claim 11. The combination as defined in claim 4 wherein the lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, or an ACAT inhibitor.

Claim 11 reads on a combination comprising the approved product.

Claim 12. The combination as defined in claim 11 wherein the lipid lowering agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, atavastatin, rosuvastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, and/or LY295427.

Claim 12 reads on a combination comprising the approved product.

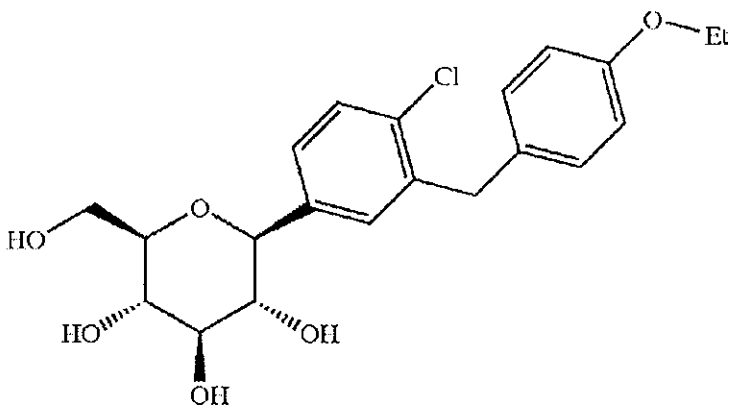
Claim 13. The combination as defined in claim 11 wherein the SGLT2 inhibitor is present in a weight ratio to the lipid-lowering agent within the range from about 0.01 to about 300:1.

Claim 13 reads on a combination comprising the approved product.

Claim 14. A method for treating or delaying the progression or onset of diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension, or for increasing high density lipoprotein levels, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

Claim 14 reads on a method for using the approved product.

Claim 15. The method as defined in claim 14 where the SGLT2 inhibitor compound has the structure



Claim 15 reads on a method for using the approved product.

Claim 16. A method for treating type II diabetes which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in claim 1 alone or in combination with another antidiabetic agent, an agent for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an anti-atherosclerotic agent and/or a hypolipidemic agent.

Claim 16 reads on a method for using the approved product.

Thus,

Claim 1 reads on the approved product.

Claim 2 reads on the approved product.

Claim 3 reads on the approved product.

Claim 4 reads on a combination comprising the approved product.

Claim 5 reads on a combination comprising the approved product

Claim 6 reads on a combination comprising the approved product

Claim 7 reads on a combination comprising the approved product

Claim 8 reads on a combination comprising the approved product

Claim 9 reads on a combination comprising the approved product

Claim 10 reads on a combination comprising the approved product

Claim 11 reads on a combination comprising the approved product

Claim 12 reads on a combination comprising the approved product

Claim 13 reads on a combination comprising the approved product

Claim 14 reads on a method for using the approved product.

Claim 15 reads on a method for using the approved product.

Claim 16 reads on a method for using the approved product.

(10) A statement beginning on a new page of the relevant dates and information pursuant to 35 U.S.C. 156(g) in order to enable the Secretary of Health and Human Services or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period as follows:

(i) For a patent claiming a human drug, antibiotic, or human biological product:

(A) The effective date of the investigational new drug (IND) application and the IND number;

(B) The date on which a new drug application (NDA) or a Product License Application (PLA) was initially submitted and the NDA or PLA number; and

(C) The date on which the NDA was approved or the Product License issued;

The following dates are relevant for a determination of the length of the Patent Term Extension available to applicant:

An Investigational New Drug (IND) application, No. 68,652 was filed November 20, 2003 (copy of FDA letter acknowledgment attached hereto as **Exhibit H**). The effective date of the IND application was December 21, 2003.

A New Drug Application (NDA), No. 202293 was filed December 27, 2010 (copy of FDA letter acknowledgment attached hereto as **Exhibit I**).

An Approval letter for NDA No. 202293 was signed January 8, 2014 (copy of FDA letter attached hereto as **Exhibit C**).

(11) A brief description beginning on a new page of the significant activities undertaken by the applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities;

Applicant submits a log of activities before the FDA as **Exhibit I**. The following provides a brief description of significant activities undertaken by the applicant's predecessor-in-interest ("BMS") during the regulatory review period with respect to the approved product, with significant dates:

- The original IND submission (IND 68,652) for FARXIGA® (dapagliflozin) was submitted on **November 20, 2003**.

- In **2003,** letter, telephonic and facsimile correspondence between BMS and FDA regarding initial submission of application, permission to proceed with studies and comments and recommendations from FDA on **November 21, November 25, December 15, December 19, December 22** and **December 23.**

- In **2004**, protocol and information amendments submitted on **February 23, March 12, March 18, March 24, May 20, July 16** (multiple), **August 23, September 21, November 23** and **December 8**; letter from FDA to BMS requesting additional information regarding July 16 amendment on **July 27** and BMS response submitted on **September 14**.

- In **2005**, protocol and information amendments submitted on **February 23, April 1, May 13, July 13, August 17, September 1, September 19, September 29, December 8** and **December 22**; BMS submitted an IND annual report for period December 1, 2003 through November 30, 2004 on **February 14**; telephonic correspondence between BMS and FDA regarding toxicity studies and safety on **April 25** and **April 29,** and BMS responded by providing requested data on **May**

16 and **August 17;** FDA letter regarding amendment dated April 1, 2005 on **May 12**; BMS submitted IND Safety Report on **December 15**.

- In **2006**, protocol and information amendments submitted on **January 5** (multiple), **February 3, February 15, February 21, March 6, March 15, March 28, April 7, April 24, May 8, May 16, May 17, June 1, June 5, July 12, August 23, September 18, September 22, October 25, November 2, November 6, November 27, December 6, December 14** and **December 15**; BMS submitted an IND annual report for period December 1, 2004 through November 30, 2005 on **February 16**; FDA letter providing comments and recommendations relating to BMS's January 5 submission on **April 24;** telephonic correspondence between BMS and FDA regarding time period required for review of protocol MB102009 on **July 10** and request for review of MB102009 protocol on **July 26**; BMS responded to agency's review of MB102009 on **September 25;** BMS submitted request for special protocol assessment on **November 6** with FDA acknowledging receipt of protocols on **November 15**; BMS responded to FDA request for information on **November 27**.

- In **2007**, protocol and information amendments submitted on **January 2, January 3, January 4, January 25** (multiple), **January 29, January 31, February 1, February 13** (multiple), **February 28** (multiple), **March 9, March 26, March 29, May 11, June 6, July 2, July 16, July 19, July 24, August 6, August 15, August 31, September 10, September 14, September 19, September 25, September 27, October 17, October 31, November 15, November 21** (multiple), **December 5, December 11** and **December 13**; BMS submitted an IND annual report for period December 1, 2005 through November 30, 2006 on **February 15**; BMS requested information on **July 3**; BMS requested an End-of-Phase 2 meeting to review results of clinical trials and relevant preclinical studies supporting the Phase 3 clinical development program on **July 12** and resubmitted request on **August 6;** FDA letter encouraging submission of another End-of-Phase 2 meeting after submission of study report for MB102-008 on **August 1**; BMS submitted End-of-Phase 2 briefing package for Sept. 11 meeting on **August**

9; BMS submitted IND Safety Report on **September 5**; correspondence from FDA to BMS containing pre-meeting minutes regarding QTc study and extensive comments on the QTc study on **September 7**; meeting minutes and slides for September 11 meeting submitted on **September 25** and **October 11** and request made for meeting/background document regarding September 11 meeting on **December 17**; BMS's response to Division's comments relating to BMS's amendments on **December 20**; FDA letter denying request for meeting on **December 27**.

- In **2008**, protocol and information amendments submitted on **January 7** (multiple), **January 9, January 18, February 8, February 14, March 13, April 4** (multiple), **April 9, April 24, April 30, May 21, May 30, June 18, July 2, July 15, July 31, August 8, August 13, August 22, August 28, August 29, September 3, September 25, October 15, November 12, December 3, December 5, December 8, December 10, December 15,** and **December 19** (multiple).

- In **2008,** BMS submitted a Safety Report on **January 16, September 2, October 16, November 21, November 25** and **December 22**.

- Correspondence between BMS and FDA in **2008** including: FDA letter denying request for meeting and providing response to BMS's questions on December 17, 2007 amendment on **February 29**; FDA email correspondence providing comments on protocols MB102030 & MB102033 on **October 7** and BMS's response and submission of core statistical analysis plan on **October 22;** BMS email correspondence regarding carcinogenicity studies and request for ECAC comment on **October 7** and **October 8**; BMS correspondence to FDA to provide transparency in regard to an error in information submitted to FDA regarding randomized treatment on **November 25**.

- BMS submitted information to the FDA in **2008** including: an IND annual report for period December 1, 2006 through November 30, 2007 on **February 15**; information to ensure that the an evaluation of available blinded & unblended

safety data was conducted in support of Study MB102021 on **July 30**; SAP for clinical study MB102009 on **August 19;** responses to the agency comments received on October 24, 2008 on **November 7.**

- BMS requested a CMC-Type B meeting on **August 6, 2008** and BMS submitted briefing document for October 9, 2008 meeting on **September 5, 2008**.

- BMS requested comment on modified dissolution method on **November 26, 2008**.

- In **2009**, protocol and information amendments submitted on **January 15, February 5, February 11, February 13, February 19, February 26, March 4, March 12, March 16, March 20, March 25, April 21, April 22, May 20, May 29, June 2, June 8, June 15, June 16, June 25, July 1, July 8, July 13, July 22, July 23, August 5, August 19, August 25, September 16, October 1** (multiple), **October 2** (multiple), **October 5, October 6, October 8, October 19, October 22, November 10, November 12, November 17, November 19, November 20** (multiple), **December 15** and **December 17.**

- In **2009,** BMS submitted a Safety Report on **January 6, February 13, February 23, March 11, March 12, March 30, May 5, June 26, July 15, July 28, August 3, September 2, November 2, November 10, November 30,** and **December 18.**

- Correspondence between BMS and FDA in **2009** including: BMS and FDA correspondence regarding safety reports on **February 12, February 24, February 26, March 2, March 3** and BMS response to FDA request for summary of safety information on **March 13**; BMS and FDA email correspondence regarding revised dissolution method on **March 4;** BMS responded to FDA request for information **May 14**; FDA email correspondence confirming non-requirement of study MB102020 for NDA submission on **July 22.**

- BMS submitted information to the FDA in **2009** including: an IND annual report for period December 1, 2007 through November 30, 2008 on **February 13**; an amended core statistical analysis plan originally sent on October 22, 2008 on **May 6;** a statistical analysis plan for various protocols on **August 27;** a response to FDA request for information providing updated informed consent form for study MB102020 on **June 23;** notice of pending IND for dapagliflozin for Type I diabetes on **August 24;** statistical analysis plan on **December 9.**

- BMS submitted clinical information in support of amended study MB102020 on **May 1** and **May 4, 2009** (electronic copy of response), FDA provided comments and requested additional information on **May 15, 2009** and indicated that reviewers did not object to start of protocol on MB102020 on **May 19, 2009.**

- BMS requested Type A meeting to discuss the proposed CV-analysis plan in support of dapagliflozin as a treatment for type 2 diabetes mellitus on **June 18, 2009** and FDA denied meeting request on **June 23, 2009;** BMS made a second request for a Type A meeting to discuss CV-analysis plan on **October 19, 2009** and FDA granted meeting on **October 21, 2009.**

- On **June 18, 2009** the FDA requested additional information to provide a description of microbial limits testing and provide description of water activity in tablet form of drug product and BMS responded by providing microbial testing method on **July 2, 2009.**

- In **2010**, protocol and information amendments submitted on **January 6, January 12, January 13, January 25, February 2, February 18, February 24, March 1, March 11, March 15, March 16, March 17, March 25, March 30, March 31** (multiple), **April 5, April 16, May 5, May 7, May 12, May 21, May 26, June 9, June 15, June 17** (multiple), **July 7, July 16, July 22** (multiple), **August 3, August 10, August 12, August 31, September 10, September 23, September 29, October 5, October 12, October 13, October 15, October 21, November 3, November 4, November 8, November 11, November 16, November 17, November 22,** and **December 21.**

- In **2010,** BMS submitted a Safety Report on **February 11, February 16, February 17, March 8, March 31, April 12, September 13, September 17, October 7, October 12, November 8,** and **December 21.**

- Correspondence between BMS and FDA in **2010** including: email correspondence from BMS showing intent to submit dapagliflozin NDA on December 10 on **February 4;** FDA letter providing feedback on **April 29;** FDA letter requesting feedback on format and content for planned NDA on **August 23;** email correspondence providing FDA feedback on upcoming dapagliflozin NDA format and content on **August 27;** email correspondence providing response to FDA comments and requesting feedback to Type C meeting request on **August 31;** FDA letter pertaining to amendment dated March 25, 2010 containing bone safety data on **September 17;** email correspondence from FDA requesting information on **September 23;** email correspondence providing pre-NDA meeting package on **October 21;** FDA letter providing preliminary responses to questions for pre-NDA meeting on **November 8;** email correspondence between BMS and FDA regarding site level data on **November 9, November 21, December 1,** and **December 2;** FDA email correspondence regarding NDA on **December 6.**

- On **August 27, 2010** BMS requested a pre-NDA meeting, FDA granted the request on **September 15, 2010,** BMS submitted a briefing book on **October 12, 2010,** and Pre-NDA meeting minutes were sent to BMS on **December 2, 2010** and amendment to meeting minutes on **December 3, 2010.**

- BMS submitted information to the FDA in **2010** including: core statistical analysis plan and SAP for protocol MB102035 on **January 5**; an IND annual report for period December 1, 2008 through November 30, 2009 on **February 16**; SAP on **March 3, April 21** and **November 18;** Core Statistical Plan on **April 9;** letter from DMC on **April 13;** revised CEC charter addressing FDA request on **May 26;** pediatric plan and request for partial waiver on **August 5**; DMC charter for MB102029 on **August 5,** review letter on **October 29** and DMC charter minutes on **November 5.**

- In **2010,** BMS submitted a response to FDA request on **February 8** (response to FDA letter dated December 19, 2008), **February 18** (providing full developmental data package concerning the revised dissolution method), **March 25** (providing bone marker data), **April 27** (response to FDA letter dated December 30, 2009), **June 11** (concerning revised dissolution method for dapagliflozin tablets), **October 14** (providing study information), **October 19** (response to FDA request dated September 17, 2010).

- On **December 27, 2010** BMS submitted a New Drug Application.

- In **2011**, protocol and information amendments were submitted on **January 7, January 13, February 14, February 15, March 3, March 15, March 24, April 21, April 29, May 3, May 11, May 20, May 26, June 23, June 29, July 12, July 21, August 18, September 1, September 13, October 5, October 13** (multiple), **October 17, October 25, November 8, November 9, November 10, November 22, November 23, December 20,** and **December 22.**

- In **2011,** BMS submitted a Safety Report on **March 24, May 4, May 9, May 26, June 30, July 12, July 20, September 20, October 3,** and **December 22.**

- BMS submitted information to the FDA in **2011** including: hepatic adjudication committee charter and data monitoring committee review letter on **February 24;** an IND annual report for period December 1, 2010 through February 13, 2011 on **April 12;** DMC charter regarding MB102029 on **June 2** and review letter on **June 28;** draft protocol MB102091for FDA comments on **July 26;** statistical analysis plan and data monitoring committee meeting minutes on **October 31;** synopsis of study CV181169 on **December 21.**

- On **January 5 and November 11, 2011,** BMS submitted additional patent information relating to NDA submission.

- On **March 4, 2011,** the FDA sent a letter confirming that the NDA was sufficiently complete to permit a substantive review.

- On **April 28, 2011,** BMS submitted a 4-month clinical safety update for NDA.

- On **May 2, 2011,** the FDA sent a letter requesting confirmation of routine BIMO inspections to be conducted by FDA to determine if facilities are in accordance with regulations.

- On **May 25, 2011**, BMS requested to conduct first study in Type I patients under current dapagliflozin IND.

- On **June 2, 2011** BMS requested Type-C meeting, FDA granted request on **June 22, 2011,** and minutes discussing the design of proposed CV outcomes and overall pharmacovigilance plan were submitted on **November 3, 2011**.

- On **September 1, 2011,** FDA sent a letter to BMS notifying BMS of deficiencies which precluded discussion of labeling and postmarking requirements.

- In **2011,** BMS submitted a response to an FDA request for the NDA on **January 27** (relating to efficacy programs), **January 28** (relating to site-level data), **January 31** (relating to updated Montreal heart institute data set), **February 16** (relating to clarification on efficacy analyses); **March 23** (response to FDA request for information on March 4, 2011), **March 30** (response to SCE analysis questions), **April 11** (relating to CEC Charter information), **April 12** (relating to disintegration method), **April 13** (relating to RMP Annexes), **April 14** (relating to population pharmacokinetics dataset), **April 22** (relating to program files and response documents for each phase 3 study); **May 9** (relating to clinical pharmacology and pharmacology tox information), **May 12** (corrected response regarding lab parameters), **May 13** (relating to clinical safety and D1690C0004 control), **May 16** (providing additional data for proposed waiver of microbial testing), **May 18** (relating to clinical safety and efficacy information), **May 19** (relating to Hy's law and 4-month safety update), **May 20** (providing additional clinical safety information), **May 23** (relating to CMC stability update and providing EMDAC briefing document), **May 24** (relating to clinical safety information and providing response to FDA questions), **June 2** (response to

request for additional CMC information), **June 3** (providing additional clinical information), **June 10** (relating to information on eDISH analysis), **June 13** (relating to additional clinical pharmacology information), **June 14** (relating to June 7 FDA request), **June 16** (relating to clinical safety information for study D1690C0012), **June 17** (relating to additional clinical safety information), **June 24** (relating to additional CMC information), **July 13** (response to FDA request of July 8, 2011 for clinical information), **August 12** (response to FDA request for clinical information), **August 17 and September 9** (relating to microbial limits), **August 19** (relating to clinical information), **August 22** (relating to pediatric plan), **September 14** (relating to CETERO), **September 19** (responding to questions raised at EMDAC meeting), **October 27** (response to August 15, 2011 information request), **November 2** (response to August 15, 2011 information request), **November 8** (response to August 15, 2011 information request), **November 9** (response to information request), **November 16** (response to information request), **November 22** (response to information request), **December 6** (response to information request), **December 7** (providing response to request for additional information).

- BMS submitted information to the FDA for the NDA in **2011** including: safety assessment on **June 22;** updated site level data on **July 22**; datasets on **August 25;** 6-month data from studies D1690C00018 & D1690C00019 on **August 30,** and a response to FDA request relating to 6-month studies on **October 20, 2011**; new USPI and medication guide on **September 1;** preliminary CV meta-analysis on **September 20;** a draft protocol on **November 10**; study datasets on **November 15**.

- On **December 29, 2011**, BMS submitted updated carton and container labels.

- In **2012**, protocol and information amendments were submitted on **January 5, January 6, January 31, February 28, March 5, March 29, April 6, April 27, April 30, May 18, May 30, June 13, June 28, June 29, July 3, July 24, August**

7, August 23, August 27 (multiple), **September 7, September 19, October 18, November 13, November 19** (multiple), **November 27,** and **December 14.**

- In **2012,** BMS submitted a Safety Report on **January 27, February 29, March 12, March 28, April 6, April 11, April 25, May 1, May 10, August 7, August 30, September 5, September 19,** and **October 10.**

- BMS submitted information to the FDA in **2012** including: CVOT protocol and clinical events committee charter for review on **April 2;** an IND annual report for period February 14, 2011 through February 13, 2012 on **April 11;** amendment to pediatric plan on **June 1;** draft CVOT protocol for review, responded to agency's comments on **August 6;** updated CVOT draft protocol for review on **September 11;** resubmitted agency form FDA 3674 and provided national trial number on **November 28.**

- In **2012,** BMS submitted response to FDA request for information for the NDA on **January 9** (response to FDA request for additional information dated January 4, 2012), **February 15** (providing information on protocol amendments), **April 27** (response to FDA request for additional information dated April 20, 2012); **May 30** (response to FDA request for additional information dated May 16, 2012), **August 6** (relating to waiver from reporting study endpoints as serious adverse events), **August 29** (submitting information on a patient and information re;ated to study recommendation), **December 11** (providing table of studies the sponsor plans to submit in support of resubmission).

- The FDA sent a complete response letter (CRL) for the NDA on **January 17, 2012,** BMS requested a Type B meeting to discuss CRL on **January 19, 2012,** FDA granted meeting request on **January 26, 2012,** BMS submitted meeting materials on **March 30** and official meeting meetings were submitted on **May 9.** On **October 26, 2012** BMS requested feedback from the FDA on NDA resubmission plan in response to CRL and FDA responded on **November 19, 2012.**

- For the NDA, on **February 7, 2012** BMS requested a Type C meeting to discuss the benefit/risk required for diabetes drugs and inquiry of views about the need for new classes of drugs versus the known benefits/risks of existing drugs and the FDA granted meeting request on **February 9,** BMS submitted meeting materials on **March 30,** FDA provided preliminary comments on **April 27** and official meeting meetings were submitted on **May 9.**

- On **July 18, 2012** BMS submitted a formal dispute resolution request and a request for a Type A meeting to discuss request for the NDA.

- In **2013**, protocol and information amendments submitted on **January 9, January 31, February 5, February 8, February 19, February 27, March 11, April 18, May 9, May 17, June 5, June 21, July 2, August 27, September 12, October 2, October 11, October 15, November 1, November 12, November 20, November 21, December 26,** and **December 31.**

- In **2013**, BMS submitted a Safety Report on **April 26, May 31, June 7, June 13, June 14, July 2, July 3, August 5, August 29, September 5, October 11, October 17, October 28, October 30, November 1, November 5, November 18** (multiple), **November 20, November 21, December 2, December 5, December 16, December 17, December 18, December 27,** and **December 31.**

- BMS submitted information to the FDA in **2013** including: draft clinical events committee charter for CVOT on **January 29;** Medwatch form as requested by FDA on **February 27;** an IND annual report for period February 14, 2012 through February 13, 2013 on **April 10;** Statistical analysis plans on **June 3;** Dapa-pediatric PK/PD study amendment on **July 31;** revised statistical analysis plan, response to agency's comment and revised DMC charter on **September 4;** request for Type B End of phase 2 meeting on **December 20.**

- In **2013,** BMS submitted responses to FDA requests for information for the NDA on **August 7** (providing most up-to-date and comprehensive datasets for the core 21 clinical trials), **September 6** (response to FDA request dated August 21,

2013); **September 17** (response to FDA request dated September 11, 2013); **October 4** (response to FDA questions dated October 2, 2013 regarding 30-month safety update) **October 18** (relating to SGLT2 inhibitors); **October 25** (response to FDA request for information dated October 9, 2013) and **December 6** (information regarding renal impairment/failure and volume depletion).

- On **April 18, 2013** a telephonic conference was held between FDA and BMS to discuss resubmission of NDA. On **July 11, 2013** BMS resubmitted the NDA in response to the CRL.

- On **October 10, 2013** BMS submitted a 30-Month safety update and a 30- month update errata on **November 5, 2013** for the NDA.

- On **October 16, 2013** BMS submitted additional patent information for the NDA.

- On **October 16, November 4,** and **December 24** submitted proposed Trade and Sample Carton/Container labels for the NDA.

- In **2014**, protocol and information amendments submitted on **January 3, January 7** and **January 8**.

- An Approval letter for NDA No. 202293 was signed **January 8, 2014.**

(12) A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of extension claimed, including how the length of extension was determined;

Applicant submits that U.S. Patent No. 6,515,117 is entitled to patent term extension according to the provisions of 35 U.S.C. § 156. Applicant believes that the length of the extension of the patent term is equal to 1,825 days, pursuant to the provisions of 35 U.S.C. §§ 156(c) and (g).

The length of the patent term extension requested in this application is 1,825 days, comprising half of the period from December 21, 2003 until December 27, 2010 (a total of 2563/2 = 1,281 days) plus the period from December 27, 2010 until January 8, 2014 (1,109 days), for a total of 2,390 days, as limited by the proviso of 35 U.S.C. §156(g)(6) that the total patent term extension is limited to be no longer than five (5) years (1,825 days), and further limited by the proviso of 35 U.S.C. §156(c)(3) that the total patent term is limited to be no longer than fourteen (14) years from the date of marketing approval, calculated as follows:

Length of regulatory review period under IND:

December 21, 2003	- December 20, 2004 =	366 days
December 21, 2004	- December 20, 2005 =	365 days
December 21, 2005	- December 20, 2006 =	365 days
December 21, 2006	- December 20, 2007 =	365 days
December 21, 2007	- December 20, 2008 =	366 days
December 21, 2008	- December 20, 2009 =	365 days
December 21, 2009	- December 20, 2010 =	365 days
December 21, 2010	- December 26, 2010 =	6 days
Total		= 2,563 days

Length of regulatory review under NDA:

December 27, 2010 - December 31, 2010	=	5 days
January 1, 2011 - December 31, 2011	=	365 days
January 1, 2012 - December 31, 2012	=	366 days
January 1, 2013 – December 31, 2013	=	365 days
January 1, 2014 - January 8, 2014	=	8 days
Total	=	1,109 days

Length of time from current expiration date of U.S. Patent No. 6,515,117 and fourteen years from January 8, 2014:

October 4, 2020 - October 3, 2021	=	365 days
October 4, 2021 - October 3, 2022	=	365 days
October 4, 2022 - October 3, 2023	=	365 days
October 4, 2023 - October 3, 2024	=	366 days
October 4, 2024 - October 3, 2025	=	365 days
October 4, 2025 - October 3, 2026	=	365 days
October 4, 2026 - October 3, 2027	=	365 days
October 4, 2027 - January 8, 2028	=	97 days
Total	=	2,653 days

Applicant is applying for a patent term extension to the fullest extent that the patent deserves under the circumstances of regulatory delay set forth herein. Applicant believes the length of the patent term extension determined above is the appropriate length pursuant to the statute. Despite Applicant's diligent efforts, if the total number of days to which U.S. Patent No. 6,515,117 is greater than the number of days (1,825) requested here, Applicant requests the U.S. Patent and Trademark Office recalculate the correct length of patent term extension and award a patent term extension to U.S. Patent No. 6,515,117 for the correct number of days.

(13) A statement that applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought;

Applicant and its undersigned agent acknowledges a duty to disclose to the Director of the U.S. Patent and Trademark Office and the Secretary of Health and Human

Services any information that is material to the determination of entitlement to the patent term extension sought in this application.

(14) The prescribed fee for receiving and acting upon the application for extension pursuant to 37 C.F.R. § 120(j)

The U.S. Patent and Trademark Office is hereby authorized to charge any fees that may be required, including the prescribed fee of one thousand one hundred twenty dollars ($1,120.00) as set forth in 37 C.F.R. § 1.20(j), for the filing of this paper to Deposit Account No. 26-0166.

(15) The name, address, and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed.

Inquiries and correspondence relating to this patent term extension application should be addressed to:

David M. Gryte
AstraZeneca
1800 Concord Pike
P.O. Box 15437
Wilmington, DE 19850-5437
(302) 885-6609 (direct)
David.Gryte@astrazeneca.com

A Rule 3.73(b) document is appended hereto as **Exhibit K**.

If the Examiner or other Patent Office official reviewing this application believes it to be helpful, he or she is invited to contact the undersigned attorney by telephone at (302) 885-6609.

Respectfully submitted,

Date: March 6, 2014

By: _____

David M. Gryte
Senior Patent Attorney
Reg. No. 41,809
Tel. (302) 885 6609

LIST OF EXHIBITS

Exhibit A:	U.S. Patent No. 6,515,117
Exhibit B:	U.S. Patent and Trademark Office assignment record for U.S. Patent No. 6,515,117
Exhibit C:	FARXIGA® FDA approval letter
Exhibit D:	Copy of a receipt for payment of the first maintenance fee, paid July 7, 2006
Exhibit E:	Copy of a receipt for payment of the second maintenance fee, paid July 8, 2010
Exhibit F:	Copy of a Terminal Disclaimer, filed August 19, 2002
Exhibit G:	Copy of a Certificate of Correction, issued October 23, 2008
Exhibit H:	FDA acknowledgement letter for filing an Investigational New Drug (IND) application, No. 68,652
Exhibit I:	FDA acknowledgment letter for filing a New Drug Application (NDA), No. 202293
Exhibit J:	FDA Log
Exhibit K:	Rule 3.73(b) statement

EXHIBIT A

US006515117B2

(12) **United States Patent**
Ellsworth et al.

(10) **Patent No.: US 6,515,117 B2**
(45) **Date of Patent: Feb. 4, 2003**

(54) **C-ARYL GLUCOSIDE SGLT2 INHIBITORS AND METHOD**

(75) Inventors: **Bruce Ellsworth**, Princeton, NJ (US); **William N. Washburn**, Titusville, NJ (US); **Philip M. Sher**, Plainsboro, NJ (US); **Gang Wu**, Princeton, NJ (US); **Wei Meng**, Pennington, NJ (US)

(73) Assignee: **Bristol-Myers Squibb Company**, Princeton, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **10/151,436**

(22) Filed: **May 20, 2002**

(65) **Prior Publication Data**

US 2002/0137903 A1 Sep. 26, 2002

Related U.S. Application Data

(63) Continuation-in-part of application No. 09/679,027, filed on Oct. 4, 2000, now Pat. No. 6,414,126.
(60) Provisional application No. 60/194,615, filed on Apr. 5, 2000, and provisional application No. 60/158,773, filed on Oct. 12, 1999.

(51) **Int. Cl.**[7] **C07H 15/20**; A61K 31/70
(52) **U.S. Cl.** **536/17.2**; 536/1.11; 536/17.3; 536/17.4; 536/17.5; 536/18.4; 514/866; 514/25
(58) **Field of Search** 536/1.11, 17.2, 536/17.3, 17.4, 17.5, 18.4; 514/866, 25

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,414,126 B1 * 7/2002 Ellsworth et al. 536/17.2

FOREIGN PATENT DOCUMENTS

EP	0 598359 A		5/1994
EP	0 684 254 B1		11/1995
EP	0 773 226 B1		5/1997
EP	0 850 948 A1		1/1998
JP	8-27006		1/1996
JP	9124685		7/1997
JP	9188625		7/1997
JP	10245391		9/1998
JP	9124684		5/1999
WO	WO 9831697 A	*	7/1998
WO	WO 98/31697	*	7/1998
WO	WO 0 018918		4/2000

OTHER PUBLICATIONS

T. Kuribayashi et al., Journal of Carbohydrate Chemistry, (1999) vol. 18, No. 4, pp. 371–382.
W. Gaffield et al., Tetrahedron, (1978) vol. 34, No. 20, pp. 3089–3096.
Benhaddou et al. Carbohydrate Research 260 (1994) pp. 243–250.
Hongu et al. Chemical Phar. Bull. (1998) vol. 46, No. 10, pp. 1545–1565.
Tsujihara et al. Chemical Pharm. Bull. (1996) vol. 44. No. 6. pp. 1174–1180.
Hongu et al. Chem. Pharm. Bull. (1998) vol. 46. No. 1, pp. 22–23.
Oku et al. Diabetes. vol. 48 (1999) pp. 1794–1800.

* cited by examiner

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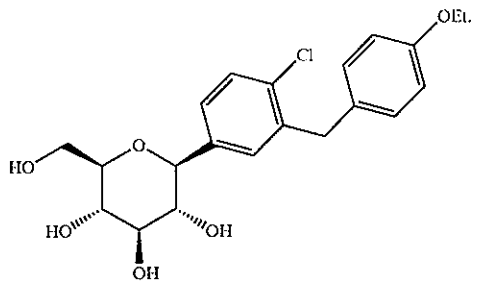
Assistant Examiner—Devesh Khare
(74) *Attorney, Agent, or Firm*—Jonathan Provoost; Burton Rodney

(57) **ABSTRACT**

An SGLT2 inhibiting compound is provided having the formula



A method is also provided for treating diabetes and related diseases employing an SGLT2 inhibiting amount of the above compound alone or in combination with another antidiabetic agent or other therapeutic agent.

17 Claims, No Drawings

C-ARYL GLUCOSIDE SGLT2 INHIBITORS AND METHOD

This application is a continuation-in-part under 37 C.F.R. §1.53(b)(2) of U.S. Ser. No. 09/679,027, filed Oct. 4, 2000, which claims the benefit of provisional application 60/194,615, filed Apr. 5, 2000 and provisional application 60/158,773, filed Oct. 12, 1999.

FIELD OF THE INVENTION

The present invention relates to C-aryl glucosides which are inhibitors of sodium dependent glucose transporters found in the intestine and kidney (SGLT2) and to a method for treating diabetes, especially type II diabetes, as well as hyperglycemia, hyperinsulinemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis and related diseases, employing such C-aryl glucosides alone or in combination with one, two or more other type antidiabetic agent and/or one, two or more other type therapeutic agents such as hypolipidemic agents.

BACKGROUND OF THE INVENTION

Approximately 100 million people worldwide suffer from type II diabetes (NIDDM), which is characterized by hyperglycemia due to excessive hepatic glucose production and peripheral insulin resistance, the root causes for which are as yet unknown. Hyperglycemia is considered to be the major risk factor for the development of diabetic complications, and is likely to contribute directly to the impairment of insulin secretion seen in advanced NIDDM. Normalization of plasma glucose in NIDDM patients would be predicted to improve insulin action, and to offset the development of diabetic complications. An inhibitor of the sodium-dependent glucose transporter SGLT2 in the kidney would be expected to aid in the normalization of plasma glucose levels, and perhaps body weight, by enhancing glucose excretion.

The development of novel, safe, and orally active antidiabetic agents is also desired in order to complement existing therapies, including the sulfonylureas, thiazolidinediones, metformin, and insulin, and to avoid the potential side effects associated with the use of these other agents.

Hyperglycemia is a hallmark of type II diabetes (NIDDM); consistent control of plasma glucose levels in diabetes can offset the development of diabetic complications and beta cell failure seen in advanced disease. Plasma glucose is normally filtered in the kidney in the glomerulus and actively reabsorbed in the proximal tubule. SGLT2 appears to be the major transporter responsible for the reuptake of glucose at this site. The SGLT specific inhibitor phlorizin or closely related analogs inhibit this reuptake process in diabetic rodents and dogs resulting in normalization of plasma glucose levels by promoting glucose excretion without hypoglycemic side effects. Long term (6 month) treatment of Zucker diabetic rats with an SGLT2 inhibitor has been reported to improve insulin response to glycemia, improve insulin sensitivity, and delay the onset of nephropathy and neuropathy in these animals, with no detectable pathology in the kidney and no electrolyte imbalance in plasma. Selective inhibition of SGLT2 in diabetic patients would be expected to normalize plasma glucose by enhancing the excretion of glucose in the urine, thereby improving insulin sensitivity, and delaying the development of diabetic complications.

Ninety percent of glucose reuptake in the kidney occurs in the epithelial cells of the early S1 segment of the renal

cortical proximal tubule, and SGLT2 is likely to be the major transporter responsible for this reuptake. SGLT2 is a 672 amino acid protein containing 14 membrane-spanning segments that is predominantly expressed in the early S1 segment of the renal proximal tubules. The substrate specificity, sodium dependence, and localization of SGLT2 are consistent with the properties of the high capacity, low affinity, sodium-dependent glucose transporter previously characterized in human cortical kidney proximal tubules. In addition, hybrid depletion studies implicate SGLT2 as the predominant Na^+/glucose cotransporter in the S1 segment of the proximal tubule, since virtually all Na-dependent glucose transport activity encoded in mRNA from rat kidney cortex is inhibited by an antisense oligonucleotide specific to rat SGLT2. SGLT2 is a candidate gene for some forms of familial glucosuria, a genetic abnormality in which renal glucose reabsorption is impaired to varying degrees. None of these syndromes investigated to date map to the SGLT2 locus on chromosome 16. However, the studies of highly homologous rodent SGLTs strongly implicate SGLT2 as the major renal sodium-dependent transporter of glucose and suggest that the glucosuria locus that has been mapped encodes an SGLT2 regulator. Inhibition of SGLT2 would be predicted to reduce plasma glucose levels via enhanced glucose excretion in diabetic patients.

SGLT1, another Na-dependent glucose cotransporter that is 60% identical to SGLT2 at the amino acid level, is expressed in the small intestine and in the more distal S3 segment of the renal proximal tubule. Despite their sequence similarities, human SGLT1 and SGLT2 are biochemically distinguishable. For SGLT1, the molar ratio of Na^+ to glucose transported is 2:1, whereas for SGLT2, the ratio is 1:1. The K_m for Na^+ is 32 and 250–300 mM for SGLT1 and SGLT2, respectively. K_m values for uptake of glucose and the nonmetabolizable glucose analog α-methyl-D-glucopyranoside (AMG) are similar for SGLT1 and SGLT2, i.e. 0.8 and 1.6 mM (glucose) and 0.4 and 1.6 mM (AMG) for SGLT1 and SGLT2 transporters, respectively. However, the two transporters do vary in their substrate specificities for sugars such as galactose, which is a substrate for SGLT1 only.

Administration of phlorizin, a specific inhibitor of SGLT activity, provided proof of concept in vivo by promoting glucose excretion, lowering fasting and fed plasma glucose, and promoting glucose utilization without hypoglycemic side effects in several diabetic rodent models and in one canine diabetes model. No adverse effects on plasma ion balance, renal function or renal morphology have been observed as a consequence of phlorizin treatment for as long as two weeks. In addition, no hypoglycemic or other adverse effects have been observed when phlorizin is administered to normal animals, despite the presence of glycosuria. Administration of an inhibitor of renal SGLTs for a 6-month period (Tanabe Seiyaku) was reported to improve fasting and fed plasma glucose, improve insulin secretion and utilization in obese NIDDM rat models, and offset the development of nephropathy and neuropathy in the absence of hypoglycemic or renal side effects.

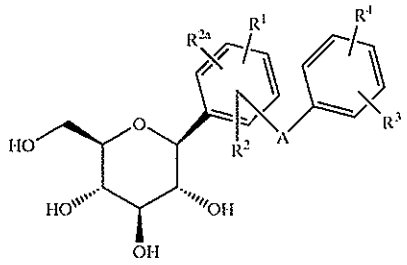
Phlorizin itself is unattractive as an oral drug since it is a nonspecific SGLT1/SGLT2 inhibitor that is hydrolyzed in the gut to its aglycone phloretin, which is a potent inhibitor of facilitated glucose transport. Concurrent inhibition of facilitative glucose transporters (GLUTs) is undesirable since such inhibitors would be predicted to exacerbate peripheral insulin resistance as well as promote hypoglycemia in the CNS. Inhibition of SGLT1 could also have serious adverse consequences as is illustrated by the hereditary

syndrome glucose/galactose malabsorption (GGM), in which mutations in the SGLT1 cotransporter result in impaired glucose uptake in the intestine, and life-threatening diarrhea and dehydration. The biochemical differences between SGLT2 and SGLT1, as well as the degree of sequence divergence between them, allow for identification of selective SGLT2 inhibitors.

The familial glycosuria syndromes are conditions in which intestinal glucose transport, and renal transport of other ions and amino acids, are normal. Familial glycosuria patients appear to develop normally, have normal plasma glucose levels, and appear to suffer no major health deficits as a consequence of their disorder, despite sometimes quite high (110–114 g/daily) levels of glucose excreted. The major symptoms evident in these patients include polyphagia, polyuria and polydipsia, and the kidneys appear to be normal in structure and function. Thus, from the evidence available thus far, defects in renal reuptake of glucose appear to have minimal long term negative consequences in otherwise normal individuals.

The following references disclose C-aryl glucosides SGLT2 inhibitors for treating diabetes.

WO 01/27128 discloses compounds of the structure



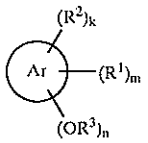
where

A is O, S, NH, or $(CH_2)_n$ where n is 0–3;

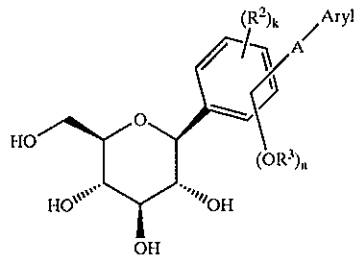
R^1, R^2 and R^{2a} are independently hydrogen, OH, OR^5, alkyl, CF_3, $OCHF_2$, OCF_3, SR^5 or halogen, etc;

R^3 and R^4 are independently hydrogen, OH, OR^{5a}, OAryl, OCH_2Aryl, alkyl, cycloalkyl, CF_3, —$OCHF_2$, —OCF_3, halogen, etc. These compounds are reported to be inhibitors of the SGLT2 transporter and consequently represent a mode for treatment of diabetes and complications thereof.

WO 98/31697 discloses compounds of the structure



Where Ar includes, among others, phenyl, biphenyl, diphenylmethane, diphenylethane, and diphenylether, and R^1 is a glycoside, R^2 is H, OH, amino, halogen, carboxy, alkyl, cycloalkyl, or carboxamido, and R^3 is hydrogen, alkyl, or acyl, and k, m, and n are independently 1–4. A subset of compounds disclosed in WO 98/31697 contains compounds of the following structures

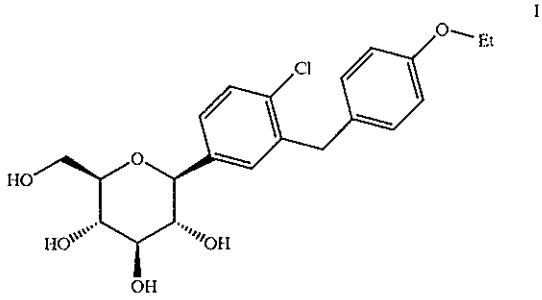


A or O or $(CH_2)_x$ where x = 0–3
R^3 is hydrogen, alkyl or acyl group where n is 1–4
R^2 is hydrogen, alkyl, OH, NH_2, halogen, CO_2H or carboximide where k is 1–4

which are disclosed for use in the treatment or prevention of inflammatory diseases, autoimmune diseases, infections, cancer, and cancer metastasis, reperfusion disorders, thrombosis, ulcer, wounds, osteoporosis, diabetes mellitus and atherosclerosis, among others.

DESCRIPTION OF THE INVENTION

In accordance with the present invention, a C-aryl glucoside compound is provided which has the structure



I

including pharmaceutically acceptable salts thereof, all stereoisomers thereof, and all prodrug esters thereof.

The compound of formula I possesses activity as inhibitors of the sodium dependent glucose transporters found in the intestine and kidney of mammals and is useful in the treatment of diabetes and the micro- and macrovascular complications of diabetes such as retinopathy, neuropathy, nephropathy, and wound healing.

The present invention provides for compound of formula I, pharmaceutical compositions employing such a compound and for methods of using such a compound.

In addition, in accordance with the present invention, a method is provided for treating or delaying the progression or onset of diabetes, especially type I and type II diabetes, including complications of diabetes, including retinopathy, neuropathy, nephropathy and delayed wound healing, and related diseases such as insulin resistance (impaired glucose homeostasis), hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, obesity, hyperlipidemia including hypertriglyceridemia, Syndrome X, atherosclerosis and hypertension, and for increasing high density lipoprotein levels, wherein a therapeutically effective amount of a compound of structure I is administered to a human patient in need of treatment.

In addition, in accordance with the present invention, a method is provided for treating diabetes and related diseases as defined above and hereinafter, wherein a therapeutically effective amount of a combination of a compound of structure I and another type of antidiabetic agent and/or another type of therapeutic agent such as a hypolipidemic agent is administered to a human patient in need of treatment.

The conditions, diseases, and maladies collectively referred to as "Syndrome X" (also known as Metabolic Syndrome) are detailed in Johannsson *J. Clin. Endocrinol. Metab.*, 82, 727–34 (1997).

The term "other type of therapeutic agents" as employed herein refers to one or more antidiabetic agents (other than SGLT2 inhibitors of formula I), one or more anti-obesity agents, anti-hypertensive agents, anti-platelet agents, anti-atherosclerotic agents and/or one or more lipid-lowering agents (including anti-atherosclerosis agents).

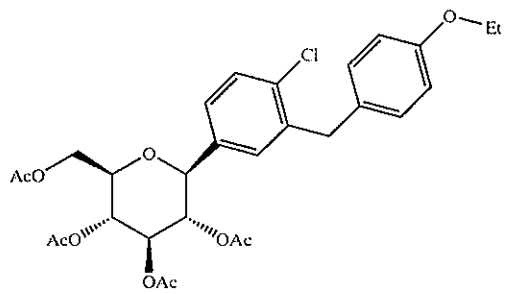
In the above method of the invention, the compound of structure I of the invention will be employed in a weight ratio to the one, two or more antidiabetic agent and/or one, two or more other type therapeutic agent (depending upon its mode of operation) within the range from about 0.01:1 to about 300:1, preferably from about 0.1:1 to about 10:1.

DETAILED DESCRIPTION OF THE INVENTION

The compound of formula I of the invention can be prepared as shown in the following reaction scheme and description thereof wherein temperatures are expressed in degrees Centigrade.

Compound of formula I can be prepared as shown in Scheme 1 by treatment of compound of formula II

II

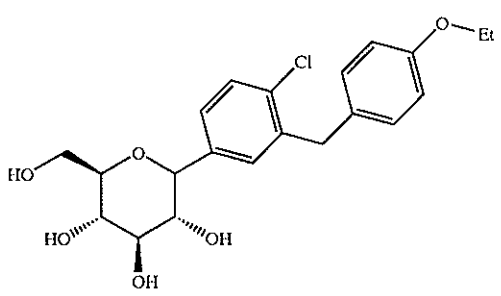


with a base such as LiOH or NaOH in a solvent such as a 1:2:3 mixture of H_2O/THF/MeOH or aq. MeOH or aq. EtOH.

The compound of formula II (which is a novel intermediate that readily crystallizes) provides a convenient means to purify crude compound of formula Ia which was obtained as a mixture of α and β anomers.

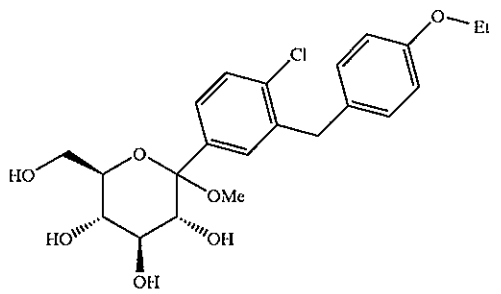
The compound of formula II can be prepared by treatment of compound of formula Ia with Ac_2O in a solvent such as CH_2Cl_2 containing pyridine and a catalyst such as dimethylaminopyridine (DMAP).

Ia



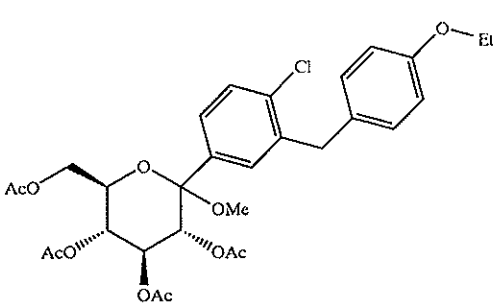
Compounds of formula Ia can be prepared by reduction of a compound of formula III with a reducing agent such as Et_3SiH in a solvent such as 1:1 CH_2Cl_2/MeCN at −10° in the presence of a Lewis acid catalyst such as $BF_3.Et_2O$.

III



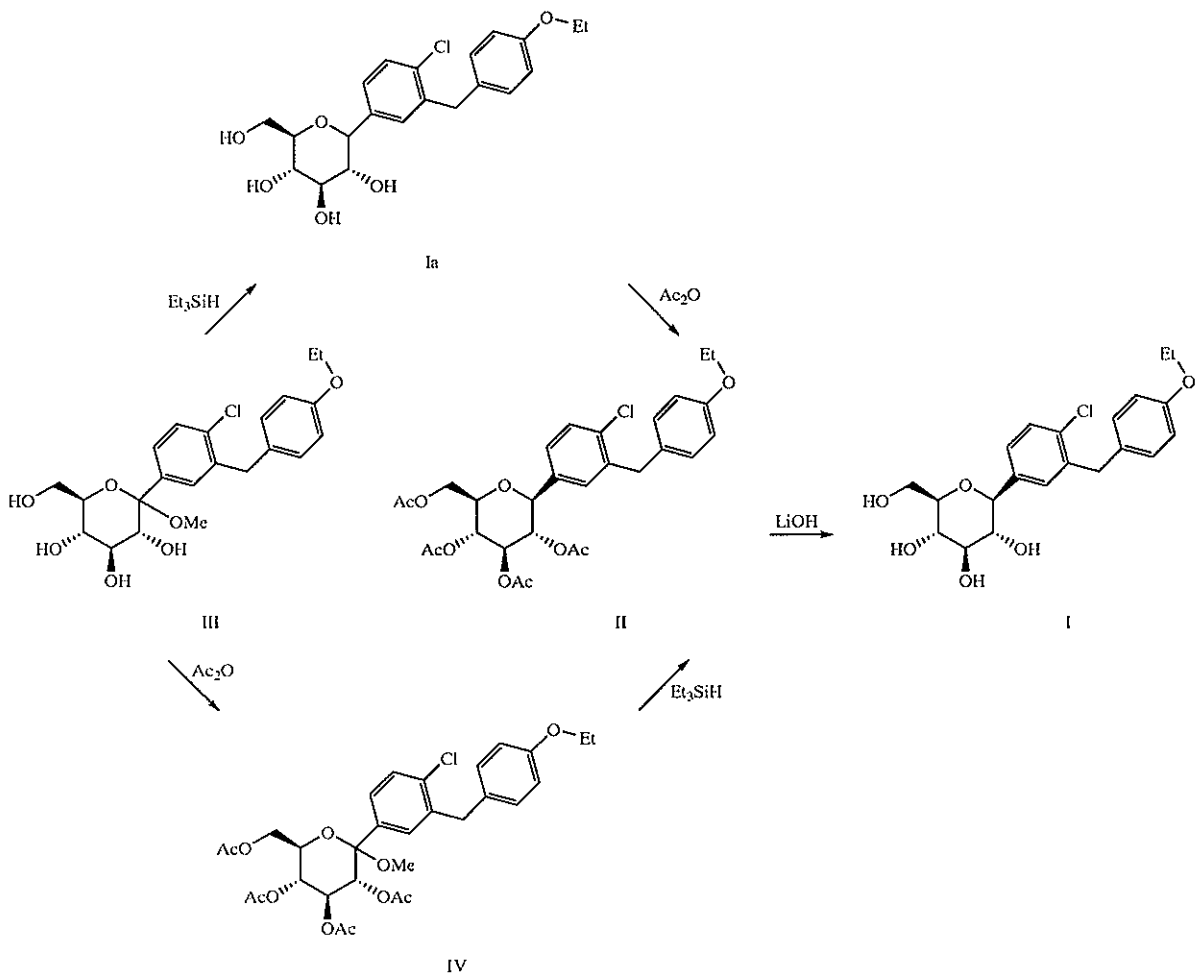
The compound of formula II can alternatively be prepared from compound of formula III by first acetylating compound of formula III with Ac_2O in a solvent such toluene or CH_2Cl_2 containing a base such as Hunig's base or Et_3N and a catalyst such as DMAP to generate compound of formula IV.

IV

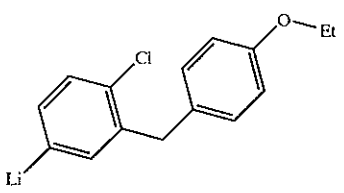


Subsequent conversion of compound of formula IV to compound of formula II can be achieved by treatment at 20° treatmentwith a reducing agent such as Et_3SiH in a solvent such as MeCN containing 1 equiv of H_2O and a Lewis acid catalyst such as $BF_3.Et_2O$.

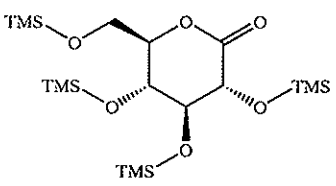
Scheme 1



The compound of formula III can be prepared, as outlined in Scheme 2, by 1) addition of a cold THF solution of an aryl lithium of formula V to a persilylated gluconolactone of formula VI in a solvent such as toluene at −75°. Subsequently, a methanol solution of a protic acid such methanesulfonic acid (MSA) is added after 30 min and the solution stirred at 20° until transformation of the intermediary lactol to III is complete.



V

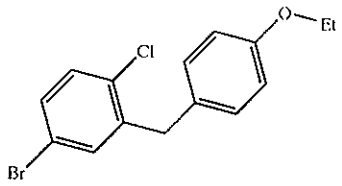


VI

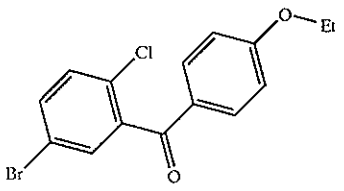
The compound of formula VI can be prepared by treatment of commercially available D-gluconolactone with a silylating agent such as trimethylsilyl chloride in a solvent such as THF containing a base such as N-methylmorpholine.

The compound of formula V can be prepared by treatment of compound of formula VII with an alkyl lithium such as n-BuLi or t-BuLi in a solvent such as THF at −75°.

VII



The compound of formula VII can be readily prepared by treatment of compound of formula VIII with a reducing agent such as Et_3SiH in a solvent such as 1:1 CH_2Cl_2/MeCN at 0°–20° in the presence of a Lewis acid catalyst such as $BF_3.Et_2O$.

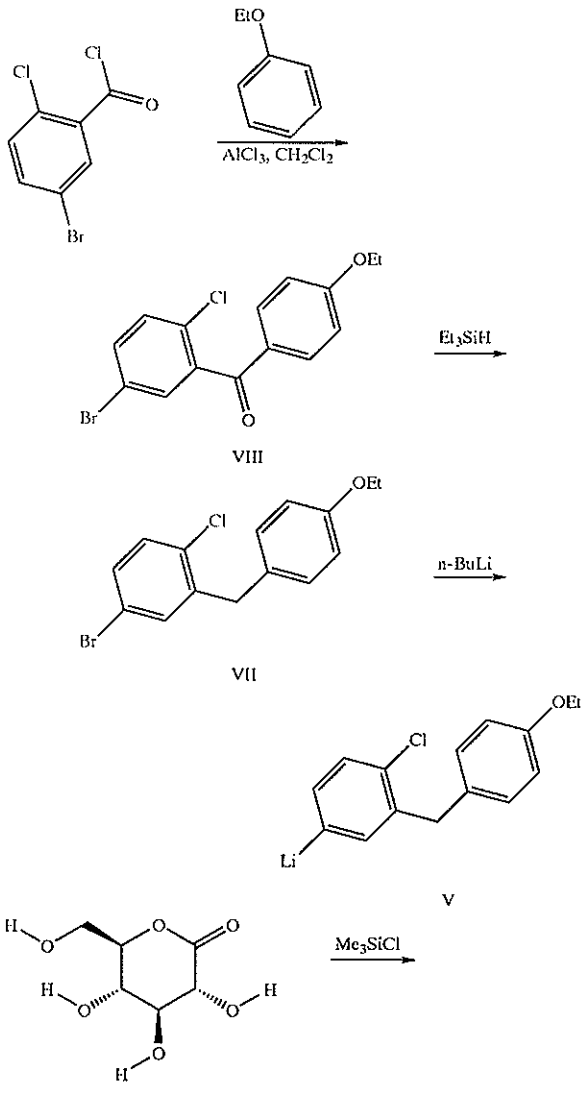


VIII

The compound of formula VIII can be prepared by Friedel-Craft acylation of commercially available ethoxybenzene (phenetole) with 2-chloro-5-bromobenzoyl chloride in a solvent such as CH_2Cl_2 containing an equivalent of a Lewis Acid such as $AlCl_3$ or $AlBr_3$.

2-Chloro-5-bromobenzoyl chloride is readily prepared from commercially available 2-chloro-5-bromobenzoic acid by treatment with oxalyl chloride in a solvent such as CH_2Cl_2 containing a catalytic amount of DMF.

Scheme 2



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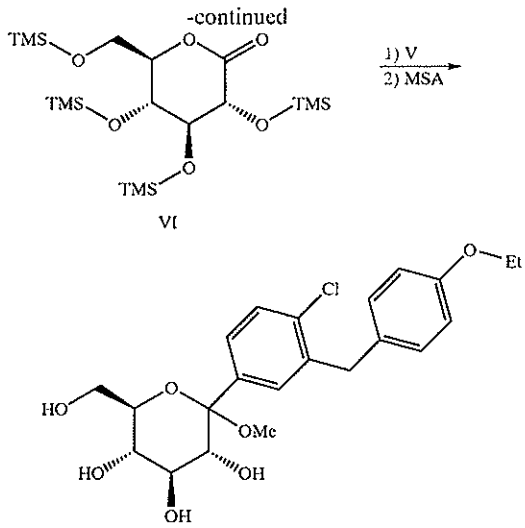


VI

III

Listed below are definitions of various terms used in the description of the instant invention. These definitions apply to the terms as they are used throughout the specification (unless they are otherwise limited in specific instances) either individually or as part of a larger group.

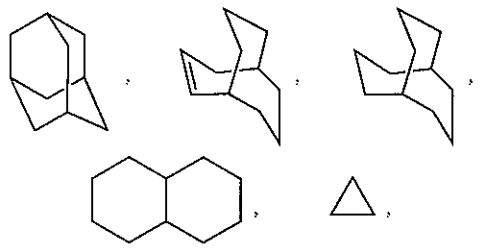
The following abbreviations are employed herein:

Ph=phenyl
Bn=benzyl
t-Bu=tertiary butyl
Me=methyl
Et=ethyl
TMS=trimethylsilyl
TBS=tert-butyldimethylsilyl
THF=tetrahydrofuran
Et_2O=diethyl ether
EtOAc=ethyl acetate
DMF=dimethyl formamide
MeOH=methanol
EtOH=ethanol
i-PrOH=isopropanol
HOAc or AcOH=acetic acid
TFA=trifluoroacetic acid
i-Pr_2NEt=diisopropylethylamine
Et_3N=triethylamine
DMAP=4-dimethylaminopyridine
$NaBH_4$=sodium borohydride
n-BuLi=n-butyllithium
Pd/C=palladium on carbon
KOH=potassium hydroxide
NaOH=sodium hydroxide
LiOH=lithium hydroxide
K_2CO_3=potassium carbonate
$NaHCO_3$=sodium bicarbonate
Ar=argon
N_2=nitrogen
min=minute(s)
h or hr=hour(s)
L=liter
mL=milliliter
μL=microliter
g=gram(s)
mg=milligram(s)
mol=moles
mmol=millimole(s)
meq=milliequivalent

RT=room temperature
sat or sat'd=saturated
aq.=aqueous
TLC=thin layer chromatography
HPLC=high performance liquid chromatography
LC/MS=high performance liquid chromatography/mass spectrometry
MS or Mass Spec=mass spectrometry
NMR=nuclear magnetic resonance
mp=melting point

Unless otherwise indicated, the term "lower alkyl" as employed herein alone or as part of another group includes both straight and branched chain hydrocarbons containing 1 to 8 carbons, and the terms "alkyl" and "alk" as employed herein alone or as part of another group includes both straight and branched chain hydrocarbons containing 1 to 20 carbons, preferably 1 to 10 carbons, more preferably 1 to 8 carbons, in the normal chain, such as methyl, ethyl, propyl, isopropyl, butyl, t-butyl, isobutyl, pentyl, hexyl, isohexyl, heptyl, 4,4-dimethylpentyl, octyl, 2,2,4-trimethylpentyl, nonyl, decyl, undecyl, dodecyl, the various branched chain isomers thereof, and the like as well as such groups including 1 to 4 substituents such as halo, for example F, Br, Cl or I or CF_3, alkyl, alkoxy, aryl, aryloxy, aryl(aryl) or diaryl, arylalkyl, arylalkyloxy, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, cycloalkylalkyloxy, optionally substituted amino, hydroxy, hydroxyalkyl, acyl, alkanoyl, heteroaryl, heteroaryloxy, cycloheteroalkyl, arylheteroaryl, arylalkoxycarbonyl, heteroarylalkyl, heteroarylalkoxy, aryloxyalkyl, aryloxyaryl, alkylamido, alkanoylamino, arylcarbonylamino, nitro, cyano, thiol, haloalkyl, trihaloalkyl and/or alkylthio.

Unless otherwise indicated, the term "cycloalkyl" as employed herein alone or as part of another group includes saturated or partially unsaturated (containing 1 or 2 double bonds) cyclic hydrocarbon groups containing 1 to 3 rings, including monocyclicalkyl, bicyclicalkyl and tricyclicalkyl, containing a total of 3 to 20 carbons forming the rings, preferably 3 to 10 carbons, forming the ring and which may be fused to 1 or 2 aromatic rings as described for aryl, which include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclodecyl and cyclododecyl, cyclohexenyl,



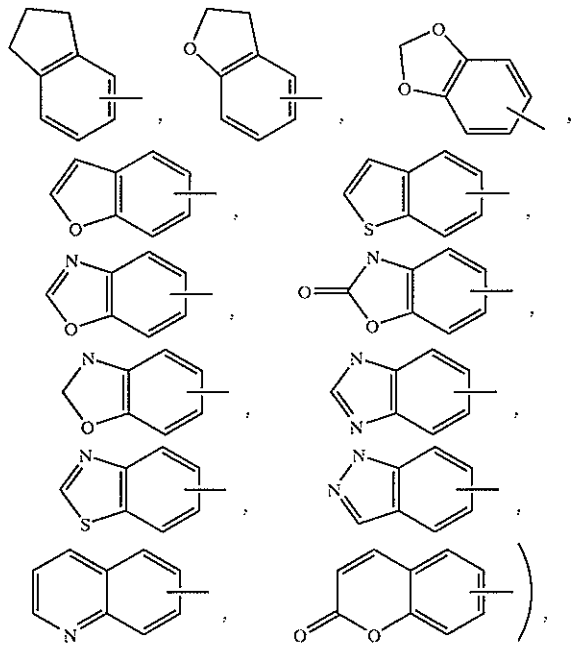
any of which groups may be optionally substituted with 1 to 4 substituents such as halogen, alkyl, alkoxy, hydroxy, aryl, aryloxy, arylalkyl, cycloalkyl, alkylamido, alkanoylamino, oxo, acyl, arylcarbonylamino, amino, nitro, cyano, thiol and/or alkylthio and/or any of the alkyl substituents.

The term "alkanoyl" as used herein alone or as part of another group refers to alkyl linked to a carbonyl group.

The term "halogen" or "halo" as used herein alone or as part of another group refers to chlorine, bromine, fluorine, and iodine, with chlorine or fluorine being preferred.

The term "metal ion" refers to alkali metal ions such as sodium, potassium or lithium and alkaline earth metal ions such as magnesium and calcium, as well as zinc and aluminum.

Unless otherwise indicated, the term "aryl" or "Aryl" as employed herein alone or as part of another group refers to monocyclic and bicyclic aromatic groups containing 6 to 10 carbons in the ring portion (such as phenyl or naphthyl including 1-naphthyl and 2-naphthyl) and may optionally include one to three additional rings fused to a carbocyclic ring or a heterocyclic ring (such as aryl, cycloalkyl, heteroaryl or cycloheteroalkyl rings for example



and may be optionally substituted through available carbon atoms with 1, 2, or 3 groups selected from hydrogen, halo, haloalkyl, alkyl, haloalkyl, alkoxy, haloalkoxy, alkenyl, trifluoromethyl, trifluoromethoxy, alkynyl, cycloalkyl-alkyl, cycloheteroalkyl, cycloheteroalkylalkyl, aryl, heteroaryl, arylalkyl, aryloxy, aryloxyalkyl, arylalkoxy, alkoxycarbonyl, arylcarbonyl, arylalkenyl, aminocarbonylaryl, arylthio, arylsulfinyl, arylazo, heteroarylalkyl, heteroarylalkenyl, heteroarylheteroaryl, heteroaryloxy, hydroxy, nitro, cyano, amino, substituted amino wherein the amino includes 1 or 2 substituents (which are alkyl, aryl or any of the other aryl compounds mentioned in the definitions), thiol, alkylthio, arylthio, heteroarylthio, arylthioalkyl, alkoxyarylthio, alkylcarbonyl, arylcarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aminocarbonyl, alkylcarbonyloxy, arylcarbonyloxy, alkylcarbonylamino, arylcarbonylamino, arylsulfinyl, arylsulfinylalkyl, arylsulfonylamino and arylsulfonaminocarbonyl and/or any of the alkyl substituents set out herein.

Unless otherwise indicated, the term "lower alkoxy", "alkoxy", "aryloxy" or "aralkoxy" as employed herein alone or as part of another group includes any of the above alkyl, aralkyl or aryl groups linked to an oxygen atom.

Unless otherwise indicated, the term "lower alkylthio", "alkylthio", "arylthio" or "aralkylthio" as employed herein alone or as part of another group includes any of the above alkyl, aralkyl or aryl groups linked to a sulfur atom.

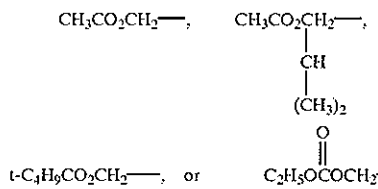
The term "polyhaloalkyl" as used herein refers to an "alkyl" group as defined above which includes from 2 to 9, preferably from 2 to 5, halo substituents, such as F or Cl, preferably F, such as CF_3CH_2, CF_3 or $CF_3CF_2CH_2$.

The term "polyhaloalkyloxy" as used herein refers to an "alkoxy" or "alkyloxy" group as defined above which

includes from 2 to 9, preferably from 2 to 5, halo substituents, such as F or Cl, preferably F, such as CF_3CH_2O, CF_3O or $CF_3CF_2CH_2O$.

The term "prodrug esters" as employed herein includes esters and carbonates formed by reacting one or more hydroxyls of compounds of formula I with alkyl, alkoxy, or aryl substituted acylating agents employing procedures known to those skilled in the art to generate acetates, pivalates, methylcarbonates, benzoates and the like. In addition, prodrug esters which are known in the art for carboxylic and phosphorus acid esters such as methyl, ethyl, benzyl and the like.

Examples of such prodrug esters include



Where the compound of structure I are in acid form they may form a pharmaceutically acceptable salt such as alkali metal salts such as lithium, sodium or potassium, alkaline earth metal salts such as calcium or magnesium as well as zinc or aluminum and other cations such as ammonium, choline, diethanolamine, lysine (D or L), ethylenediamine, t-butylamine, t-octylamine, tris-(hydroxymethyl) aminomethane (TRIS), N-methyl glucosamine (NMG), triethanolamine and dehydroabietylamine.

All stereoisomers of the compound of the instant invention are contemplated, either in admixture or in pure or substantially pure form. The compound of the present invention can have asymmetric centers at any of the carbon atoms including any one of the R substituents. Consequently, compound of formula I can exist in enantiomeric or diastereomeric forms or in mixtures thereof. The processes for preparation can utilize racemates, enantiomers or diastereomers as starting materials. When diastereomeric or enantiomeric products are prepared, they can be separated by conventional methods for example, chromatographic or fractional crystallization.

Where desired, the compound of structure I may be used in combination with one or more other types of antidiabetic agents and/or one or more other types of therapeutic agents which may be administered orally in the same dosage form, in a separate oral dosage form or by injection.

The other type of antidiabetic agent which may be optionally employed in combination with the SGLT2 inhibitor of formula I may be 1,2,3 or more antidiabetic agents or antihyperglycemic agents including insulin secretagogues or insulin sensitizers, or other antidiabetic agents preferably having a mechanism of action different from SGLT2 inhibition and may include biguanides, sulfonyl ureas, glucosidase inhibitors, PPAR γ agonists such as thiazolidinediones, aP2 inhibitors, PPAR α/γ dual agonists, dipeptidyl peptidase IV (DP4) inhibitors, and/or meglitinides, as well as insulin, glucagon-like peptide-1 (GLP-1), PTP1B inhibitors, glycogen phosphorylase inhibitors and/or glucos-6-phosphatase inhibitors.

The other types of therapeutic agents which may be optionally employed in combination with the SGLT2 inhibitor of formula I include anti-obesity agents, antihypertensive agents, antiplatelet agents, antiatherosclerotic agents and/or lipid lowering agents.

The SGLT2 inhibitor of formula I may also be optionally employed in combination with agents for treating complications of diabetes. These agents include PKC inhibitors and/or AGE inhibitors.

It is believed that the use of the compound of structure I in combination with 1, 2, 3 or more other antidiabetic agents produces antihyperglycemic results greater than that possible from each of these medicaments alone and greater than the combined additive anti-hyperglycemic effects produced by these medicaments.

The other antidiabetic agent may be an oral antihyperglycemic agent preferably a biguanide such as metformin or phenformin or salts thereof, preferably metformin HCl.

Where the other antidiabetic agent is a biguanide, the compound of structure I will be employed in a weight ratio to biguanide within the range from about 0.01:1 to about 100:1, preferably from about 0.1:1 to about 5:1.

The other antidiabetic agent may also preferably be a sulfonyl urea such as glyburide (also known as glibenclamide), glimepiride (disclosed in U.S. Pat. No. 4,379,785), glipizide, gliclazide or chlorpropamide, other known sulfonylureas or other antihyperglycemic agents which act on the ATP-dependent channel of the β-cells, with glyburide and glipizide being preferred, which may be administered in the same or in separate oral dosage forms.

The compound of structure I will be employed in a weight ratio to the sulfonyl urea in the range from about 0.01:1 to about 100:1, preferably from about 0.2:1 to about 10:1.

The oral antidiabetic agent may also be a glucosidase inhibitor such as acarbose (disclosed in U.S. Pat. No. 4,904,769) or miglitol (disclosed in U.S. Pat. No. 4,639, 436), which may be administered in the same or in a separate oral dosage forms.

The compound of structure I will be employed in a weight ratio to the glucosidase inhibitor within the range from about 0.01:1 to about 100:1, preferably from about 0.5:1 to about 50:1.

The compound of structure I may be employed in ombination with a PPAR γ agonist such as a thiazolidinedione oral anti-diabetic agent or other insulin sensitizers (which has an insulin sensitivity effect in NIDDM patients) such as troglitazone (Warner-Lambert's Rezulin®, disclosed in U.S. Pat. No. 4,572,912), rosiglitazone (SKB), pioglitazone (Takeda), Mitsubishi's MCC-555 (disclosed in U.S. Pat. No. 5,594,016), Glaxo-Welcome's GL-262570, englitazone (CP-68722, Pfizer) or darglitazone (CP-86325, Pfizer, isaglitazone (MIT/J&J), JTT-501 (JPNT/P&U), L-895645 (Merck), R-119702 (Sankyo/WL), NN-2344 (Dr. Reddy/NN), or YM-440 (Yamanouchi), preferably rosiglitazone and pioglitazone.

The compound of structure I will be employed in a weight ratio to the thiazolidinedione in an amount within the range from about 0.01:1 to about 100:1, preferably from about 0.2:1 to about 10:1.

The sulfonyl urea and thiazolidinedione in amounts of less than about 150 mg oral antidiabetic agent may be incorporated in a single tablet with the compound of structure I.

The compound of structure I may also be employed in combination with an antihyperglycemic agent such as insulin or with glucagon-like peptide-1 (GLP-1) such as GLP-1(1–36) amide, GLP-1(7–36) amide, GLP-1(7–37) (as disclosed in U.S. Pat. No. 5,614,492 to Habener, the disclosure of which is incorporated herein by reference), as well as AC2993 (Amylen) and LY-315902 (Lilly), which may be administered via injection, intranasal, or by transdermal or buccal devices.

Where present, metformin, the sulfonyl ureas, such as glyburide, glimepiride, glipyride, glipizide, chlorpropamide

and gliclazide and the glucosidase inhibitors acarbose or miglitol or insulin (injectable, pulmonary, buccal, or oral) may be employed in formulations as described above and in amounts and dosing as indicated in the Physician's Desk Reference (PDR).

Where present, metformin or salt thereof may be employed in amounts within the range from about 500 to about 2000 mg per day which may be administered in single or divided doses one to four times daily.

Where present, the thiazolidinedione anti-diabetic agent may be employed in amounts within the range from about 0.01 to about 2000 mg/day which may be administered in single or divided doses one to four times per day.

Where present insulin may be employed in formulations, amounts and dosing as indicated by the Physician's Desk Reference.

Where present GLP-1 peptides may be administered in oral buccal formulations, by nasal administration or parenterally as described in U.S. Pat. No. 5,346,701 (TheraTech), U.S. Pat. Nos. 5,614,492 and 5,631,224 which are incorporated herein by reference.

The other antidiabetic agent may also be a PPAR α/γ dual agonist such as AR-HO39242 (Astra/Zeneca), GW-409544 (Glaxo-Wellcome), KRP297 (Kyorin Merck) as well as those disclosed by Murakami et al, "A Novel Insulin Sensitizer Acts As a Coligand for Peroxisome Proliferation—Activated Receptor Alpha (PPAR alpha) and PPAR gamma. Effect on PPAR alpha Activation on Abnormal Lipid Metabolism in Liver of Zucker Fatty Rats", Diabetes 47, 1841–1847 (1998), and in U.S. provisional application No. 60/155,400, filed Sep. 22, 1999, (attorney file LA29) the disclosure of which is incorporated herein by reference, employing dosages as set out therein, which compounds designated as preferred are preferred for use herein.

The other antidiabetic agent may be an aP2 inhibitor such as disclosed in U.S. application Ser. No. 09/391,053, filed Sep. 7, 1999, and in U.S. provisional application No. 60/127,745, filed Apr. 5, 1999 (attorney file LA27*), employing dosages as set out herein. Preferred are the compounds designated as preferred in the above application.

The other antidiabetic agent may be a DP4 inhibitor such as disclosed in WO99/38501, WO99/46272, WO99/67279 PROBIODRUG), WO99/67278 (PROBIODRUG), WO99/61431 (PROBIODRUG), NVP-DPP728A (1-[[[2-[(5-cyanopyridin-2-yl)amino]ethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine) (Novartis) (preferred) as disclosed by Hughes et al, Biochemistry, 38(36), 11597–11603, 1999, TSL-225 (tryptophyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (disclosed by Yamada et al, Bioorg. & Med. Chem. Lett. 8 (1998) 1537–1540, 2-cyanopyrrolidides and 4-cyanopyrrolidides as disclosed by Ashworth et al, Bioorg. & Med. Chem. Lett., Vol. 6, No. 22, pp 1163–1166 and 2745–2748 (1996) employing dosages as set out in the above references.

The meglitinide which may optionally be employed in combination with the compound of formula I of the invention may be repaglinide, nateglinide (Novartis) or KAD1229 (PF/Kissei), with repaglinide being preferred.

The SGLT2 inhibitor of formula I will be employed in a weight ratio to the meglitinide, PPAR γ agonist, PPAR α/γ dual agonist, aP2 inhibitor or DP4 inhibitor within the range from about 0.01:1 to about 100:1, preferably from about 0.2:1 to about 10:1.

The hypolipidemic agent or lipid-lowering agent which may be optionally employed in combination with the compounds of formula I of the invention may include 1,2,3 or more MTP inhibitors, HMG CoA reductase inhibitors, squalene synthetase inhibitors, fibric acid derivatives, ACAT inhibitors, lipoxygenase inhibitors, cholesterol absorption inhibitors, ileal Na^+/bile acid cotransporter inhibitors, upregulators of LDL receptor activity, bile acid sequestrants, and/or nicotinic acid and derivatives thereof.

MTP inhibitors employed herein include MTP inhibitors disclosed in U.S. Pat. Nos. 5,595,872, 5,739,135, 5,712,279, 5,760,246, 5,827,875, 5,885,983 and U.S. application Ser. No. 09/175,180 filed Oct. 20, 1998, now U.S. Pat. No. 5,962,440. Preferred are each of the preferred MTP inhibitors disclosed in each of the above patents and applications. All of the above U.S. Patents and applications are incorporated herein by reference.

The hypolipidemic agent may be an HMG CoA reductase inhibitor which includes, but is not limited to, mevastatin and related compounds as disclosed in U.S. Pat. No. 3,983,140, lovastatin (mevinolin) and related compounds as disclosed in U.S. Pat. No. 4,231,938, pravastatin and related compounds such as disclosed in U.S. Pat. No. 4,346,227, simvastatin and related compounds as disclosed in U.S. Pat. Nos. 4,448,784 and 4,450,171. The hypolipidemic agent may also be the compounds disclosed in U.S. provisional application Nos. 60/211,594 and 60/211,595. Other HMG CoA reductase inhibitors which may be employed herein include, but are not limited to, fluvastatin, disclosed in U.S. Pat. No. 5,354,772, cerivastatin disclosed in U.S. Pat. Nos. 5,006,530 and 5,177,080, atorvastatin disclosed in U.S. Pat. Nos. 4,681,893, 5,273,995, 5,385,929 and 5,686,104, atavastatin (Nissan/Sankyo's nisvastatin (NK-104)) disclosed in U.S. Pat. No. 5,011,930, Shionogi-Astra/Zeneca visastatin (ZD-4522) disclosed in U.S. Pat. No. 5,260,440, and related statin compounds disclosed in U.S. Pat. No. 5,753,675, pyrazole analogs of mevalonolactone derivatives as disclosed in U.S. Pat. No. 4,613,610, indene analogs of mevalonolactone derivatives as disclosed in PCT application WO 86/03488, 6-[2-(substituted-pyrrol-1-yl)-alkyl)pyran-2-ones and derivatives thereof as disclosed in U.S. Pat. No. 4,647,576, Searle's SC-45355 (a 3-substituted pentanedioic acid derivative) dichloroacetate, imidazole analogs of mevalonolactone as disclosed in PCT application WO 86/07054, 3-carboxy-2-hydroxy-propane-phosphonic acid derivatives as disclosed in French Patent No. 2,596,393, 2,3-disubstituted pyrrole, furan and thiophene derivatives as disclosed in European Patent Application No. 0221025, naphthyl analogs of mevalonolactone as disclosed in U.S. Pat. No. 4,686,237, octahydronaphthalenes such as disclosed in U.S. Pat. No. 4,499,289, keto analogs of mevinolin (lovastatin) as disclosed in European Patent Application No.0,142,146 A2, and quinoline and pyridine derivatives disclosed in U.S. Pat. Nos. 5,506,219 and 5,691,322.

In addition, phosphinic acid compounds useful in inhibiting HMG CoA reductase suitable for use herein are disclosed in GB 2205837.

The squalene synthetase inhibitors suitable for use herein include, but are not limited to, α-phosphono-sulfonates disclosed in U.S. Pat. No. 5,712,396, those disclosed by Biller et al, J. Med. Chem., 1988, Vol. 31, No. 10, pp 1869–1871, including isoprenoid (phosphinyl-methyl) phosphonates as well as other known squalene synthetase inhibitors, for example, as disclosed in U.S. Pat. Nos. 4,871,721 and 4,924,024 and in Biller, S. A., Neuenschwander, K., Ponpipom, M. M., and Poulter, C. D., Current Pharmaceutical Design, 2, 1–40 (1996).

In addition, other squalene synthetase inhibitors suitable for use herein include the terpenoid pyrophosphates disclosed by P. Ortiz de Montellano et al, J. Med. Chem., 1977, 20, 243–249, the farnesyl diphosphate analog A and

presqualene pyrophosphate (PSQ-PP) analogs as disclosed by Corey and Volante, J. Am. Chem. Soc., 1976, 98, 1291–1293, phosphinylphosphonates reported by McClard, R. W. et al, J.A.C.S., 1987, 109, 5544 and cyclopropanes reported by Capson, T. L., PhD dissertation, June, 1987, Dept. Med. Chem. U of Utah, Abstract, Table of Contents, pp 16, 17, 40–43, 48–51, Summary.

Other hypolipidemic agents suitable for use herein include, but are not limited to, fibric acid derivatives, such as fenofibrate, gemfibrozil, clofibrate, bezafibrate, ciprofibrate, clinofibrate and the like, probucol, and related compounds as disclosed in U.S. Pat. No. 3,674,836, probucol and gemfibrozil being preferred, bile acid sequestrants such as cholestyramine, colestipol and DEAE-Sephadex (Secholex®, Policexide®), as well as lipostabil (Rhone-Poulenc), Eisai E-5050 (an N-substituted ethanolamine derivative), imanixil (HOE-402), tetrahydrolipstatin (THL), istigmastanylphos-phorylcholine (SPC, Roche), aminocyclodextrin (Tanabe Seiyoku), Ajinomoto AJ-814 (azulene derivative), melinamide (Sumitomo), Sandoz 58-035, American Cyanamid CL-277,082 and CL-283,546 (disubstituted urea derivatives), nicotinic acid, acipimox, acifran, neomycin, p-aminosalicylic acid, aspirin, poly (diallylmethylamine) derivatives such as disclosed in U.S. Pat. No. 4,759,923, quaternary amine poly (diallyldimethylammonium chloride) and ionenes such as disclosed in U.S. Pat. No. 4,027,009, and other known serum cholesterol lowering agents.

The other hypolipidemic agent may be an ACAT inhibitor such as disclosed in, Drugs of the Future 24, 9–15 (1999), (Avasimibe); "The ACAT inhibitor, Cl-1011 is effective in the prevention and regression of aortic fatty streak area in hamsters", Nicolosi et al, Atherosclerosis (Shannon, Irel). (1998), 137(1), 77–85; "The pharmacological profile of FCE 27677: a novel ACAT inhibitor with potent hypolipidemic activity mediated by selective suppression of the hepatic secretion of ApoB100-containing lipoprotein", Ghiselli, Giancarlo, Cardiovasc. Drug Rev. (1998), 16(1), 16–30; "RP 73163: a bioavailable alkylsulfinyl-diphenylimidazole ACAT inhibitor", Smith, C., et al, Bioorg. Med. Chem. Lett. (1996), 6(1), 47–50; "ACAT inhibitors: physiologic mechanisms for hypolipidemic and anti-atherosclerotic activities in experimental animals", Krause et al, Editor(s): Ruffolo, Robert R., Jr.; Hollinger, Mannfred A., Inflammation: Mediators Pathways (1995), 173–98, Publisher: CRC, Boca Raton, Fla.; "ACAT inhibitors: potential anti-atherosclerotic agents", Sliskovic et al, Curr. Med. Chem. (1994), 1(3), 204–25; "Inhibitors of acyl-CoA:cholesterol O-acyl transferase (ACAT) as hypocholesterolemic agents. 6. The first water-soluble ACAT inhibitor with lipid-regulating activity. Inhibitors of acyl-CoA:cholesterol acyltransferase (ACAT). 7. Development of a series of substituted N-phenyl-N'-[(1-phenylcyclopentyl)methyl]ureas with enhanced hypocholesterolemic activity", Stout et al, Chemtracts: Org. Chem. (1995), 8(6), 359–62, or TS-962 (Taisho Pharmaceutical Co. Ltd).

The hypolipidemic agent may be an upregulator of LD2 receptor activity such as MD-700 (Taisho Pharmaceutical Co. Ltd) and LY295427 (Eli Lilly).

The hypolipidemic agent may be a cholesterol absorption inhibitor preferably Schering-Plough's SCH48461 as well as those disclosed in Atherosclerosis 115, 45–63 (1995) and J. Med. Chem. 41, 973 (1998).

The hypolipidemic agent may be an ileal Na^+/bile acid cotransporter inhibitor such as disclosed in Drugs of the Future, 24, 425–430 (1999).

Preferred hypolipidemic agents are pravastatin, lovastatin, simvastatin, atorvastatin, fluvastatin, cerivastatin, atavastatin and rosuvastatin.

The above-mentioned U.S. patents are incorporated herein by reference. The amounts and dosages employed will be as indicated in the Physician's Desk Reference and/or in the patents set out above.

The compound of formula I of the invention will be employed in a weight ratio to the hypolipidemic agent (where present), within the range from about 500:1 to about 1:500, preferably from about 100:1 to about 1:100.

The dose administered must be carefully adjusted according to age, weight and condition of the patient, as well as the route of administration, dosage form and regimen and the desired result.

The dosages and formulations for the hypolipidemic agent will be as disclosed in the various patents and applications discussed above.

The dosages and formulations for the other hypolipidemic agent to be employed, where applicable, will be as set out in the latest edition of the Physicians' Desk Reference.

For oral administration, a satisfactory result may be obtained employing the MTP inhibitor in an amount within the range of from about 0.01 mg/kg to about 500 mg and preferably from about 0.1 mg to about 100 mg, one to four times daily.

A preferred oral dosage form, such as tablets or capsules, will contain the MTP inhibitor in an amount of from about 1 to about 500 mg, preferably from about 2 to about 400 mg, and more preferably from about 5 to about 250 mg, one to four times daily.

For oral administration, a satisfactory result may be obtained employing an HMG CoA reductase inhibitor, for example, pravastatin, lovastatin, simvastatin, atorvastatin, fluvastatin or cerivastatin in dosages employed as indicated in the Physician's Desk Reference, such as in an amount within the range of from about 1 to 2000 mg, and preferably from about 4 to about 200 mg.

The squalene synthetase inhibitor may be employed in dosages in an amount within the range of from about 10 mg to about 2000 mg and preferably from about 25 mg to about 200 mg.

A preferred oral dosage form, such as tablets or capsules, will contain the HMG CoA reductase inhibitor in an amount from about 0.1 to about 100 mg, preferably from about 5 to about 80 mg, and more preferably from about 10 to about 40 mg.

A preferred oral dosage form, such as tablets or capsules will contain the squalene synthetase inhibitor in an amount of from about 10 to about 500 mg, preferably from about 25 to about 200 mg.

The other hypolipidemic agent may also be a lipoxygenase inhibitor including a 15-lipoxygenase (15-LO) inhibitor such as benzimidazole derivatives as disclosed in WO 97/12615, 15-LO inhibitors as disclosed in WO 97/12613, isothiazolones as disclosed in WO 96/38144, and 15-LO inhibitors as disclosed by Sendobry et al "Attenuation of diet-induced atherosclerosis in rabbits with a highly selective 15-lipoxygenase inhibitor lacking significant antioxidant properties, Brit. J. Pharmacology (1997) 120, 1199–1206, and Cornicelli et al, "15-Lipoxygenase and its Inhibition: A Novel Therapeutic Target for Vascular Disease", Current Pharmaceutical Design, 1999, 5, 11–20.

The compounds of formula I and the hypolipidemic agent may be employed together in the same oral dosage form or in separate oral dosage forms taken at the same time.

The compositions described above may be administered in the dosage forms as described above in single or divided doses of one to four times daily. It may be advisable to start a patient on a low dose combination and work up gradually to a high dose combination.

The preferred hypolipidemic agents are pravastatin, simvastatin, lovastatin, atorvastatin, fluvastatin, cerivastatin, atavastatin and rosuvastatin.

When the other type of therapeutic agent which may be optionally employed with the SGLT2 inhibitor of formula I is 1, 2, 3 or more of an anti-obesity agent, it may include a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta drug, an anorectic agent, an NPY antagonist, a Leptin analog and/or an MC4 agonist.

The beta 3 adrenergic agonist which may be optionally employed in combination with a compound of formula I may be AJ9677 (Takeda/Dainippon), L750355 (Merck), or CP331648 (Pfizer) or other known beta 3 agonists as disclosed in U.S. Pat. Nos. 5,541,204, 5,770,615, 5,491,134, 5,776,983 and 5,488,064, with AJ9677, L750,355 and CP331648 being preferred.

The lipase inhibitor which may be optionally employed in combination with a compound of formula I may be orlistat or ATL-962 (Alizyme), with orlistat being preferred.

The serotonin (and dopamine) reuptake inhibitor which may be optionally employed in combination with a compound of formula I may be sibutramine, topiramate (Johnson & Johnson) or axokine (Regeneron), with sibutramine and topiramate being preferred.

The thyroid receptor beta compound which may be optionally employed in combination with a compound of formula I may be a thyroid receptor ligand as disclosed in WO97/21993 (U. Cal SF), WO99/00353 (KaroBio) and GB98/284425 (KaroBio), with compounds of the KaroBio applications being preferred.

The anorectic agent which may be optionally employed in combination with a compound of formula I may be dexamphetamine, phentermine, phenylpropanolamine or mazindol, with dexamphetamine being preferred.

The various anti-obesity agents described above may be employed in the same dosage form with the compound of formula I or in different dosage forms, in dosages and regimens as generally known in the art or in the PDR.

Examples of the anti-platelet agent(s) which may be optionally employed in combinations of this invention include abciximab, ticlopidine, eptifibatide, dipyridamole, aspirin, anagrelide, tirofiban and/or clopidogrel.

Examples of the anti-hypertensive agent(s) which may be optionally employed in combinations of this invention include ACE inhibitors, calcium antagonists, alpha-blockers, diuretics, centrally acting agents, angiotensin-II antagonists, beta-blockers and vasopeptidase inhibitors.

Examples of ACE inhibitors include lisinopril, enalapril, quinapril, benazepril, fosinopril, ramipril, captopril, enalaprilat, moexipril, trandolapril and perindopril; examples of calcium antagonists include amlodipine, diltiazem, nifedipine, verapamil, felodipine, nisoldipine, isradipine and nicardipine; examples of alpha-blockers include terazosin, doxazosin and prazosin; examples of diuretics include hydrochlorothiazide, torasemide, furosemide, spironolactone and indapamide; examples of centrally acting agents include clonidine and guanfacine; examples of angiotensin-II antagonists include losartan, valsartan, irbesartan, candesartan and telmisartan; examples of beta-blockers include metoprolol, propranolol, atenolol, carvedilol and sotalol; and examples of vasopeptidase inhibitors include omapatrilat and gemopatrilat.

In carrying out the method of the invention, a pharmaceutical composition will be employed containing the compound of structure I, with or without another antidiabetic agent and/or antihyperlipidemic agent, or other type therapeutic agent, in association with a pharmaceutical vehicle or diluent. The pharmaceutical composition can be formulated employing conventional solid or liquid vehicles or diluents and pharmaceutical additives of a type appropriate to the mode of desired administration. The compounds can be administered to mammalian species including humans, monkeys, dogs, etc. by an oral route, for example, in the form of tablets, capsules, granules or powders, or they can be administered by a parenteral route in the form of injectable preparations, or they can be administered intranasally or in transdermal patches. The dose for adults is preferably between 10 and 2,000 mg per day, which can be administered in a single dose or in the form of individual doses from 1–4 times per day.

A typical injectable preparation is produced by aseptically placing 250 mg of compounds of structure I into a vial, aseptically freeze-drying and sealing. For use, the contents of the vial are mixed with 2 mL of physiological saline, to produce an injectable preparation.

SGLT2 inhibitor activity of the compounds of the invention may be determined by use of an assay system as set out below.

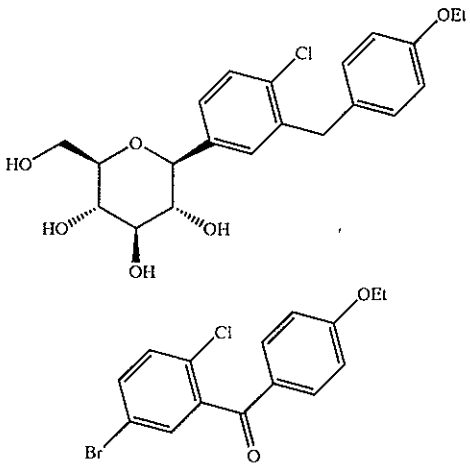
Assay for SGLT2 Activity

The mRNA sequence for human SGLT2 (GenBank #M95549) was cloned by reverse-transcription and amplification from human kidney mRNA, using standard molecular biology techniques. The cDNA sequence was stably transfected into CHO cells, and clones were assayed for SGLT2 activity essentially as described in Ryan et al. (1994). Evaluation of inhibition of SGLT2 activity in a clonally selected cell line was performed essentially as described in Ryan et al., with the following modifications. Cells were grown in 96-well plates for 2–4 days to 75,000 or 30,000 cells per well in F-12 nutrient mixture (Ham's F-12), 10% fetal bovine serum, 300 ug/ml Geneticin and penicillin-streptomycin. At confluence, cells were washed twice with 10 mM Hepes/Tris, pH 7.4, 137 mM N-methyl-D-glucamine, 5.4 mM KCl, 2.8 mM $CaCl_2$, 1.2 mM $MgSO_4$. Cells then were incubated with 10 μM [^{14}C]AMG, and 10 μM inhibitor (final DMSO=0.5%) in 10 mM Hepes/Tris, pH 7.4, 137 mM NaCl, 5.4 mM KCl, 2.8 mM $CaCl_2$, 1.2 mM $MgSO_4$ at 37° C. for 1.5 hr. Uptake assays were quenched with ice cold 1×PBS containing 0.5 mM phlorizin, and cells were then lysed with 0.1% NaOH. After addition of MicroScint scintillation fluid, the cells were allowed to shake for 1 hour, and then [^{14}C]AMG was quantitated on a TopCount scintillation counter. Controls were performed with and without NaCl. For determination of EC_{50} values, 10 inhibitor concentrations were used over 2 log intervals in the appropriate response range, and triplicate plates were averaged across plates.

Ryan M J, Johnson G, Kirk J, Fuerstenberg S M, Zager R A and Torok-Storb B. 1994. HK-2: an immortalized proximal tubule epithelial cell line from normal adult human kidney. Kidney International 45: 48–57.

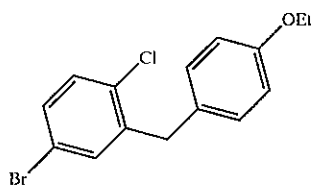
The following Working Examples represent preferred embodiments of the present invention. All temperatures are expressed in degrees Centigrade unless otherwise indicated.

EXAMPLE



A. 5-Bromo-2-chloro-4'-ethoxybenzophenone

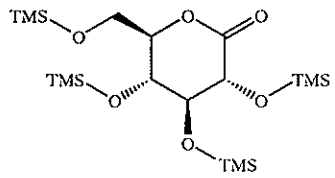
To a stirred suspension of commercial 5-bromo-2-chlorobenzoic acid (250 g, 1.06 mol) in 450 mL of CH_2Cl_2 containing oxalyl chloride (1.1 mol) was added 1.5 mL of DMF. Once the vigorous evolution of gas ceased, the reaction was stirred overnight prior to removal of the volatiles under vacuum using a rotary evaporator. After dissolving the crude 5-bromo-2-chlorobenzoyl chloride in 200 ml of CH_2Cl_2, the yellow solution was transferred to a 2 L 3-neck flask equipped with an overhead stirrer and an internal thermometer. The stirred mixture was cooled to −3° prior to adding phenetole (130 g, 1.08 mol). $AlCl_3$ (140 g, 1.07 mol) was added via a solid addition funnel over 30 min to insure that the temperature did not exceed 4°. The copious amounts of HCl gas which began to evolve after 60% of the $AlCl_3$ had been added were trapped by passing the gas over a stirred conc. NaOH solution. HPLC revealed the reaction to be 95% complete 10 minutes after the addition was finished. After the mixture was stirred at 4° for 1 hr, the reaction was quenched by pouring over ice. Subsequently, the suspension was diluted with H_2O (1 L) and extracted 3× with CH_2Cl_2. The combined organic extracts were washed 2× with 1N HCl, 1× with H_2O, 2× with 1M NaOH, and 2× with brine prior to drying over Na_2SO_4. After removal of the volatiles, HPLC revealed the residue to be a 1:7 mixture of ortho/para isomers. Recrystallization 2× from 400 mL of absolute EtOH yielded 230 g (64%) of 5-bromo-2-chloro-4'-ethoxybenzophenone.



B. 5-Bromo-2-chloro-4'-ethoxydiphenylmethane

To a stirred solution of Et_3SiH (400 mL, 2.51 mol and 5-bromo-2-chloro-4'-ethoxybenzophenone (390 g, 1.15 mol) in 900 mL of a 1:2 mixture 1,2-dichloroethane/MeCN at 10° C. was added $BF_3.Et_2O$ (150 mL, 1.58 mol) at such a rate that the temperature did not exceed 20°. Caution a moderate exotherm insues during the addition. After stirring overnight at 20° C., HPLC revealed the reaction to be 90% complete. After adding an additional 40 mL Et_3SiH and 15 mL of $BF_3.Et_2O$, the reaction was heated to 50° for 3 hr. (Note elevated temperatures increase formation of the Ritter reaction product N-acetyl 5-bromo-2-chloro-4'-ethoxydiphenylmethylamine). Upon cooling, the reaction was quenched with 120 g of KOH in 300 mL of H_2O. After stirring 2 hr, the layers were separated. The aqueous layer was extracted 2× with CH_2Cl_2; the combined organic layers were washed 1× with 300 mL portions of 2M KOH, 2× with H_2O containing 10% brine to aid phase separation and with brine 2× prior to drying over Na_2SO_4. After removal of the volatiles, the residue was recrystallized from absolute EtOH to yield 230 g of 5-bromo-2-chloro-4'-ethoxydiphenylmethane as a white solid.

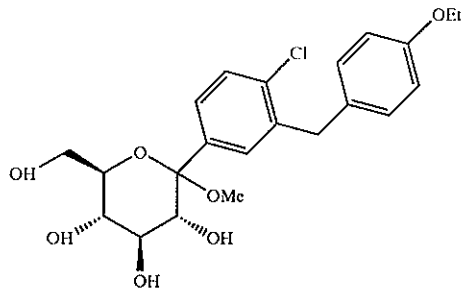
C.



C. 2,3,4,6-tetra-O-Trimethylsilyl-β-D-glucolactone

To a stirred −5° C. solution of gluconolactone (239 g, 1.34 mol and N-methylmorpholine (1180 mL, 10.73 mol) in 2.4 L of THF under Ar was added trimethylsilyl chloride (1022 mL, 8.05 mol) via dropping funnel at a rate such that the temperature did not exceed 5° C. After 1 hr the stirred reaction was heated to 35° C. for 5 hr whereupon it was allowed to cool to 20° C. as the reaction stirred overnight. After dilution with 3.6 L of toluene, the mixture was cooled to 0–5° C. prior to cautiously adding 7 L of H_2O at a rate such that the temperature did not exceed 10° C. Note, a severe exotherm results upon addition of the first portion of H_2O. After mixing, the phases were allowed to separate and then split. The organic phase was washed with aq. NaH_2PO_4 (2 L), H_2O (1 L), and brine (1 L). The organic layer was then concentrated under vacuum using a rotary evaporator; the resultant light yellow oil was twice taken up 250 mL of toluene and reconcentrated to yield 616 g of title compound.

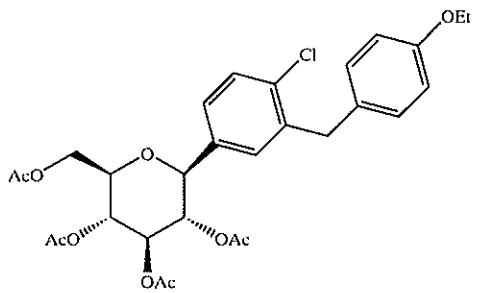
D.



To a stirred −78° solution of Part B 5-bromo-2-chloro-4'-ethoxydiphenylmethane (150 g, 0.46 mol) in 1.15 L of 1:2 dry THF/toluene under Ar was added 184 mL of 2.5 M n-BuLi in hexane dropwise to insure the temperature remained below −70°. After stirring for 30 minutes following the addition, this solution was transferred by cannula to a stirred −78° solution of Part C 2,3,4,6-tetra-O-

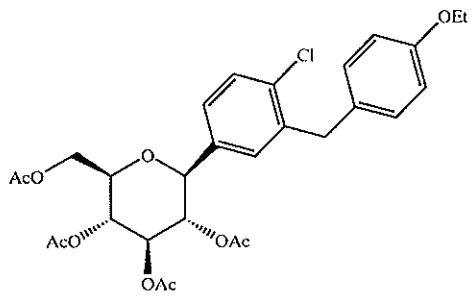
trimethylsilyl-β-D-glucolactone (236 g, 0.51 mol) in 1.1 L of toluene at a rate that maintained the reaction below −70°. The solution was stirred for 30 min at −78° prior to quenching by addition of 1 L of MeOH containing methanesulfonic acid (41.8 mL, 0.64 mol). The reaction stirred overnight as the temperature rose to 20° C. HPLC analysis reveals two new peaks corresponding to the mass of the expected O-methylglucoside; the ratio typically varies from 95:5 to 80:20. The desired product corresponds to the major one with shorter retention time. Note longer reaction times or addition of 50% more methanesulfonic acid will convert all of the isomeric product to the desired O-methylglucoside. The reaction, once complete, was quenched by the addition of $NaHCO_3$ (37 g, 0.37 mol) in 200 mL of H_2O. If the pH was not weakly basic, more $NaHCO_3$ was added prior to dilution 2 fold with H_2O and 3 extractions with EtOAc. The combined EtOAc fractions were washed with brine and dried over Na_2SO_4. After concentration using a rotary evaporator, the residue was dissolved in hot toluene (150 mL). The resulting solution was poured into a liter of stirred hexane. The precipitate was collected by vacuum filtration; the resulting filter cake was washed 2× with 500 mL of hexane and then air dried to yield 171 g of title compound in the form of a white solid.

E.



To a stirred −10° solution of Part D O-methylglucoside (123 g, 0.28 mol) in 1.2 L of 1:1 CH_2Cl_2/MeCN was added Et_3SiH (65.27 g, 0.56 mol) followed by addition of $BF_3.Et_2O$ (59.75 g, 0.42 mol) at a rate such that the temperature was maintained between −5°—10°. The stirred solution was allowed to warm to 0° over 5 hr. When HPLC analysis revealed that the reaction was complete, the reaction was quenched by addition of satd. aq $NaHCO_3$ (310 mL). The organic volatiles were removed under vacuum using a rotary evaporator. The residue was partitioned between 2 L each of EtOAc and H_2O. After separating phases, the H_2O layer was extracted 2× with 2 L portions of EtOAc. The combined organic phases were washed with H_2O (2 L) and with brine (2 L) prior to drying over $MgSO_4$ and then concentrated using a rotary evaporator to yield 104.6 g of yellow solidified foam. After dissolution of this residue in CH_2Cl_2 (750 mL), pyridine (200 g, 2.53 mol) was added followed by Ac_2O (261.1 g, 2.56 mol) in one portion. After the resulting exotherm raising the temperature from 28° to 47° had subsided, DMAP (1.56 g, 13 mmol) was added. The reaction was quenched after 1.5 hr by addition of H_2O (1.8 L) once HPLC analysis indicated the reaction to be complete. The mixture was extracted 2× with CH_2Cl_2 (total volume 2.7 L); the combined organic layers were washed 2× with 1N HCL (1.8 L), 2× with brine (1.8 L) prior to drying over $MgSO_4$. The residue, after concentration using a rotary evaporator, was recrystallized from absolute EtOH (750 mL) to yield 89.5 g of the desired tetraacetylated β-C-glucoside as a white solid. The mother liquors contained the corresponding α-C-glucoside as well as a more polar furanose isomer.

F.

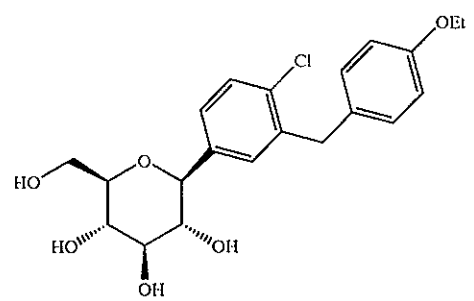


Alternatively the O-methylglucoside of Part D can first be aceylated and then reduced to yield the desired tetraacetylated C-arylglucoside utilizing the following procedure.

A solution of Part D O-methylglucoside (3.0 g, 6.8 mmol) in toluene (45 mL) containing diisopropylethylamine (6.9 mL, 40 mmol) was cooled to 0° prior to addition of acetic anhydride (3.35 mL, 35.5 mmol) and DMAP (84 mg, 0.68 mmol). The solution was allowed to gradually warm to 20°; after six hours, tlc analysis revealed complete conversion to tetraacetate. The reaction was quenched by addition of 50 mL of 20% H_3PO_4. After separation of the layers, the aq. phase was extracted 2× with toluene. The combined organic phases were washed 1× with 50 mL of H_2O prior to concentration under vacuum. The resultant oil was dissolved in 20 mL of toluene and reconcentrated to yield a thick oil (4.15 g) that was used without further purification.

A solution of the above crude oil(4.15 g, 6.8 mmol) in MeCN (60 mL) containing one eqivalent of H_2O (123 mg, 6.8 mmol) was cooled to 0° prior to addition of Et_3SiH (3.27 mL, 20.5 mmol) followed by $BF_3.Et_2O$ (1.73 mL, 13.7 mmol). After stirring for 1 hr, the solution was allowed to warm to 20°. After 4 hr, once periodic HPLC analysis revealed that the reaction was no longer progressing beyond 60%, an additional 2 mL of Et_3SiH and 1 mL of $BF_3.Et_2O$ was added. Two hours later, no starting material remained by HPLC analysis. After adding aq $NaHCO_3$ to quench the reaction, the mixture was stirred 30 min prior to being extracted 3× with EtOAc. The combined organic layers were washed 1× with aq $NaHCO_3$ and brine prior to drying over Na_2SO_4. The oil obtained after concentration under vacuum was dissolved in 70 mL of hot 25% EtOAc/hexane. Upon cooling, 2.45 g of desired tetraacetylated β-C-arylglucoside crystallized which was subsequently isolated by filtration.

G.



To a stirred 20° solution of tetraacetylated β-C-glucoside (27.2 g, 49 mmol) (prepared as described in Part E), in 480 mL of 2:3:1 THF/MeOH/H_2O was added $LiOH.H_2O$ (2.3 g,

57 mmol). After stirring overnight, the volatiles were removed using a rotary evaporator. The residue, after being dissolved in EtOAc (300 mL), was washed 1× with brine (150 mL), 1× with brine (50 mL) containing 10 mL of 5% aq KHSO4 and finally with brine (50 mL) prior to drying over Na_2SO_4. The volatiles were removed using a rotary evaporator and the resultant oil in the minimum amount of CH_2Cl_2 foamed under vacuum to yield 20.4 g of desired title C-arylglucoside as a glassy off white solid containing 0.11 mol % of EtOAc.

HPLC retention time: 7.08 min, 94% pure, YMC S5 C-18 4.6×50 mm column, 2.5 mL/min, detection at 220 nM; 8 min gradient 0–100% B hold 5 min at 100% B. Solvent A: 10% MeOH/H_2O+0.2% H_3PO_4. Solvent B: 90% MeOH/H_2O+ 0.2% H_3PO_4.

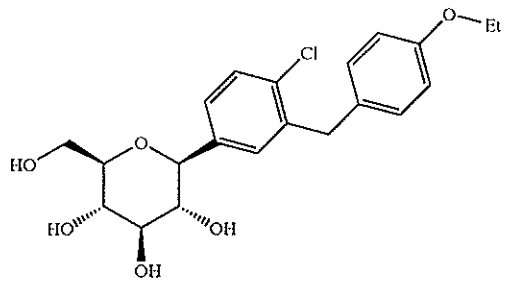
^1H NMP (500 MHz, CD_3OD) δ7.33 (d, 1H, J=6 Hz), 7.31 (d, 1H, J=2.2 Hz), 7.31 (dd, 1H, J=6 Hz, J=2.2 Hz), 7.07 (d, 2H, J=8.8 Hz), 6.78 (d, 2H, J=8.8 Hz), 4.07–3.90 (m, 7H), 3.85 (d, 1H, J=10.6 Hz), 3.69 (dd, 1H, J=5.3, 10.6 Hz), 3.42–3.25 (m, 4H) Hz), 1.34 (t, 3H, J=7 Hz).

^{13}C NMP (125 MHz, CD_3OD) δ158.8, 140.0, 139.9, 134.4, 132.9, 131.9, 130.8, 130.1, 128.2, 115.5, 82.9, 82.2, 79.7, 76.4, 71.9, 64.5, 63.1, 39.2, 15.2.

Anal Calcd for $C_{21}H_{25}ClO_6$ LC-MS [M+Na^+]431; found 431.

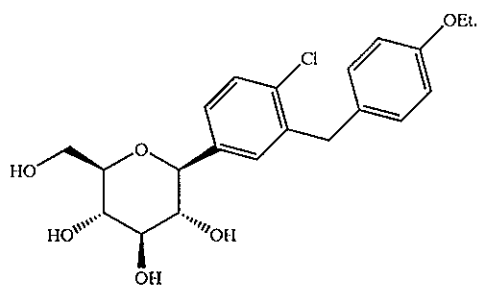
What is claimed:

1. A compound having the structure



or a pharmaceutically acceptable salt, a stereoisomer thereof, or a prodrug ester thereof.

2. The compound as defined in claim 1 having the structure



3. A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

4. A pharmaceutical combination comprising an SGLT2 inhibitor compound as defined in claim 3 and an antidiabetic agent other than an SGLT2 inhibitor, an agent for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent, and/or a lipid-lowering agent.

5. The pharmaceutical combination as defined in claim 4 comprising said SGLT2 inhibitor compound and an antidiabetic agent.

6. The combination as defined in claim 5 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR γ agonist, a PPAR α/γ dual agonist, an aP2 inhibitor, a DP4 inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1), insulin, a meglitinide, a PTP1B inhibitor, a glycogen phosphorylase inhibitor, and/or a glucos-6-phosphatase inhibitor.

7. The combination as defined in claim 6 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, GI-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, and/or NVP-DPP-728A.

8. The combination as defined in claim 5 wherein the SGLT2 inhibitor compound is present in a weight ratio to the antidiabetic agent within the range from about 0.01 to about 300:1.

9. The combination as defined in claim 4 wherein the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor beta compound, and/or an anorectic agent.

10. The combination as defined in claim 9 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, and/or mazindol.

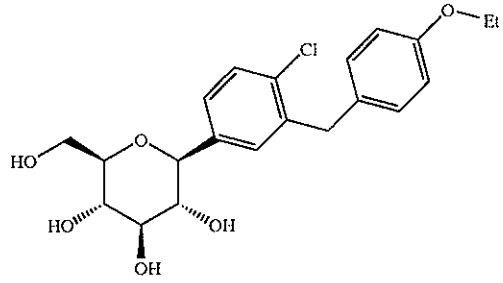
11. The combination as defined in claim 4 wherein the lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, or an ACAT inhibitor.

12. The combination as defined in claim 11 wherein the lipid lowering agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, nisvastatin, visastatin, atavastatin, rosuvastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, and/or LY295427.

13. The combination as defined in claim 11 wherein the SGLT2 inhibitor is present in a weight ratio to the lipid-lowering agent within the range from about 0.01 to about 300:1.

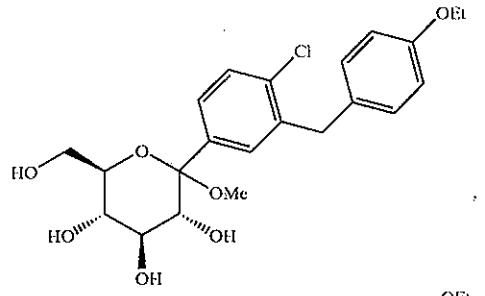
14. A method for treating or delaying the progression or onset of diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension, or for increasing high density lipoprotein levels, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in claim 1.

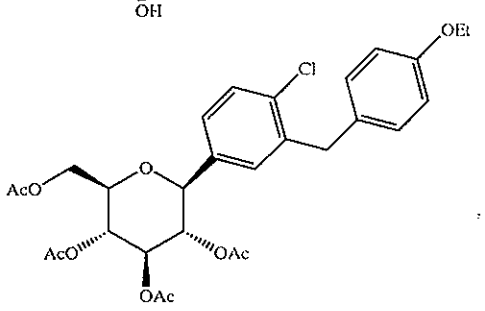
15. The method as defined in claim 14 where the SGLT2 inhibitor compound has the structure



16. A method for treating type II diabetes which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in claim 1 alone or in combination with another antidiabetic agent, an agent for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an anti-atherosclerotic agent and/or a hypolipidemic agent.

17. A compound having the structure





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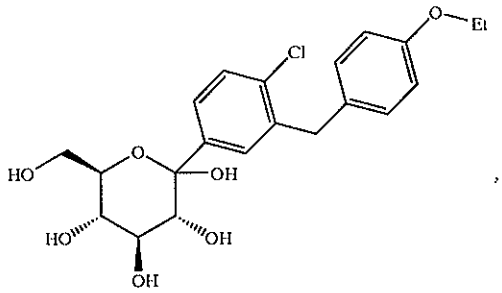
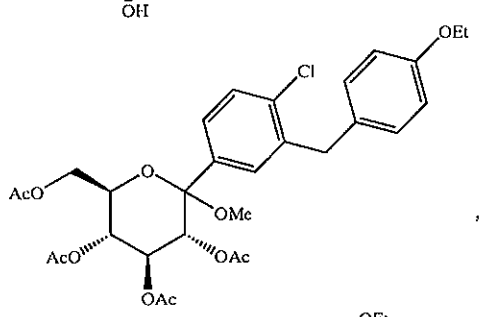
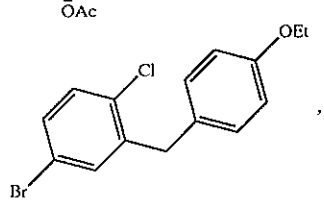
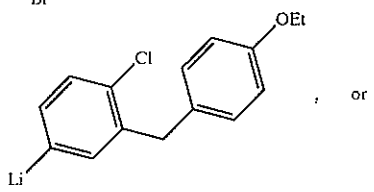
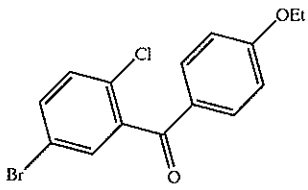










or a pharmaceutically acceptable salt thereof, all stereoisomers thereof, or a prodrug ester thereof.

* * * * *

EXHIBIT B

Patent Assignment Abstract of Title

NOTE:Results display only for issued patents and published applications. For pending or abandoned applications please consult USPTO staff.

Total Assignments: 2

Patent #: 6515117 **Issue Dt:** 02/04/2003 **Application #:** 10151436 **Filing Dt:** 05/20/2002

Publication #: 20020137903 **Pub Dt:** 09/26/2002

Inventors: Bruce Ellsworth, William N. Washburn, Philip M. Sher, Gang Wu, Wei Meng

Title: C-ARYL GLUCOSIDE SGLT2 INHIBITORS AND METHOD

Assignment: 1

Reel/Frame: 012918/0698 **Recorded:** 05/20/2002 **Pages:** 5

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignors: ELLSWORTH, BRUCE **Exec Dt:** 05/08/2002

WASHBURN, WILLIAM N. **Exec Dt:** 05/08/2002

SHER, PHILIP M. **Exec Dt:** 05/08/2002

WU, GANG **Exec Dt:** 05/08/2002

MENG, WEI **Exec Dt:** 05/08/2002

Assignee: BRISTOL-MYERS SQUIBB COMPANY
LAWRENCEVILLE-PRINCETON ROAD
PRINCETON, NEW JERSEY 08543

Correspondent: BRISTOL-MYERS SQUIBB COMPANY
STEPHEN B. DAVIS
PATENT DEPARTMENT
P.O. BOX 4000
PRINCETON, NEW JERSEY 08543-4000

Assignment: 2

Reel/Frame: 032347/0115 **Recorded:** 03/04/2014 **Pages:** 36

Conveyance: ASSIGNMENT OF ASSIGNORS INTEREST (SEE DOCUMENT FOR DETAILS).

Assignor: BRISTOL-MYERS SQUIBB COMPANY **Exec Dt:** 01/30/2014

Assignee: ASTRAZENECA AB
SE-151 85
SODERTALJE, SWEDEN

Correspondent: MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DR.
CHICAGO, IL 60606

EXHIBIT C

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202293

NDA APPROVAL

Bristol-Myers Squibb
Attention: Amy A. Jennings, Ph.D.
Director, Global Regulatory Sciences - U.S.
5 Research Parkway
Wallingford, CT 06492-7660

Dear Dr. Jennings:

Please refer to your New Drug Application (NDA) dated December 27, 2010, received December 28, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Farxiga (dapagliflozin) tablets 5 mg and 10 mg.

We acknowledge receipt of your amendments dated January 5, 12, 28 (2), and 31, February 1 and 16, March 23 and 30, April 11, 12, 13, 14, 22 and 27, May 9, 13, 16,18, 20 (2), 23, and 24, June 2, 3 (2), 8, 13 (2), 14, 16, 17, 22, 24, and 30, July 13 and 25, August 1, 12, 17, 19, 22, 26, 29, and 30, September 2 (2), 7, 9, 14, 19, 20, and 26, October 18, 20, and 27, November 2, 8, 9, 10 (2), 16 (2), and 22, and December 2, 6, 7, 12, 19, and 29, 2011, and January 10, 11, 19, and 24, February 7, March 30 (2), April 2, 27, and 30, May 9 and 30, June 4 and 27, July 17, August 6 and 31, October 26, November 21, and December 12, 2012, and January 30, February 4 and 28, May 13, July 11 and 16, August 7, September 3, 5, 6, 9, and 17, October 4, 10, 16 (2), 18, 22, and 25, November 4, 5, and 21, and December 6, 18, 24, 26, and 31, 2013. We also acknowledge receipt of your email dated January 7, 2014, which includes the agreed-upon labeling.

The July 11, 2013, submission constituted a complete response to our January 17, 2012, action letter.

This new drug application provides for the use of Farxiga (dapagliflozin) as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA

automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (package insert and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels submitted on December 24, 2013, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202293.**" Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 through 9 years because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group.

We are deferring submission of your pediatric studies for ages 10 to 17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

2121-1 Complete a randomized, multicenter, parallel, single-dose study to explore the pharmacokinetics (PK) and pharmacodynamics (PD) of dapagliflozin in children, 10 to 17 years of age with type 2 diabetes mellitus (T2DM) receiving one of the three dose levels of dapagliflozin over the range of 2.5 to 10 mg. At least 30% of randomized subjects in each dose group will be 10 - 15 years of age.

Final Protocol Submission:	April 2012
Study Completion:	August 2014
Final Report Submission:	February 2015

2121-2 A 26-week randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of dapagliflozin for the treatment of pediatric subjects ages 10 to <18 years of age with type 2 diabetes mellitus (T2DM), as add-on to metformin or as monotherapy, followed by a 26-week double-blind, placebo- or active-controlled extension period (Week 26 to Week 52). At least 30% of randomized subjects will be 10 to 14 years of age and at least one-third and not more than two-thirds of subjects in both age subsets (10 to 14 years and 15 to <18 years) will be female. Secondary safety endpoints should include the effect of dapagliflozin on mineral and bone metabolism, and the effect of dapagliflozin on growth.

Final Protocol Submission:	August 2015
Study Completion:	February 2020
Final Report Submission:	August 2020

Submit the protocol(s) to your IND 068652, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess signals of serious risks of bladder cancers, serious hepatic abnormalities and adverse pregnancy outcomes in patients treated with Farxiga (dapagliflozin).

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

2121-3 Conduct a study to evaluate dapagliflozin in an orthotopic rodent bladder tumor promotion model.

The timetable you submitted on December 20, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	November 2014
Study Completion:	November 2015
Final Report Submission:	August 2016

2121-4 An assessment and analysis of all foreign and domestic spontaneous reports of serious hepatic abnormalities and pregnancy outcomes in patients treated with dapagliflozin. The enhanced pharmacovigilance study should continue for 5 years.

The timetable you submitted on December 20, 2013, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	September 2014
Interim Report Submissions:	March 2015
	March 2016
	March 2017
	March 2018
	March 2019
Study Completion:	September 2019
Final Report Submission:	March 2020

Finally, we have determined that only a clinical trial (rather than an observational study) will be sufficient to assess a signal of a serious risk of bladder cancer in patients treated with Farxiga (dapagliflozin). Furthermore, there have been signals of a serious risk of cardiovascular events with some medications developed for the treatment of type 2 diabetes mellitus and available data have not definitively excluded the potential for this serious risk with Farxiga (dapagliflozin). As such, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess a signal of a serious risk of major adverse cardiovascular events with antidiabetic medications, including Farxiga (dapagliflozin).

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

2121-5 A randomized, double-blind, placebo-controlled trial (the DECLARE trial) evaluating the effect of dapagliflozin on the incidence of major adverse cardiovascular events (MACE) in patients with type 2 diabetes mellitus. The primary objective of the trial should be to demonstrate that the upper bound of the 2-sided 95% confidence interval for the estimated risk ratio comparing the incidence of MACE (non-fatal myocardial infarction, non-fatal stroke, cardiovascular death) observed with dapagliflozin to that observed in the placebo group is less than 1.3. The long-term effects of dapagliflozin on the incidence of liver toxicity, bone fractures, nephrotoxicity/acute kidney injury, breast and bladder cancer, complicated genital infections, complicated urinary tract infections/pyelonoephritis/urosepsis, serious events related to hypovolemia and serious hypersensitivity reactions should also be assessed. The estimated glomerular filtration rate (eGFR) should also be monitored over time to assess for worsening of renal function.

The timetable you submitted on December 20, 2013, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	submitted May 9, 2013
Trial Completion:	June 2019
Final Report Submission:	June 2020

2121-6 To assess the risk of bladder cancer associated with dapagliflozin, conduct adequate follow-up beyond completion of the cardiovascular outcomes trial (DECLARE) to observe a total of 66 events of bladder cancer, with 80% power to exclude a relative risk of 2.0 for dapagliflozin versus placebo, assuming a 2-sided alpha of 5%.

The timetable you submitted on December 20, 2013, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	January 2015
Trial Completion:	June 2024
Final Report Submission:	December 2024

Submit the protocol(s) to your IND 068652, with a cross-reference letter to this NDA. Submit all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)," "Required Postmarketing Final Report Under 505(o)," "Required Postmarketing Correspondence Under 505(o)."**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

EXPIRY DATING PERIOD

A 24-month expiry dating period is granted for Farxiga (dapagliflozin) tablets when stored at 25°C (77°F) with excursions permitted from 15° to 30°C (59° to 86 °F).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new

biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Abolade (Bola) Adeolu, Regulatory Project Manager, at (301) 796-4264.

Sincerely,

{See appended electronic signature page}

Curtis J. Rosebraugh, MD, MPH
Director
Office of Drug Evaluation II
Office of New Drugs
Center for Drug Evaluation and Research

Enclosures:
Package Insert
Medication Guide
Carton and Container Labeling

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FARXIGA safely and effectively. See full prescribing information for FARXIGA.

FARXIGA (dapagliflozin) tablets, for oral use
Initial U.S. Approval: 2014

----------INDICATIONS AND USAGE----------

FARXIGA is a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. (1)

Limitation of use:

- Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis. (1.1)

----------DOSAGE AND ADMINISTRATION----------

- The recommended starting dose is 5 mg once daily, taken in the morning, with or without food. (2.1)
- Dose can be increased to 10 mg once daily in patients tolerating FARXIGA who require additional glycemic control. (2.1)
- Assess renal function before initiating FARXIGA. Do not initiate FARXIGA if eGFR is below 60 mL/min/1.73 m^2. (2.2)
- Discontinue FARXIGA if eGFR falls persistently below 60 mL/min/1.73 m^2. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

- Tablets: 5 mg and 10 mg (3)

----------CONTRAINDICATIONS----------

- History of serious hypersensitivity reaction to FARXIGA. (4)
- Severe renal impairment, end-stage renal disease, or dialysis. (4)

----------WARNINGS AND PRECAUTIONS----------

- *Hypotension:* Before initiating FARXIGA, assess volume status and correct hypovolemia in the elderly, in patients with renal impairment or low systolic blood pressure, and in patients on diuretics. Monitor for signs and symptoms during therapy. (5.1, 6.1)
- *Impairment in renal function:* Monitor renal function during therapy. (5.2)
- *Hypoglycemia:* In patients taking insulin or an insulin secretagogue with FARXIGA, consider a lower dose of insulin or the insulin secretagogue to reduce the risk of hypoglycemia. (5.3)
- *Genital mycotic infections:* Monitor and treat if indicated. (5.4)
- *Increased LDL-C:* Monitor and treat per standard of care. (5.5)
- *Bladder Cancer:* An imbalance in bladder cancers was observed in clinical trials. FARXIGA should not be used in patients with active bladder cancer and should be used with caution in patients with a prior history of bladder cancer. (5.6)
- *Macrovascular outcomes:* There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with FARXIGA or any other antidiabetic drug. (5.7)

----------ADVERSE REACTIONS----------

- The most common adverse reactions associated with FARXIGA (5% or greater incidence) were female genital mycotic infections, nasopharyngitis, and urinary tract infections. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bristol-Myers Squibb at 1-800-721-5072 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

----------USE IN SPECIFIC POPULATIONS----------

- *Pregnancy:* There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. (8.1)
- *Nursing Mothers:* Discontinue FARXIGA or discontinue nursing. (8.3)
- *Geriatrics:* Higher incidence of adverse reactions related to reduced intravascular volume. (5.1, 8.5)
- *Renal Impairment:* Higher incidence of adverse reactions related to reduced intravascular volume and renal function. (5.2, 6.1, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 1/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

[illegible]

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FARXIGA (dapagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus [see *Clinical Studies (14)*].

1.1 Limitation of Use

FARXIGA is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

The recommended starting dose of FARXIGA is 5 mg once daily, taken in the morning, with or without food. In patients tolerating FARXIGA 5 mg once daily who require additional glycemic control, the dose can be increased to 10 mg once daily.

In patients with volume depletion, correcting this condition prior to initiation of FARXIGA is recommended [see *Warnings and Precautions (5.1)*, *Use in Specific Populations (8.5, 8.6)*, and *Patient Counseling Information (17)*].

2.2 Patients with Renal Impairment

Assessment of renal function is recommended prior to initiation of FARXIGA therapy and periodically thereafter.

FARXIGA should not be initiated in patients with an eGFR less than 60 mL/min/1.73 m^2.

No dose adjustment is needed in patients with mild renal impairment (eGFR of 60 mL/min/1.73 m^2 or greater).

FARXIGA should be discontinued when eGFR is persistently less than 60 mL/min/1.73 m^2 [see *Warnings and Precautions (5.2)* and *Use in Specific Populations (8.6)*].

3 DOSAGE FORMS AND STRENGTHS

- FARXIGA 5 mg tablets are yellow, biconvex, round, film-coated tablets with "5" engraved on one side and "1427" engraved on the other side.
- FARXIGA 10 mg tablets are yellow, biconvex, diamond-shaped, film-coated tablets with "10" engraved on one side and "1428" engraved on the other side.

4 CONTRAINDICATIONS

- History of a serious hypersensitivity reaction to FARXIGA [see *Adverse Reactions (6.1)*].
- Severe renal impairment, end-stage renal disease (ESRD), or patients on dialysis [see *Use in Specific Populations (8.6)*].

5 WARNINGS AND PRECAUTIONS

5.1 Hypotension

FARXIGA causes intravascular volume contraction. Symptomatic hypotension can occur after initiating FARXIGA [see *Adverse Reactions (6.1)*] particularly in patients with impaired renal function (eGFR less than 60 mL/min/1.73 m^2), elderly patients, or patients on loop diuretics. Before initiating FARXIGA in patients with one or more of these characteristics, volume status should be assessed and corrected. Monitor for signs and symptoms of hypotension after initiating therapy.

5.2 Impairment in Renal Function

FARXIGA increases serum creatinine and decreases eGFR. Elderly patients and patients with impaired renal function may be more susceptible to these changes. Adverse reactions related to renal function can occur after initiating FARXIGA [see *Adverse Reactions (6.1)*]. Renal function should be evaluated prior to initiation of FARXIGA and monitored periodically thereafter.

5.3 Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues

Insulin and insulin secretagogues are known to cause hypoglycemia. FARXIGA can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue [see *Adverse Reactions (6.1)*]. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when these agents are used in combination with FARXIGA.

5.4 Genital Mycotic Infections

FARXIGA increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections were more likely to develop genital mycotic infections [see *Adverse Reactions (6.1)*]. Monitor and treat appropriately.

5.5 Increases in Low-Density Lipoprotein Cholesterol (LDL-C)

Increases in LDL-C occur with FARXIGA [see *Adverse Reactions (6.1)*]. Monitor LDL-C and treat per standard of care after initiating FARXIGA.

5.6 Bladder Cancer

Across 22 clinical studies, newly diagnosed cases of bladder cancer were reported in 10/6045 patients (0.17%) treated with FARXIGA and 1/3512 patient (0.03%) treated with placebo/comparator. After excluding patients in whom exposure to study drug was less than one year at the time of diagnosis of bladder cancer, there were 4 cases with FARXIGA and no cases with placebo/comparator. Bladder cancer risk factors and hematuria (a potential indicator of pre-existing tumors) were balanced between treatment arms at baseline. There were too few cases to determine whether the emergence of these events is related to FARXIGA.

There are insufficient data to determine whether FARXIGA has an effect on pre-existing bladder tumors. Consequently, FARXIGA should not be used in patients with active bladder cancer. In patients with prior history of bladder cancer, the benefits of glycemic control versus unknown risks for cancer recurrence with FARXIGA should be considered.

5.7 Macrovascular Outcomes

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with FARXIGA or any other antidiabetic drug.

6 ADVERSE REACTIONS

The following important adverse reactions are described below and elsewhere in the labeling:

- Hypotension [see *Warnings and Precautions (5.1)*]
- Impairment in Renal Function [see *Warnings and Precautions (5.2)*]
- Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues [see *Warnings and Precautions (5.3)*]

- Genital Mycotic Infections [see *Warnings and Precautions (5.4)*]
- Increases in Low-Density Lipoprotein Cholesterol (LDL-C) [see *Warnings and Precautions (5.5)*]
- Bladder Cancer [see *Warnings and Precautions (5.6)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Pool of 12 Placebo-Controlled Studies for FARXIGA 5 and 10 mg

The data in Table 1 is derived from 12 placebo-controlled studies ranging from 12 to 24 weeks. In 4 studies FARXIGA was used as monotherapy, and in 8 studies FARXIGA was used as add-on to background antidiabetic therapy or as combination therapy with metformin [see *Clinical Studies (14)*].

These data reflect exposure of 2338 patients to FARXIGA with a mean exposure duration of 21 weeks. Patients received placebo (N=1393), FARXIGA 5 mg (N=1145), or FARXIGA 10 mg (N=1193) once daily. The mean age of the population was 55 years and 2% were older than 75 years of age. Fifty percent (50%) of the population were male; 81% were White, 14% were Asian, and 3% were Black or African American. At baseline, the population had diabetes for an average of 6 years, had a mean hemoglobin A1c (HbA1c) of 8.3%, and 21% had established microvascular complications of diabetes. Baseline renal function was normal or mildly impaired in 92% of patients and moderately impaired in 8% of patients (mean eGFR 86 mL/min/1.73 m^2).

Table 1 shows common adverse reactions associated with the use of FARXIGA. These adverse reactions were not present at baseline, occurred more commonly on FARXIGA than on placebo, and occurred in at least 2% of patients treated with either FARXIGA 5 mg or FARXIGA 10 mg.

Table 1: Adverse Reactions in Placebo-Controlled Studies Reported in ≥2% of Patients Treated with FARXIGA

Adverse Reaction	% of Patients		
	Pool of 12 Placebo-Controlled Studies		
	Placebo N=1393	FARXIGA 5 mg N=1145	FARXIGA 10 mg N=1193
Female genital mycotic infections*	1.5	8.4	6.9
Nasopharyngitis	6.2	6.6	6.3
Urinary tract infections†	3.7	5.7	4.3
Back pain	3.2	3.1	4.2
Increased urination‡	1.7	2.9	3.8
Male genital mycotic infections§	0.3	2.8	2.7
Nausea	2.4	2.8	2.5
Influenza	2.3	2.7	2.3
Dyslipidemia	1.5	2.1	2.5
Constipation	1.5	2.2	1.9
Discomfort with urination	0.7	1.6	2.1
Pain in extremity	1.4	2.0	1.7

* Genital mycotic infections include the following adverse reactions, listed in order of frequency reported for females: vulvovaginal mycotic infection, vaginal infection, vulvovaginal candidiasis, vulvovaginitis, genital infection, genital candidiasis, fungal genital infection, vulvitis, genitourinary tract infection, vulval abscess, and vaginitis bacterial. (N for females: Placebo=677, FARXIGA 5 mg=581, FARXIGA 10 mg=598).

† Urinary tract infections include the following adverse reactions, listed in order of frequency reported: urinary tract infection, cystitis, *Escherichia* urinary tract infection, genitourinary tract infection, pyelonephritis, trigonitis, urethritis, kidney infection, and prostatitis.

‡ Increased urination includes the following adverse reactions, listed in order of frequency reported: pollakiuria, polyuria, and urine output increased.

§ Genital mycotic infections include the following adverse reactions, listed in order of frequency reported for males: balanitis, fungal genital infection, balanitis candida, genital candidiasis, genital infection male, penile infection, balanoposthitis, balanoposthitis infective, genital infection, posthitis. (N for males: Placebo=716, FARXIGA 5 mg=564, FARXIGA 10 mg=595).

Pool of 13 Placebo-Controlled Studies for FARXIGA 10 mg

The safety and tolerability of FARXIGA 10 mg was also evaluated in a larger placebo-controlled study pool. This pool combined 13 placebo-controlled studies, including 3 monotherapy studies, 9 add-on to background antidiabetic therapy studies, and an initial combination with metformin study. Across these 13 studies, 2360 patients were treated once daily with FARXIGA 10 mg for a mean duration of exposure of 22 weeks. The mean age of the population was 59 years and 4% were older than 75 years. Fifty-eight percent (58%) of the population were male; 84% were White, 9% were Asian, and 3% were Black or African American. At baseline, the population had diabetes for an average of 9 years, had a mean HbA1c of 8.2%, and 30% had established

microvascular disease. Baseline renal function was normal or mildly impaired in 88% of patients and moderately impaired in 11% of patients (mean eGFR 82 mL/min/1.73 m^2).

Volume Depletion

FARXIGA causes an osmotic diuresis, which may lead to reductions in intravascular volume. Adverse reactions related to volume depletion (including reports of dehydration, hypovolemia, orthostatic hypotension, or hypotension) are shown in Table 2 for the 12-study and 13-study, short-term, placebo-controlled pools [see *Warnings and Precautions (5.1)*].

Table 2: Adverse Reactions of Volume Depletion* in Clinical Studies with FARXIGA

	Pool of 12 Placebo-Controlled Studies			Pool of 13 Placebo-Controlled Studies	
	Placebo	**FARXIGA 5 mg**	**FARXIGA 10 mg**	**Placebo**	**FARXIGA 10 mg**
Overall population N (%)	N=1393 5 (0.4%)	N=1145 7 (0.6%)	N=1193 9 (0.8%)	N=2295 17 (0.7%)	N=2360 27 (1.1%)
Patient Subgroup n (%)					
Patients on loop diuretics	n=55 1 (1.8%)	n=40 0	n=31 3 (9.7%)	n=267 4 (1.5%)	n=236 6 (2.5%)
Patients with moderate renal impairment with eGFR ≥30 and <60 mL/min/1.73 m^2	n=107 2 (1.9%)	n=107 1 (0.9%)	n=89 1 (1.1%)	n=268 4 (1.5%)	n=265 5 (1.9%)
Patients ≥65 years of age	n=276 1 (0.4%)	n=216 1 (0.5%)	n=204 3 (1.5%)	n=711 6 (0.8%)	n=665 11 (1.7%)

* Volume depletion includes reports of dehydration, hypovolemia, orthostatic hypotension, or hypotension.

Impairment of Renal Function

Use of FARXIGA was associated with increases in serum creatinine and decreases in eGFR (see Table 3). In patients with normal or mildly impaired renal function at baseline, serum creatinine and eGFR returned to baseline values at Week 24. Renal-related adverse reactions, including renal failure and blood creatinine increase, were more frequent in patients treated with FARXIGA (see Table 4). Elderly patients and patients with impaired renal function were more susceptible to these adverse reactions (see Table 4). Sustained decreases in eGFR were seen in patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m^2).

Table 3: Changes in Serum Creatinine and eGFR Associated with FARXIGA in the Pool of 12 Placebo-Controlled Studies and Moderate Renal Impairment Study

		Pool of 12 Placebo-Controlled Studies		
		Placebo N=1393	**FARXIGA 5 mg N=1145**	**FARXIGA 10 mg N=1193**
Baseline Mean	Serum Creatinine (mg/dL)	0.853	0.860	0.847
	eGFR (mL/min/1.73 m^2)	86.0	85.3	86.7
Week 1 Change	Serum Creatinine (mg/dL)	−0.003	0.029	0.041
	eGFR (mL/min/1.73 m^2)	0.4	−2.9	−4.1
Week 24 Change	Serum Creatinine (mg/dL)	−0.005	−0.001	0.001
	eGFR (mL/min/1.73 m^2)	0.8	0.8	0.3
		Moderate Renal Impairment Study		
		Placebo N=84	**FARXIGA 5 mg N=83**	**FARXIGA 10 mg N=85**
Baseline Mean	Serum Creatinine (mg/dL)	1.46	1.53	1.52
	eGFR (mL/min/1.73 m^2)	45.6	44.2	43.9
Week 1 Change	Serum Creatinine (mg/dL)	0.01	0.13	0.18
	eGFR (mL/min/1.73 m^2)	0.5	−3.8	−5.5
Week 24 Change	Serum Creatinine (mg/dL)	0.02	0.08	0.16
	eGFR (mL/min/1.73 m^2)	0.03	−4.0	−7.4
Week 52 Change	Serum Creatinine (mg/dL)	0.10	0.06	0.15
	eGFR (mL/min/1.73 m^2)	−2.6	−4.2	−7.3

Table 4: Proportion of Patients with at Least One Renal Impairment-Related Adverse Reaction

	Pool of 6 Placebo-Controlled Studies (up to 104 weeks)*			Pool of 9 Placebo-Controlled Studies (up to 104 weeks)†	
Baseline Characteristic	**Placebo**	**FARXIGA 5 mg**	**FARXIGA 10 mg**	**Placebo**	**FARXIGA 10 mg**
Overall population Patients (%) with at least one event	n=785 13 (1.7%)	n=767 14 (1.8%)	n=859 16 (1.9%)	n=1956 82 (4.2%)	n=2026 136 (6.7%)
65 years of age and older Patients (%) with at least one event	n=190 4 (2.1%)	n=162 5 (3.1%)	n=159 6 (3.8%)	n=655 52 (7.9%)	n=620 87 (14.0%)
eGFR ≥30 and <60 mL/min/1.73 m^2 Patients (%) with at least one event	n=77 5 (6.5%)	n=88 7 (8.0%)	n=75 9 (12.0%)	n=249 40 (16.1%)	n=251 71 (28.3%)
65 years of age and older and eGFR ≥30 and <60 mL/min/1.73 m^2 Patients (%) with at least one event	n=41 2 (4.9%)	n=43 3 (7.0%)	n=35 4 (11.4%)	n=141 27 (19.1%)	n=134 47 (35.1%)

* Subset of patients from the pool of 12 placebo-controlled studies with long-term extensions.

† Subset of patients from the pool of 13 placebo-controlled studies with long-term extensions.

The safety of FARXIGA was evaluated in a study of patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m^2) [see *Clinical Studies (14)*]. In this study 13 patients experienced bone fractures for treatment durations up to 104 weeks. No fractures occurred in the placebo group, 5 occurred in the FARXIGA 5 mg group, and 8 occurred in the FARXIGA 10 mg group. Eight of these 13 fractures were in patients who had a baseline eGFR of 30 to 45 mL/min/1.73 m^2. Eleven of the 13 fractures were reported within the first 52 weeks. There was no apparent pattern with respect to the anatomic site of fracture.

Hypoglycemia

The frequency of hypoglycemia by study [see *Clinical Studies (14)*] is shown in Table 5. Hypoglycemia was more frequent when FARXIGA was added to sulfonylurea or insulin [see *Warnings and Precautions (5.3)*].

Table 5: Incidence of Major* and Minor† Hypoglycemia in Placebo-Controlled Studies

	Placebo	FARXIGA 5 mg	FARXIGA 10 mg
Monotherapy* (24 weeks)	**N=75**	**N=64**	**N=70**
Major [n (%)]	0	0	0
Minor [n (%)]	0	0	0
Add-on to Metformin* (24 weeks)	**N=137**	**N=137**	**N=135**
Major [n (%)]	0	0	0
Minor [n (%)]	0	2 (1.5)	1 (0.7)
Active Control Add-on to Metformin versus Glipizide (52 weeks)	**N=408**	–	**N=406**
Major [n (%)]	3 (0.7)	–	0
Minor [n (%)]	147 (36.0)	–	7 (1.7)
Add-on to Glimepiride* (24 weeks)	**N=146**	**N=145**	**N=151**
Major [n (%)]	0	0	0
Minor [n (%)]	3 (2.1)	8 (5.5)	9 (6.0)
Add-on to Pioglitazone* (24 weeks)	**N=139**	**N=141**	**N=140**
Major [n (%)]	0	0	0
Minor [n (%)]	0	3 (2.1)	0
Add-on to DPP4 inhibitor (24 weeks)	**N=226**	–	**N=225**
Major [n (%)]	0	–	1 (0.4)
Minor [n (%)]	3 (1.3)	–	4 (1.8)

Table 5: Incidence of Major* and Minor† Hypoglycemia in Placebo-Controlled Studies

	Placebo	FARXIGA 5 mg	FARXIGA 10 mg
Add-on to Insulin with or without other OADs‡ (24 weeks)	**N=197**	**N=212**	**N=196**
Major [n (%)]	1 (0.5)	1 (0.5)	1 (0.5)
Minor [n (%)]	67 (34.0)	92 (43.4)	79 (40.3)

* Major episodes of hypoglycemia were defined as symptomatic episodes requiring external (third party) assistance due to severe impairment in consciousness or behavior with a capillary or plasma glucose value <54 mg/dL and prompt recovery after glucose or glucagon administration.

† Minor episodes of hypoglycemia were defined as either a symptomatic episode with a capillary or plasma glucose measurement <63 mg/dL regardless of need for external assistance, or an asymptomatic capillary or plasma glucose measurement <63 mg/dL that does not qualify as a major episode.

‡ OAD = oral antidiabetic therapy

Genital Mycotic Infections

Genital mycotic infections were more frequent with FARXIGA treatment. Genital mycotic infections were reported in 0.9% of patients on placebo, 5.7% on FARXIGA 5 mg, and 4.8% on FARXIGA 10 mg, in the 12-study placebo-controlled pool. Discontinuation from study due to genital infection occurred in 0% of placebo-treated patients and 0.2% of patients treated with FARXIGA 10 mg. Infections were more frequently reported in females than in males (see Table 1). The most frequently reported genital mycotic infections were vulvovaginal mycotic infections in females and balanitis in males. Patients with a history of genital mycotic infections were more likely to have a genital mycotic infection during the study than those with no prior history (10.0%, 23.1%, and 25.0% versus 0.8%, 5.9%, and 5.0% on placebo, FARXIGA 5 mg, and FARXIGA 10 mg, respectively).

Hypersensitivity Reactions

Hypersensitivity reactions (e.g., angioedema, urticaria, hypersensitivity) were reported with FARXIGA treatment. Across the clinical program, serious anaphylactic reactions and severe cutaneous adverse reactions and angioedema were reported in 0.2% of comparator-treated patients and 0.3% of FARXIGA-treated patients. If hypersensitivity reactions occur, discontinue use of FARXIGA; treat per standard of care and monitor until signs and symptoms resolve.

Laboratory Tests

Increase in Hematocrit

In the pool of 13 placebo-controlled studies, increases from baseline in mean hematocrit values were observed in FARXIGA-treated patients starting at Week 1 and continuing up to Week 16, when the maximum mean difference from baseline was observed. At Week 24, the mean changes from baseline in hematocrit were −0.33% in the placebo group and 2.30% in the FARXIGA 10 mg group. By Week 24, hematocrit values >55% were reported in 0.4% of placebo-treated patients and 1.3% of FARXIGA 10 mg–treated patients.

Increase in Serum Inorganic Phosphorus

In the pool of 13 placebo-controlled studies, increases from baseline in mean serum phosphorus levels were reported at Week 24 in FARXIGA-treated patients compared with placebo-treated patients (mean increase of 0.13 versus −0.04 mg/dL, respectively). Higher proportions of patients with marked laboratory abnormalities of hyperphosphatemia (≥5.6 mg/dL for age 17-65 years or ≥5.1 mg/dL for age ≥66 years) were reported on FARXIGA at Week 24 (0.9% versus 1.7% for placebo and FARXIGA 10 mg, respectively).

Increase in Low-Density Lipoprotein Cholesterol

In the pool of 13 placebo-controlled studies, changes from baseline in mean lipid values were reported in FARXIGA-treated patients compared to placebo-treated patients. Mean percent changes from baseline at Week 24, were 0.0% versus 2.5% for total cholesterol and −1.0% versus 2.9% for LDL cholesterol, in the placebo and FARXIGA 10 mg groups, respectively.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies of FARXIGA in pregnant women. Based on results of reproductive and developmental toxicity studies in animals, dapagliflozin may affect renal development and maturation. In a juvenile rat study, increased incidence and/or severity of renal pelvic and tubular dilatations were evident at the lowest tested dose which was approximately 15 times clinical exposure from a 10 mg dose.

These outcomes occurred with drug exposures during periods of animal development that correlate with the late second and third trimesters of human pregnancy. During pregnancy, consider appropriate alternative therapies, especially during the second and third trimesters. FARXIGA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In a juvenile toxicity study, when dapagliflozin was dosed directly to young rats from postnatal day (PND) 21 until PND 90 at doses of 1, 15, or 75 mg/kg/day, increased kidney weights and renal pelvic and tubular dilatations were reported at all levels. Exposure at the lowest tested dose was 15 times the maximum clinical dose, based on AUC. The renal pelvic and tubular dilatations observed in juvenile animals did not fully reverse within the approximate 1-month recovery period.

In a prenatal and postnatal development study, maternal rats were dosed from gestation day 6 through lactation day 21 at doses of 1, 15, or 75 mg/kg/day, and pups were indirectly exposed *in utero* and throughout lactation. Increased incidence or severity of renal pelvic dilatation was observed in adult offspring of treated dams at 75 mg/kg/day (maternal and pup dapagliflozin exposures were 1415 times and 137 times, respectively, the human values at the clinical dose). Dose-related reductions in pup body weights were observed at doses ≥1 mg/kg/day (approximately ≥19 times the clinical dose). No adverse effects on developmental endpoints were noted at 1 mg/kg/day, or approximately 19 times the clinical dose.

In embryo-fetal development studies in rats and rabbits, dapagliflozin was administered for intervals coinciding with the first trimester period of organogenesis in humans. No developmental toxicities were observed in rabbits at any dose tested. In rats, dapagliflozin was neither embryolethal nor teratogenic at doses up to 75 mg/kg/day or 1441 times the maximum clinical dose of 10 mg. At higher doses in rats, malformations of blood vessels, ribs, vertebra, manubria, and skeletal variations in fetuses at ≥150 mg/kg or 2344 times the 10 mg clinical dose were observed.

8.3 Nursing Mothers

It is not known whether FARXIGA is excreted in human milk. Dapagliflozin is excreted in rat milk reaching levels 0.49 times that found in maternal plasma. Data in juvenile rats directly exposed to dapagliflozin showed risk to the developing kidney (renal pelvic and tubular dilatations) during maturation. Since human kidney maturation occurs *in utero* and during the first 2 years of life when lactational exposure may occur, there may be risk to the developing

human kidney. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from FARXIGA, a decision should be made whether to discontinue nursing or to discontinue FARXIGA, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness of FARXIGA in pediatric patients under 18 years of age have not been established.

8.5 Geriatric Use

No FARXIGA dosage change is recommended based on age. A total of 1424 (24%) of the 5936 FARXIGA-treated patients were 65 years and older and 207 (3.5%) patients were 75 years and older in a pool of 21 double-blind, controlled, clinical safety and efficacy studies of FARXIGA. After controlling for level of renal function (eGFR), efficacy was similar for patients under age 65 years and those 65 years and older. In patients ≥65 years of age, a higher proportion of patients treated with FARXIGA had adverse reactions related to volume depletion and renal impairment or failure compared to patients treated with placebo [see *Warnings and Precautions (5.1)* and *Adverse Reactions (6.1)*].

8.6 Renal Impairment

The safety and efficacy of FARXIGA were evaluated in a study that included patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m^2). Compared to placebo-treated patients, patients with moderate renal impairment treated with FARXIGA did not have improvement in glycemic control [see *Clinical Studies (14.7)*] and had more renal-related adverse reactions and more bone fractures [see *Dosage and Administration (2.2)*, *Warnings and Precautions (5.2)*, and *Adverse Reactions (6.1)*]; therefore, FARXIGA should not be initiated in this population.

Based on its mechanism of action, FARXIGA is not expected to be effective in patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2) or ESRD [see *Contraindications (4)*].

8.7 Hepatic Impairment

No dose adjustment is recommended for patients with mild, moderate, or severe hepatic impairment. However, the benefit-risk for the use of dapagliflozin in patients with severe hepatic impairment should be individually assessed since the safety and efficacy of dapagliflozin have not been specifically studied in this population [see *Clinical Pharmacology (12.3)*].

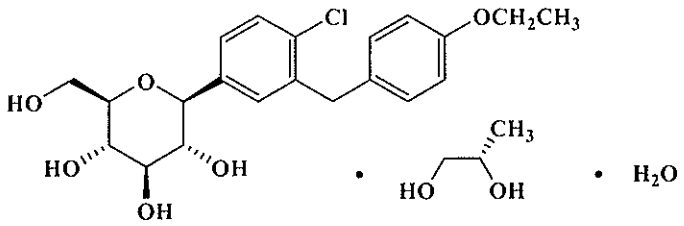
10 OVERDOSAGE

There were no reports of overdose during the clinical development program for FARXIGA.

In the event of an overdose, contact the Poison Control Center. It is also reasonable to employ supportive measures, as dictated by the patient's clinical status. The removal of dapagliflozin by hemodialysis has not been studied.

11 DESCRIPTION

Dapagliflozin is described chemically as D-glucitol, 1,5-anhydro-1-*C*-[4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl]-, (1*S*)-, compounded with (2*S*)-1,2-propanediol, hydrate (1:1:1). The empirical formula is $C_{21}H_{25}ClO_6 \bullet C_3H_8O_2 \bullet H_2O$ and the molecular weight is 502.98. The structural formula is:



FARXIGA is available as a film-coated tablet for oral administration containing the equivalent of 5 mg dapagliflozin as dapagliflozin propanediol or the equivalent of 10 mg dapagliflozin as dapagliflozin propanediol, and the following inactive ingredients: microcrystalline cellulose, anhydrous lactose, crospovidone, silicon dioxide, and magnesium stearate. In addition, the film coating contains the following inactive ingredients: polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc, and yellow iron oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

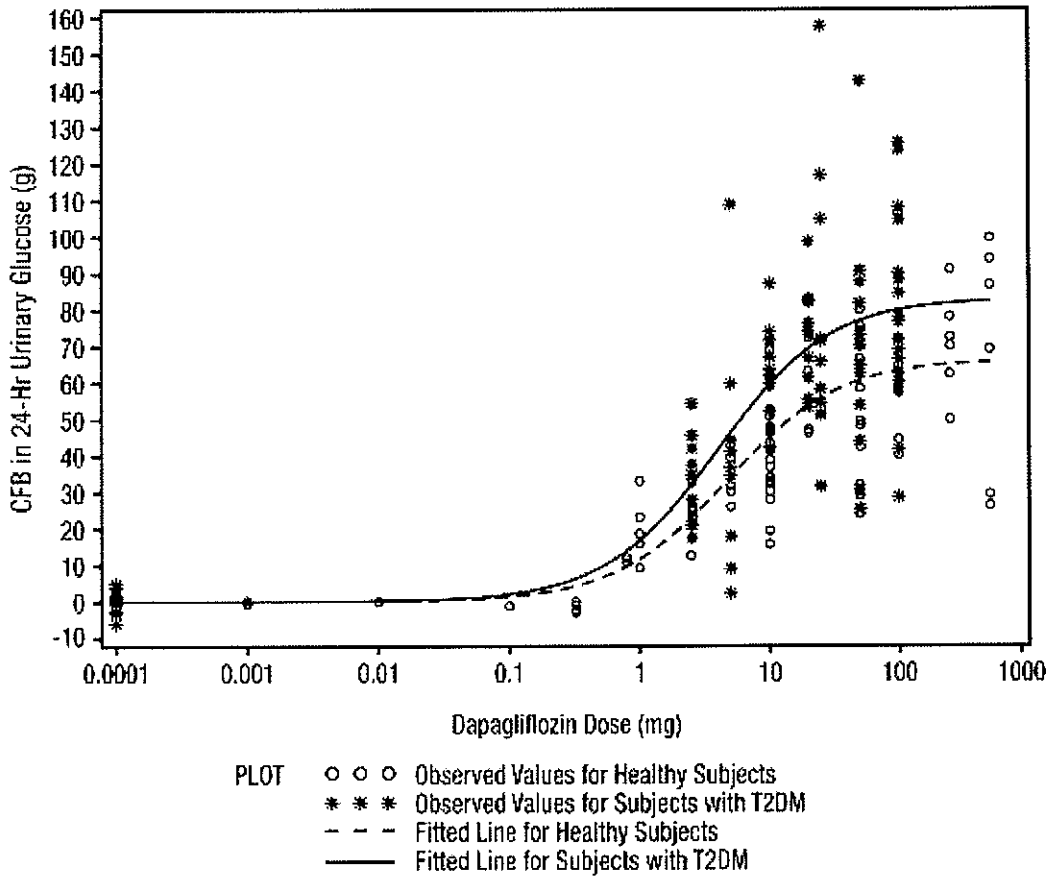
Sodium-glucose cotransporter 2 (SGLT2), expressed in the proximal renal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. Dapagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, dapagliflozin reduces reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.

12.2 Pharmacodynamics

General

Increases in the amount of glucose excreted in the urine were observed in healthy subjects and in patients with type 2 diabetes mellitus following the administration of dapagliflozin (see Figure 1). Dapagliflozin dose of 10 mg per day in patients with type 2 diabetes mellitus for 12 weeks resulted in excretion of approximately 70 grams of glucose in the urine per day at Week 12. A near maximum glucose excretion was observed at the dapagliflozin daily dose of 20 mg. This urinary glucose excretion with dapagliflozin also results in increases in urinary volume [see *Adverse Reactions (6.1)*].

Figure 1: **Scatter Plot and Fitted Line of Change from Baseline in 24-Hour Urinary Glucose Amount versus Dapagliflozin Dose in Healthy Subjects and Subjects with Type 2 Diabetes Mellitus (T2DM) (Semi-Log Plot)**



Cardiac Electrophysiology

Dapagliflozin was not associated with clinically meaningful prolongation of QTc interval at daily doses up to 150 mg (15 times the recommended maximum dose) in a study of healthy subjects. In addition, no clinically meaningful effect on QTc interval was observed following single doses of up to 500 mg (50 times the recommended maximum dose) of dapagliflozin in healthy subjects.

12.3 Pharmacokinetics

Absorption

Following oral administration of dapagliflozin, the maximum plasma concentration (C_{max}) is usually attained within 2 hours under fasting state. The C_{max} and AUC values increase dose proportionally with increase in dapagliflozin dose in the therapeutic dose range. The absolute oral bioavailability of dapagliflozin following the administration of a 10 mg dose is 78%. Administration of dapagliflozin with a high-fat meal decreases its C_{max} by up to 50% and prolongs T_{max} by approximately 1 hour, but does not alter AUC as compared with the fasted state. These changes are not considered to be clinically meaningful and dapagliflozin can be administered with or without food.

Distribution

Dapagliflozin is approximately 91% protein bound. Protein binding is not altered in patients with renal or hepatic impairment.

Metabolism

The metabolism of dapagliflozin is primarily mediated by UGT1A9; CYP-mediated metabolism is a minor clearance pathway in humans. Dapagliflozin is extensively metabolized, primarily to yield dapagliflozin 3-O-glucuronide, which is an inactive metabolite. Dapagliflozin 3-O-glucuronide accounted for 61% of a 50 mg [14C]-dapagliflozin dose and is the predominant drug-related component in human plasma.

Elimination

Dapagliflozin and related metabolites are primarily eliminated via the renal pathway. Following a single 50 mg dose of [14C]-dapagliflozin, 75% and 21% total radioactivity is excreted in urine and feces, respectively. In urine, less than 2% of the dose is excreted as parent drug. In feces, approximately 15% of the dose is excreted as parent drug. The mean plasma terminal half-life ($t_{½}$) for dapagliflozin is approximately 12.9 hours following a single oral dose of FARXIGA 10 mg.

Specific Populations

Renal Impairment

At steady state (20 mg once-daily dapagliflozin for 7 days), patients with type 2 diabetes with mild, moderate, or severe renal impairment (as determined by eGFR) had geometric mean systemic exposures of dapagliflozin that were 45%, 2.04-fold, and 3.03-fold higher, respectively, as compared to patients with type 2 diabetes with normal renal function. Higher systemic exposure of dapagliflozin in patients with type 2 diabetes mellitus with renal impairment did not result in a correspondingly higher 24-hour urinary glucose excretion. The steady-state 24-hour urinary glucose excretion in patients with type 2 diabetes and mild, moderate, and severe renal impairment was 42%, 80%, and 90% lower, respectively, than patients with type 2 diabetes with normal renal function. The impact of hemodialysis on dapagliflozin exposure is not known. [See *Dosage and Administration (2.2)*, *Warnings and Precautions (5.2)*, *Use in Specific Populations (8.6)*, and *Clinical Studies (14.7)*.]

Hepatic Impairment

In subjects with mild and moderate hepatic impairment (Child-Pugh classes A and B), mean C_{max} and AUC of dapagliflozin were up to 12% and 36% higher, respectively, as compared to healthy matched control subjects following single-dose administration of 10 mg dapagliflozin. These differences were not considered to be clinically meaningful. In patients with severe hepatic impairment (Child-Pugh class C), mean C_{max} and AUC of dapagliflozin were up to 40% and 67% higher, respectively, as compared to healthy matched controls [see *Use in Specific Populations (8.7)*].

Effects of Age, Gender, Race, and Body Weight on Pharmacokinetics

Based on a population pharmacokinetic analysis, age, gender, race, and body weight do not have a clinically meaningful effect on the pharmacokinetics of dapagliflozin and thus, no dose adjustment is recommended.

Pediatric

Pharmacokinetics in the pediatric population has not been studied.

Drug Interactions

In Vitro Assessment of Drug Interactions

In *in vitro* studies, dapagliflozin and dapagliflozin 3-O-glucuronide neither inhibited CYP 1A2, 2C9, 2C19, 2D6, or 3A4, nor induced CYP 1A2, 2B6, or 3A4. Dapagliflozin is a weak substrate of the P-glycoprotein (P-gp) active transporter, and dapagliflozin 3-O-glucuronide is a substrate for the OAT3 active transporter. Dapagliflozin or dapagliflozin 3-O-glucuronide did not meaningfully inhibit P-gp, OCT2, OAT1, or OAT3 active transporters. Overall, dapagliflozin is unlikely to affect the pharmacokinetics of concurrently administered medications that are P-gp, OCT2, OAT1, or OAT3 substrates.

Effects of Other Drugs on Dapagliflozin

Table 6 shows the effect of coadministered drugs on the pharmacokinetics of dapagliflozin. No dose adjustments are recommended for dapagliflozin.

Table 6: Effects of Coadministered Drugs on Dapagliflozin Systemic Exposure

Coadministered Drug (Dose Regimen)*	Dapagliflozin (Dose Regimen)*	Effect on Dapagliflozin Exposure (% Change [90%CI])	
		C_{max}	AUC[†]
No dosing adjustments required for the following:			
Oral Antidiabetic Agents			
Metformin (1000 mg)	20 mg	↔	↔
Pioglitazone (45 mg)	50 mg	↔	↔
Sitagliptin (100 mg)	20 mg	↔	↔
Glimepiride (4 mg)	20 mg	↔	↔
Voglibose (0.2 mg three times daily)	10 mg	↔	↔
Other Medications			
Hydrochlorothiazide (25 mg)	50 mg	↔	↔
Bumetanide (1 mg)	10 mg once daily for 7 days	↔	↔
Valsartan (320 mg)	20 mg	↓12% [↓3%, ↓20%]	↔
Simvastatin (40 mg)	20 mg	↔	↔
Anti-infective Agent			
Rifampin (600 mg once daily for 6 days)	10 mg	↓7% [↓22%, ↑11%]	↓22% [↓27%, ↓17%]

Table 6: Effects of Coadministered Drugs on Dapagliflozin Systemic Exposure

Coadministered Drug (Dose Regimen)*	Dapagliflozin (Dose Regimen)*	Effect on Dapagliflozin Exposure (% Change [90%CI])	
		C_{max}	AUC†
Nonsteroidal Anti-inflammatory Agent			
Mefenamic Acid (loading dose of 500 mg followed by 14 doses of 250 mg every 6 hours)	10 mg	↑13% [↑3%, ↑24%]	↑51% [↑44%, ↑58%]

* Single dose unless otherwise noted.

† AUC = AUC(INF) for drugs given as single dose and AUC = AUC(TAU) for drugs given in multiple doses.

↔ = no change (geometric mean ratio of test:reference within 0.80 to 1.25); ↓ or ↑ = parameter was lower or higher, respectively, with coadministration compared to dapagliflozin administered alone (geometric mean ratio of test:reference was lower than 0.80 or higher than 1.25).

Effects of Dapagliflozin on Other Drugs

Table 7 shows the effect of dapagliflozin on other coadministered drugs. Dapagliflozin did not meaningfully affect the pharmacokinetics of the coadministered drugs.

Table 7: Effects of Dapagliflozin on the Systemic Exposures of Coadministered Drugs

Coadministered Drug (Dose Regimen)*	Dapagliflozin (Dose Regimen)*	Effect on Coadministered Drug Exposure (% Change [90% CI])	
		C_{max}	AUC†
No dosing adjustments required for the following:			
Oral Antidiabetic Agents			
Metformin (1000 mg)	20 mg	↔	↔
Pioglitazone (45 mg)	50 mg	↓7% [↓25%, ↑15%]	↔
Sitagliptin (100 mg)	20 mg	↔	↔
Glimepiride (4 mg)	20 mg	↔	↑13% [0%, ↑29%]
Other Medications			
Hydrochlorothiazide (25 mg)	50 mg	↔	↔
Bumetanide (1 mg)	10 mg once daily for 7 days	↑13% [↓2%, ↑31%]	↑13% [↓1%, ↑30%]
Valsartan (320 mg)	20 mg	↓6% [↓24%, ↑16%]	↑5% [↓15%, ↑29%]
Simvastatin (40 mg)	20 mg	↔	↑19%
Digoxin (0.25 mg)	20 mg loading dose then 10 mg once daily for 7 days	↔	↔

Table 7: Effects of Dapagliflozin on the Systemic Exposures of Coadministered Drugs

Coadministered Drug (Dose Regimen)*	Dapagliflozin (Dose Regimen)*	Effect on Coadministered Drug Exposure (% Change [90% CI])	
		C_{max}	AUC†
Warfarin (25 mg)	20 mg loading dose then 10 mg once daily for 7 days	↔	↔

* Single dose unless otherwise noted.

† AUC = AUC(INF) for drugs given as single dose and AUC = AUC(TAU) for drugs given in multiple doses.

↔ = no change (geometric mean ratio of test:reference within 0.80 to 1.25); ↓ or ↑ = parameter was lower or higher, respectively, with coadministration compared to dapagliflozin administered alone (geometric mean ratio of test:reference was lower than 0.80 or higher than 1.25).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Dapagliflozin did not induce tumors in either mice or rats at any of the doses evaluated in 2-year carcinogenicity studies. Oral doses in mice consisted of 5, 15, and 40 mg/kg/day in males and 2, 10, and 20 mg/kg/day in females, and oral doses in rats were 0.5, 2, and 10 mg/kg/day for both males and females. The highest doses evaluated in mice were approximately 72 times (males) and 105 times (females) the clinical dose of 10 mg per day based on AUC exposure. In rats, the highest dose was approximately 131 times (males) and 186 times (females) the clinical dose of 10 mg per day based on AUC exposure.

Dapagliflozin was negative in the Ames mutagenicity assay and was positive in a series of *in vitro* clastogenicity assays in the presence of S9 activation and at concentrations ≥100 μg/mL. Dapagliflozin was negative for clastogenicity in a series of *in vivo* studies evaluating micronuclei or DNA repair in rats at exposure multiples >2100 times the clinical dose.

There was no carcinogenicity or mutagenicity signal in animal studies, suggesting that dapagliflozin does not represent a genotoxic risk to humans.

Dapagliflozin had no effects on mating, fertility, or early embryonic development in treated male or female rats at exposure multiples ≤1708 times and 998 times the maximum recommended human dose in males and females, respectively.

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies of FARXIGA for Type 2 Diabetes

FARXIGA has been studied as monotherapy and in combination with metformin, pioglitazone, glimepiride, sitagliptin (with or without metformin), or insulin (with or without other oral antidiabetic therapy). The efficacy of FARXIGA was compared to a sulfonylurea (glipizide) added on to metformin. FARXIGA has also been studied in patients with type 2 diabetes and moderate renal impairment.

Treatment with FARXIGA as monotherapy and in combination with metformin, glimepiride, pioglitazone, sitagliptin, or insulin produced statistically significant improvements in mean change from baseline at Week 24 in HbA1c compared to control. Reductions in HbA1c were seen across subgroups including gender, age, race, duration of disease, and baseline BMI.

14.2 Monotherapy

A total of 840 treatment-naive patients with inadequately controlled type 2 diabetes participated in 2 placebo-controlled studies to evaluate the safety and efficacy of monotherapy with FARXIGA.

In 1 monotherapy study, a total of 558 treatment-naive patients with inadequately controlled diabetes participated in a 24-week study. Following a 2-week diet and exercise placebo lead-in period, 485 patients with HbA1c $\geq$7% and $\leq$10% were randomized to FARXIGA 5 mg or FARXIGA 10 mg once daily in either the morning (QAM, main cohort) or evening (QPM), or placebo.

At Week 24, treatment with FARXIGA 10 mg QAM provided significant improvements in HbA1c and FPG compared with placebo (see Table 8).

Table 8: Results at Week 24 (LOCF*) in a Placebo-Controlled Study of FARXIGA Monotherapy in Patients with Type 2 Diabetes (Main Cohort AM Doses)

Efficacy Parameter	FARXIGA 10 mg N=70[†]	FARXIGA 5 mg N=64[†]	Placebo N=75[†]
HbA1c (%)			
Baseline (mean)	8.0	7.8	7.8
Change from baseline (adjusted mean[‡])	−0.9	−0.8	−0.2
Difference from placebo (adjusted mean[‡]) (95% CI)	−0.7[§] (−1.0, −0.4)	−0.5 (−0.8, −0.2)	
Percent of patients achieving HbA1c <7% adjusted for baseline	50.8%[¶]	44.2%[¶]	31.6%
FPG (mg/dL)			
Baseline (mean)	166.6	157.2	159.9
Change from baseline (adjusted mean[‡])	−28.8	−24.1	−4.1
Difference from placebo (adjusted mean[‡]) (95% CI)	−24.7[§] (−35.7, −13.6)	−19.9 (−31.3, −8.5)	

* LOCF: last observation (prior to rescue for rescued patients) carried forward.

† All randomized patients who took at least one dose of double-blind study medication during the short-term double-blind period.

‡ Least squares mean adjusted for baseline value.

§ p-value <0.0001 versus placebo. Sensitivity analyses yielded smaller estimates of treatment difference with placebo.

¶ Not evaluated for statistical significance as a result of the sequential testing procedure for the secondary endpoints.

14.3 Initial Combination Therapy with Metformin

A total of 1241 treatment-naive patients with inadequately controlled type 2 diabetes (HbA1c ≥7.5% and ≤12%) participated in 2 active-controlled studies of 24-week duration to evaluate the safety and efficacy of initial therapy with FARXIGA 5 mg or 10 mg in combination with metformin extended-release (XR) formulation.

In 1 study, 638 patients were randomized to 1 of 3 treatment arms following a 1-week lead-in period: FARXIGA 10 mg plus metformin XR (up to 2000 mg per day), FARXIGA 10 mg plus placebo, or metformin XR (up to 2000 mg per day) plus placebo. Metformin XR dose was up-titrated weekly in 500 mg increments, as tolerated, with a median dose achieved of 2000 mg.

The combination treatment of FARXIGA 10 mg plus metformin XR provided statistically significant improvements in HbA1c and FPG compared with either of the monotherapy treatments and statistically significant reduction in body weight compared with metformin XR alone (see Table 9 and Figure 2). FARXIGA 10 mg as monotherapy also provided statistically

significant improvements in FPG and statistically significant reduction in body weight compared with metformin alone and was noninferior to metformin XR monotherapy in lowering HbA1c.

Table 9: Results at Week 24 (LOCF*) in an Active-Controlled Study of FARXIGA Initial Combination Therapy with Metformin XR

Efficacy Parameter	FARXIGA 10 mg + Metformin XR N=211[†]	FARXIGA 10 mg N=219[†]	Metformin XR N=208[†]
HbA1c (%)			
Baseline (mean)	9.1	9.0	9.0
Change from baseline (adjusted mean[‡])	−2.0	−1.5	−1.4
Difference from FARXIGA (adjusted mean[‡]) (95% CI)	−0.5[§] (−0.7, −0.3)		
Difference from metformin XR (adjusted mean[‡]) (95% CI)	−0.5[§] (−0.8, −0.3)	0.0[¶] (−0.2, 0.2)	
Percent of patients achieving HbA1c <7% adjusted for baseline	46.6%[#]	31.7%	35.2%
FPG (mg/dL)			
Baseline (mean)	189.6	197.5	189.9
Change from baseline (adjusted mean[‡])	−60.4	−46.4	−34.8
Difference from FARXIGA (adjusted mean[‡]) (95% CI)	−13.9[§] (−20.9, −7.0)		
Difference from metformin XR (adjusted mean[‡]) (95% CI)	−25.5[§] (−32.6, −18.5)	−11.6[#] (−18.6, −4.6)	
Body Weight (kg)			
Baseline (mean)	88.6	88.5	87.2
Change from baseline (adjusted mean[‡])	−3.3	−2.7	−1.4
Difference from metformin XR (adjusted mean[‡]) (95% CI)	−2.0[§] (−2.6, −1.3)	−1.4[§] (−2.0, −0.7)	

* LOCF: last observation (prior to rescue for rescued patients) carried forward.

† All randomized patients who took at least one dose of double-blind study medication during the short-term double-blind period.

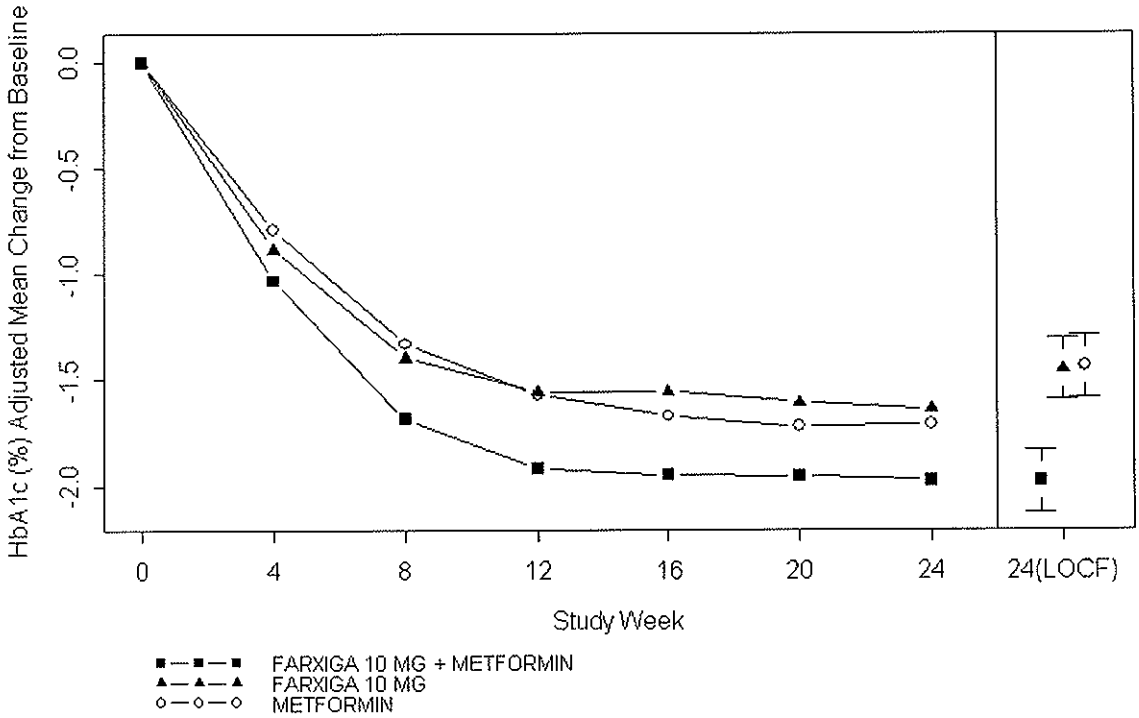
‡ Least squares mean adjusted for baseline value.

§ p-value <0.0001.

¶ Noninferior versus metformin XR.

\# p-value <0.05.

Figure 2: **Adjusted Mean Change from Baseline Over Time in HbA1c (%) in a 24-Week Active-Controlled Study of FARXIGA Initial Combination Therapy with Metformin XR**



Left side graph: Values for adjusted mean change from baseline based on a longitudinal repeated measures model, including randomized subjects who completed the study with both baseline and Week 24 HbA1c values without rescue.
Right side graph for Week 24 (LOCF): Values for adjusted mean change from baseline and 95% CIs based on an ANCOVA model, including randomized subjects with a baseline and at least one post baseline HbA1c before rescue.

In a second study, 603 patients were randomized to 1 of 3 treatment arms following a 1-week lead-in period: FARXIGA 5 mg plus metformin XR (up to 2000 mg per day), FARXIGA 5 mg plus placebo, or metformin XR (up to 2000 mg per day) plus placebo. Metformin XR dose was up-titrated weekly in 500 mg increments, as tolerated, with a median dose achieved of 2000 mg.

The combination treatment of FARXIGA 5 mg plus metformin XR provided statistically significant improvements in HbA1c and FPG compared with either of the monotherapy treatments and statistically significant reduction in body weight compared with metformin XR alone (see Table 10).

Table 10: Results at Week 24 (LOCF*) in an Active-Controlled Study of FARXIGA Initial Combination Therapy with Metformin XR

Efficacy Parameter	FARXIGA 5 mg + Metformin XR N=194[†]	FARXIGA 5 mg N=203[†]	Metformin XR N=201[†]
HbA1c (%)			
Baseline (mean)	9.2	9.1	9.1
Change from baseline (adjusted mean[‡])	−2.1	−1.2	−1.4
Difference from FARXIGA (adjusted mean[‡]) (95% CI)	−0.9[§] (−1.1, −0.6)		
Difference from metformin XR (adjusted mean[‡]) (95% CI)	−0.7[§] (−0.9, −0.5)		
Percent of patients achieving HbA1c <7% adjusted for baseline	52.4%[¶]	22.5%	34.6%
FPG (mg/dL)			
Baseline (mean)	193.4	190.8	196.7
Change from baseline (adjusted mean[‡])	−61.0	−42.0	−33.6
Difference from FARXIGA (adjusted mean[‡]) (95% CI)	−19.1[§] (−26.7, −11.4)		
Difference from metformin XR (adjusted mean[‡]) (95% CI)	−27.5[§] (−35.1, −19.8)		
Body Weight (kg)			
Baseline (mean)	84.2	86.2	85.8
Change from baseline (adjusted mean[‡])	−2.7	−2.6	−1.3
Difference from metformin XR (adjusted mean[‡]) (95% CI)	−1.4[§] (−2.0, −0.7)		

* LOCF: last observation (prior to rescue for rescued patients) carried forward.

† All randomized patients who took at least one dose of double-blind study medication during the short-term double-blind period.

‡ Least squares mean adjusted for baseline value.

§ p-value <0.0001.

¶ p-value <0.05.

14.4 Add-On to Metformin

A total of 546 patients with type 2 diabetes with inadequate glycemic control (HbA1c ≥7% and ≤10%) participated in a 24-week, placebo-controlled study to evaluate FARXIGA in combination with metformin. Patients on metformin at a dose of at least 1500 mg per day were randomized after completing a 2-week, single-blind, placebo lead-in period. Following the lead-in period, eligible patients were randomized to FARXIGA 5 mg, FARXIGA 10 mg, or placebo in addition to their current dose of metformin.

As add-on treatment to metformin, FARXIGA 10 mg provided statistically significant improvements in HbA1c and FPG, and statistically significant reduction in body weight compared with placebo at Week 24 (see Table 11 and Figure 3). Statistically significant ($p<0.05$ for both doses) mean changes from baseline in systolic blood pressure relative to placebo plus metformin were −4.5 mmHg and −5.3 mmHg with FARXIGA 5 mg and 10 mg plus metformin, respectively.

Table 11: Results of a 24-Week (LOCF*) Placebo-Controlled Study of FARXIGA in Add-On Combination with Metformin

Efficacy Parameter	FARXIGA 10 mg + Metformin N=135[†]	FARXIGA 5 mg + Metformin N=137[†]	Placebo + Metformin N=137[†]
HbA1c (%)			
Baseline (mean)	7.9	8.2	8.1
Change from baseline (adjusted mean[‡])	−0.8	−0.7	−0.3
Difference from placebo (adjusted mean[‡]) (95% CI)	−0.5[§] (−0.7, −0.3)	−0.4[§] (−0.6, −0.2)	
Percent of patients achieving HbA1c <7% adjusted for baseline	40.6%[¶]	37.5%[¶]	25.9%
FPG (mg/dL)			
Baseline (mean)	156.0	169.2	165.6
Change from baseline at Week 24 (adjusted mean[‡])	−23.5	−21.5	−6.0
Difference from placebo (adjusted mean[‡]) (95% CI)	−17.5[§] (−25.0, −10.0)	−15.5[§] (−22.9, −8.1)	
Change from baseline at Week 1 (adjusted mean[‡])	−16.5[§] (N=115)	−12.0[§] (N=121)	1.2 (N=126)
Body Weight (kg)			
Baseline (mean)	86.3	84.7	87.7
Change from baseline (adjusted mean[‡])	−2.9	−3.0	−0.9
Difference from placebo (adjusted mean[‡]) (95% CI)	−2.0[§] (−2.6, −1.3)	−2.2[§] (−2.8, −1.5)	

* LOCF: last observation (prior to rescue for rescued patients) carried forward.

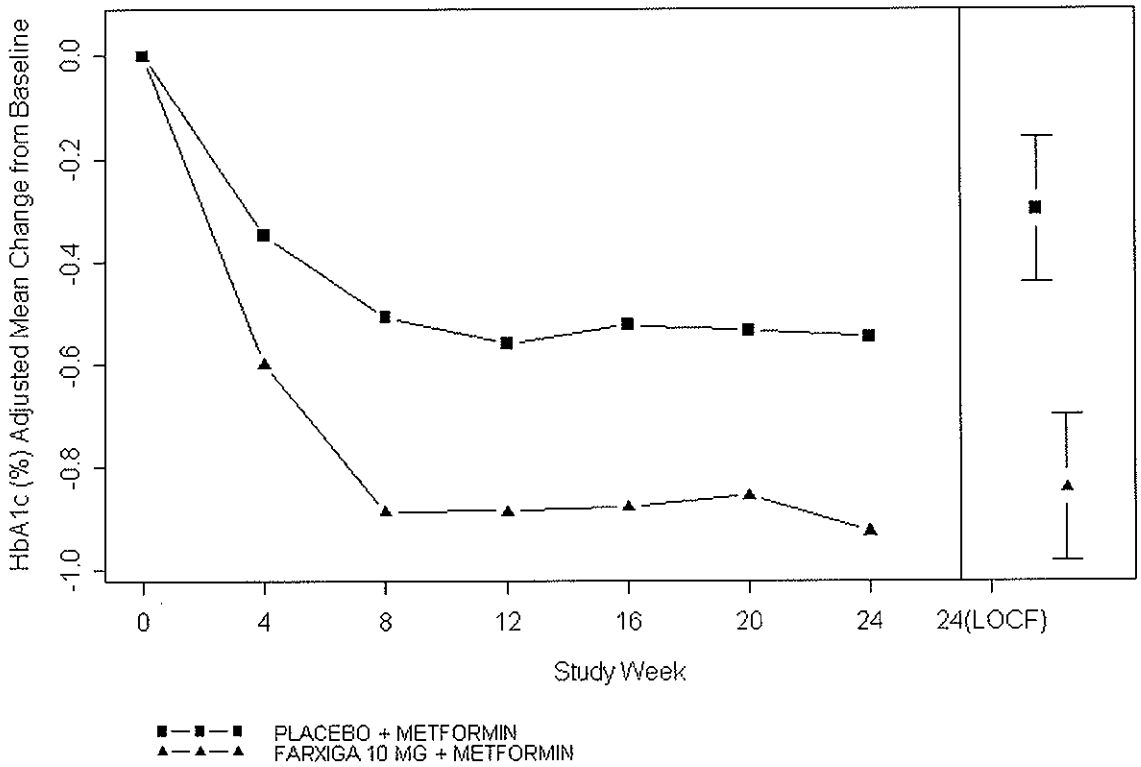
† All randomized patients who took at least one dose of double-blind study medication during the short-term double-blind period.

‡ Least squares mean adjusted for baseline value.

§ p-value <0.0001 versus placebo + metformin.

¶ p-value <0.05 versus placebo + metformin.

Figure 3: **Adjusted Mean Change from Baseline Over Time in HbA1c (%) in a 24-Week Placebo-Controlled Study of FARXIGA in Combination with Metformin**



Left side graph: Values for adjusted mean change from baseline based on a longitudinal repeated measures model, including randomized subjects who completed Short-Term Period with both baseline and Week 24 HbA1c values without rescue. Right side graph for Week 24 (LOCF): Values for adjusted mean change from baseline and 95% CIs based on an ANCOVA model, including randomized subjects with a baseline and at least one post baseline HbA1c before rescue.

14.5 Active Glipizide-Controlled Study Add-On to Metformin

A total of 816 patients with type 2 diabetes with inadequate glycemic control (HbA1c >6.5% and ≤10%) were randomized in a 52-week, glipizide-controlled, noninferiority study to evaluate FARXIGA as add-on therapy to metformin. Patients on metformin at a dose of at least 1500 mg per day were randomized following a 2-week placebo lead-in period to glipizide or dapagliflozin (5 mg or 2.5 mg, respectively) and were up-titrated over 18 weeks to optimal glycemic effect (FPG <110 mg/dL, <6.1 mmol/L) or to the highest dose level (up to glipizide 20 mg and FARXIGA 10 mg) as tolerated by patients. Thereafter, doses were kept constant, except for down-titration to prevent hypoglycemia.

At the end of the titration period, 87% of patients treated with FARXIGA had been titrated to the maximum study dose (10 mg) versus 73% treated with glipizide (20 mg). FARXIGA led to a

similar mean reduction in HbA1c from baseline at Week 52 (LOCF), compared with glipizide, thus demonstrating noninferiority (see Table 12). FARXIGA treatment led to a statistically significant mean reduction in body weight from baseline at Week 52 (LOCF) compared with a mean increase in body weight in the glipizide group. Statistically significant ($p<0.0001$) mean change from baseline in systolic blood pressure relative to glipizide plus metformin was −5.0 mmHg with FARXIGA plus metformin.

Table 12: Results at Week 52 (LOCF*) in an Active-Controlled Study Comparing FARXIGA to Glipizide as Add-On to Metformin

Efficacy Parameter	FARXIGA + Metformin N=400[†]	Glipizide + Metformin N=401[†]
HbA1c (%)		
Baseline (mean)	7.7	7.7
Change from baseline (adjusted mean[‡])	−0.5	−0.5
Difference from glipizide + metformin (adjusted mean[‡]) (95% CI)	0.0[§] (−0.1, 0.1)	
Body Weight (kg)		
Baseline (mean)	88.4	87.6
Change from baseline (adjusted mean[‡])	−3.2	1.4
Difference from glipizide + metformin (adjusted mean[‡]) (95% CI)	−4.7[¶] (−5.1, −4.2)	

* LOCF: last observation carried forward.

† Randomized and treated patients with baseline and at least 1 postbaseline efficacy measurement.

‡ Least squares mean adjusted for baseline value.

§ Noninferior to glipizide + metformin.

¶ p-value <0.0001.

14.6 Add-On Combination Therapy with Other Antidiabetic Agents

Add-On Combination Therapy with a Sulfonylurea

A total of 597 patients with type 2 diabetes and inadequate glycemic control (HbA1c ≥7% and ≤10%) were randomized in this 24-week, placebo-controlled study to evaluate FARXIGA in combination with glimepiride (a sulfonylurea).

Patients on at least half the maximum recommended dose of glimepiride as monotherapy (4 mg) for at least 8 weeks lead-in were randomized to FARXIGA 5 mg, FARXIGA 10 mg, or placebo in addition to glimepiride 4 mg per day. Down-titration of glimepiride to 2 mg or 0 mg was

allowed for hypoglycemia during the treatment period; no up-titration of glimepiride was allowed.

In combination with glimepiride, FARXIGA 10 mg provided statistically significant improvement in HbA1c, FPG, and 2-hour PPG, and statistically significant reduction in body weight compared with placebo plus glimepiride at Week 24 (see Table 13). Statistically significant ($p<0.05$ for both doses) mean changes from baseline in systolic blood pressure relative to placebo plus glimepiride were −2.8 mmHg and −3.8 mmHg with FARXIGA 5 mg and 10 mg plus glimepiride, respectively.

Add-On Combination Therapy with a Thiazolidinedione

A total of 420 patients with type 2 diabetes with inadequate glycemic control (HbA1c ≥7% and ≤10.5%) participated in a 24-week, placebo-controlled study to evaluate FARXIGA in combination with pioglitazone (a thiazolidinedione [TZD]) alone. Patients on a stable dose of pioglitazone of 45 mg per day (or 30 mg per day, if 45 mg per day was not tolerated) for 12 weeks were randomized after a 2-week lead-in period to 5 or 10 mg of FARXIGA or placebo in addition to their current dose of pioglitazone. Dose titration of FARXIGA or pioglitazone was not permitted during the study.

In combination with pioglitazone, treatment with FARXIGA 10 mg provided statistically significant improvements in HbA1c, 2-hour PPG, FPG, the proportion of patients achieving HbA1c <7%, and a statistically significant reduction in body weight compared with the placebo plus pioglitazone treatment groups (see Table 13) at Week 24. A statistically significant ($p<0.05$) mean change from baseline in systolic blood pressure relative to placebo in combination with pioglitazone was −4.5 mmHg with FARXIGA 10 mg in combination with pioglitazone.

Add-On Combination Therapy with a DPP4 Inhibitor

A total of 452 patients with type 2 diabetes who were drug naive, or who were treated at entry with metformin or a DPP4 inhibitor alone or in combination, and had inadequate glycemic control (HbA1c ≥7.0% and ≤10.0% at randomization), participated in a 24-week, placebo-controlled study to evaluate FARXIGA in combination with sitagliptin (a DPP4 inhibitor) with or without metformin.

Eligible patients were stratified based on the presence or absence of background metformin (≥1500 mg per day), and within each stratum were randomized to either FARXIGA 10 mg plus sitagliptin 100 mg once daily, or placebo plus sitagliptin 100 mg once daily. Endpoints were

tested for FARXIGA 10 mg versus placebo for the total study group (sitagliptin with and without metformin) and for each stratum (sitagliptin alone or sitagliptin with metformin). Thirty-seven percent (37%) of patients were drug naive, 32% were on metformin alone, 13% were on a DPP4 inhibitor alone, and 18% were on a DPP4 inhibitor plus metformin. Dose titration of FARXIGA, sitagliptin, or metformin was not permitted during the study.

In combination with sitagliptin (with or without metformin), FARXIGA 10 mg provided statistically significant improvements in HbA1c, FPG, and a statistically significant reduction in body weight compared with the placebo plus sitagliptin (with or without metformin) group at Week 24 (see Table 13). These improvements were also seen in the stratum of patients who received FARXIGA 10 mg plus sitagliptin alone (placebo-corrected mean change for HbA1c −0.56%; n=110) compared with placebo plus sitagliptin alone (n=111), and the stratum of patients who received FARXIGA 10 mg plus sitagliptin and metformin (placebo-corrected mean change for HbA1c −0.40; n=113) compared with placebo plus sitagliptin with metformin (n=113).

Add-On Combination Therapy with Insulin

A total of 808 patients with type 2 diabetes who had inadequate glycemic control (HbA1c ≥7.5% and ≤10.5%) were randomized in a 24-week, placebo-controlled study to evaluate FARXIGA as add-on therapy to insulin. Patients on a stable insulin regimen, with a mean dose of at least 30 IU of injectable insulin per day, for a period of at least 8 weeks prior to enrollment and on a maximum of 2 oral antidiabetic medications (OADs), including metformin, were randomized after completing a 2-week enrollment period to receive either FARXIGA 5 mg, FARXIGA 10 mg, or placebo in addition to their current dose of insulin and other OADs, if applicable. Patients were stratified according to the presence or absence of background OADs. Up- or down-titration of insulin was only permitted during the treatment phase in patients who failed to meet specific glycemic goals. Dose modifications of blinded study medication or OAD(s) were not allowed during the treatment phase, with the exception of decreasing OAD(s) where there were concerns over hypoglycemia after cessation of insulin therapy.

In this study, 50% of patients were on insulin monotherapy at baseline, while 50% were on 1 or 2 OADs in addition to insulin. At Week 24, FARXIGA 10 mg dose provided statistically significant improvement in HbA1c and reduction in mean insulin dose, and a statistically significant reduction in body weight compared with placebo in combination with insulin, with or without up to 2 OADs (see Table 13); the effect of FARXIGA on HbA1c was similar in patients treated with insulin alone and patients treated with insulin plus OAD. Statistically significant

($p<0.05$) mean change from baseline in systolic blood pressure relative to placebo in combination with insulin was −3.0 mmHg with FARXIGA 10 mg in combination with insulin.

At Week 24, FARXIGA 5 mg (−5.7 IU, difference from placebo) and 10 mg (−6.2 IU, difference from placebo) once daily resulted in a statistically significant reduction in mean daily insulin dose ($p<0.0001$ for both doses) compared to placebo in combination with insulin, and a statistically significantly higher proportion of patients on FARXIGA 10 mg (19.6%) reduced their insulin dose by at least 10% compared to placebo (11.0%).

Table 13: Results of 24-Week (LOCF*) Placebo-Controlled Studies of FARXIGA in Combination with Antidiabetic Agents

Efficacy Parameter	FARXIGA 10 mg	FARXIGA 5 mg	Placebo
In Combination with Sulfonylurea (Glimepiride)			
Intent-to-Treat Population	N=151[†]	N=142[†]	N=145[†]
HbA1c (%)			
Baseline (mean)	8.1	8.1	8.2
Change from baseline (adjusted mean[‡])	−0.8	−0.6	−0.1
Difference from placebo + glimepiride (adjusted mean[‡]) (95% CI)	−0.7[§] (−0.9, −0.5)	−0.5[§] (−0.7, −0.3)	
Percent of patients achieving HbA1c <7% adjusted for baseline	31.7%[§]	30.3%[§]	13.0%
FPG (mg/dL)			
Baseline (mean)	172.4	174.5	172.7
Change from baseline (adjusted mean[‡])	−28.5	−21.2	−2.0
Difference from placebo + glimepiride (adjusted mean[‡]) (95% CI)	−26.5[§] (−33.5, −19.5)	−19.3[§] (−26.3, −12.2)	
2-hour PPG[¶] (mg/dL)			
Baseline (mean)	329.6	322.8	324.1
Change from baseline (adjusted mean[‡])	−60.6	−54.5	−11.5
Difference from placebo + glimepiride (adjusted mean[‡]) (95% CI)	−49.1[§] (−64.1, −34.1)	−43.0[§] (−58.4, −27.5)	
Body Weight (kg)			
Baseline (mean)	80.6	81.0	80.9
Change from baseline (adjusted mean[‡])	−2.3	−1.6	−0.7
Difference from placebo + glimepiride (adjusted mean[‡]) (95% CI)	−1.5[§] (−2.2, −0.9)	−0.8[§] (−1.5, −0.2)	
In Combination with Thiazolidinedione (Pioglitazone)			
Intent-to-Treat Population	N=140[#]	N=141[#]	N=139[#]
HbA1c (%)			
Baseline (mean)	8.4	8.4	8.3
Change from baseline (adjusted mean[‡])	−1.0	−0.8	−0.4

Table 13: Results of 24-Week (LOCF*) Placebo-Controlled Studies of FARXIGA in Combination with Antidiabetic Agents

Efficacy Parameter	FARXIGA 10 mg	FARXIGA 5 mg	Placebo
Difference from placebo (adjusted mean‡) (95% CI)	−0.6§ (−0.8, −0.3)	−0.4§ (−0.6, −0.2)	
Percent of patients achieving HbA1c <7% adjusted for baseline	38.8%**	32.5%**	22.4%
FPG (mg/dL)			
Baseline (mean)	164.9	168.3	160.7
Change from baseline (adjusted mean‡)	−29.6	−24.9	−5.5
Difference from placebo (adjusted mean‡) (95% CI)	−24.1§ (−32.2, −16.1)	−19.5§ (−27.5, −11.4)	
2-hour PPG¶ (mg/dL)			
Baseline (mean)	308.0	284.8	293.6
Change from baseline (adjusted mean‡)	−67.5	−65.1	−14.1
Difference from placebo (adjusted mean‡) (95% CI)	−53.3§ (−71.1, −35.6)	−51.0§ (−68.7, −33.2)	
Body Weight (kg)			
Baseline (mean)	84.8	87.8	86.4
Change from baseline (adjusted mean‡)	−0.1	0.1	1.6
Difference from placebo (adjusted mean‡) (95% CI)	−1.8§ (−2.6, −1.0)	−1.6§ (−2.3, −0.8)	
In Combination with DPP4 Inhibitor (Sitagliptin) with or without Metformin			
Intent-to-Treat Population	**N=223†**	–	**N=224†**
HbA1c (%)			
Baseline (mean)	7.90	–	7.97
Change from baseline (adjusted mean‡)	−0.45	–	0.04
Difference from placebo (adjusted mean‡) (95% CI)	−0.48§ (−0.62, −0.34)	–	
Patients with HbA1c decrease ≥0.7% (adjusted percent)	35.4%	–	16.6%
FPG (mg/dL)			
Baseline (mean)	161.7	–	163.1
Change from baseline at Week 24 (adjusted mean‡)	−24.1	–	3.8
Difference from placebo (adjusted mean‡) (95% CI)	−27.9§ (−34.5, −21.4)	–	
Body Weight (kg)			
Baseline (mean)	91.02	–	89.23
Change from baseline (adjusted mean‡)	−2.14	–	−0.26
Difference from placebo (adjusted mean‡) (95% CI)	−1.89§ (−2.37, −1.40)	–	
In Combination with Insulin with or without up to 2 Oral Antidiabetic Therapies			
Intent-to-Treat Population	**N=194†**	**N=211†**	**N=193†**

Table 13: Results of 24-Week (LOCF*) Placebo-Controlled Studies of FARXIGA in Combination with Antidiabetic Agents

Efficacy Parameter	FARXIGA 10 mg	FARXIGA 5 mg	Placebo
HbA1c (%)			
Baseline (mean)	8.6	8.6	8.5
Change from baseline (adjusted mean‡)	−0.9	−0.8	−0.3
Difference from placebo (adjusted mean‡) (95% CI)	−0.6§ (−0.7, −0.5)	−0.5§ (−0.7, −0.4)	
FPG (mg/dL)			
Baseline (mean)	173.7	NT††	170.0
Change from baseline (adjusted mean‡)	−21.7	NT††	3.3
Difference from placebo (adjusted mean‡) (95% CI)	−25.0§ (−34.3, −15.8)	NT††	
Body Weight (kg)			
Baseline (mean)	94.6	93.2	94.2
Change from baseline (adjusted mean‡)	−1.7	−1.0	0.0
Difference from placebo (adjusted mean‡) (95% CI)	−1.7§ (−2.2, −1.2)	−1.0§ (−1.5, −0.5)	

* LOCF: last observation (prior to rescue for rescued patients) carried forward.

† Randomized and treated patients with baseline and at least 1 postbaseline efficacy measurement.

‡ Least squares mean adjusted for baseline value.

§ p-value <0.0001 versus placebo.

¶ 2-hour PPG level as a response to a 75-gram oral glucose tolerance test (OGTT).

All randomized patients who took at least one dose of double-blind study medication during the short-term, double-blind period.

** p-value <0.05 versus placebo.

†† NT: Not formally tested because of failing to achieve a statistically significant difference in an endpoint that was earlier in the testing sequence.

14.7 Use in Patients with Type 2 Diabetes and Renal Impairment

The efficacy of FARXIGA was assessed in a study of diabetic patients with moderate renal impairment (252 patients with mean eGFR 45 mL/min/1.73 m^2). FARXIGA did not show efficacy in this study. The placebo-corrected mean HbA1c change at 24 weeks was −0.1% (95% CI [−0.4%, 0.2%]) for both FARXIGA 5 mg (n=83) and 10 mg (n=82).

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

FARXIGA (dapagliflozin) tablets have markings on both sides and are available in the strengths and packages listed in Table 14.

Table 14: FARXIGA Tablet Presentations

Tablet Strength	Film-Coated Tablet Color/Shape	Tablet Markings	Package Size	NDC Code
5 mg	yellow, biconvex, round	"5" engraved on one side and "1427" engraved on the other side	Bottles of 30 Bottles of 90 Bottles of 500 Hospital Unit Dose Cartons of 100	0003-1427-11 0003-1427-12 0003-1427-13 0003-1427-14
10 mg	yellow, biconvex, diamond-shaped	"10" engraved on one side and "1428" engraved on the other side	Bottles of 30 Bottles of 90 Bottles of 500 Hospital Unit Dose Cartons of 100	0003-1428-11 0003-1428-12 0003-1428-13 0003-1428-14

Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide).

Instructions

Instruct patients to read the Medication Guide before starting treatment with FARXIGA and to reread it each time the prescription is renewed.

Inform patients of the potential risks and benefits of FARXIGA and of alternative modes of therapy. Also inform patients about the importance of adherence to dietary instructions, regular physical activity, periodic blood glucose monitoring and HbA1c testing, recognition and management of hypoglycemia and hyperglycemia, and assessment of diabetes complications. Advise patients to seek medical advice promptly during periods of stress such as fever, trauma, infection, or surgery, as medication requirements may change.

Instruct patients to take FARXIGA only as prescribed. If a dose is missed, advise patients to take it as soon as it is remembered unless it is almost time for the next dose, in which case patients should skip the missed dose and take the medicine at the next regularly scheduled time. Advise patients not to take two doses of FARXIGA at the same time.

Inform patients that the most common adverse reactions associated with use of FARXIGA are genital mycotic infections, nasopharyngitis, and urinary tract infections.

Instruct patient to immediately inform her healthcare provider if she is pregnant or plans to become pregnant. Based on animal data, FARXIGA may cause fetal harm in the second and third trimesters of pregnancy.

Instruct patient to immediately inform her healthcare provider if she is breastfeeding or planning to breastfeed. It is not known if FARXIGA is excreted in breast milk; however, based on animal data, FARXIGA may cause harm to nursing infants.

Hypotension

Inform patients that symptomatic hypotension may occur with FARXIGA and advise them to contact their healthcare provider if they experience such symptoms [see *Warnings and Precautions (5.1)*]. Inform patients that dehydration may increase the risk for hypotension, and to have adequate fluid intake.

Genital Mycotic Infections in Females (e.g., Vulvovaginitis)

Inform female patients that vaginal yeast infections may occur and provide them with information on the signs and symptoms of vaginal yeast infections. Advise them of treatment options and when to seek medical advice [see *Warnings and Precautions (5.4)*].

Genital Mycotic Infections in Males (e.g., Balanitis)

Inform male patients that yeast infections of the penis (e.g., balanitis or balanoposthitis) may occur, especially in patients with prior history. Provide them with information on the signs and symptoms of balanitis and balanoposthitis (rash or redness of the glans or foreskin of the penis). Advise them of treatment options and when to seek medical advice [see *Warnings and Precautions (5.4)*].

Hypersensitivity Reactions

Inform patients that serious hypersensitivity reactions (e.g., urticaria and angioedema) have been reported with FARXIGA. Advise patients to immediately report any signs or symptoms suggesting allergic reaction or angioedema, and to take no more of the drug until they have consulted prescribing physicians.

Urinary Tract Infections

Inform patients of the potential for urinary tract infections. Provide them with information on the symptoms of urinary tract infections. Advise them to seek medical advice if such symptoms occur.

Bladder Cancer

Inform patients to promptly report any signs of macroscopic hematuria or other symptoms potentially related to bladder cancer.

Laboratory Tests

Due to its mechanism of action, patients taking FARXIGA will test positive for glucose in their urine.

Manufactured by:
Bristol-Myers Squibb Company
Princeton, NJ 08543 USA

Marketed by:
Bristol-Myers Squibb Company
Princeton, NJ 08543
and
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

Product of Ireland

1288613

MEDICATION GUIDE
FARXIGA (far-SEE-guh)
(dapagliflozin)
tablets

What is the most important information I should know about FARXIGA?

FARXIGA can cause serious side effects, including:

- **Dehydration.** FARXIGA can cause some people to have dehydration (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, lightheaded, or weak, especially when you stand up (orthostatic hypotension). You may be at a higher risk of dehydration if you:
  - have low blood pressure
  - take medicines to lower your blood pressure, including water pills (diuretics)
  - are 65 years of age or older
  - are on a low salt diet
  - have kidney problems
- **Vaginal yeast infection.** Women who take FARXIGA may get vaginal yeast infections. Symptoms of a vaginal yeast infection include:
  - vaginal odor
  - white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese)
  - vaginal itching
- **Yeast infection of the penis (balanitis).** Men who take FARXIGA may get a yeast infection of the skin around the penis. Certain men who are not circumcised may have swelling of the penis that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of yeast infection of the penis include:
  - redness, itching, or swelling of the penis
  - rash of the penis
  - foul smelling discharge from the penis
  - pain in the skin around the penis

Talk to your healthcare provider about what to do if you get symptoms of a yeast infection of the vagina or penis. Your healthcare provider may suggest you use an over-the-counter antifungal medicine. Talk to your healthcare provider right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

- **Bladder cancer.** In studies of FARXIGA in people with diabetes, bladder cancer occurred in a few more people who were taking FARXIGA than in people who were taking other diabetes medications. There were too few cases to know if bladder cancer was related to FARXIGA. You should not take FARXIGA if you have bladder cancer. Tell your healthcare provider right away if you have any of the following symptoms:
  - blood or a red color in your urine
  - pain while you urinate

What is FARXIGA?

FARXIGA is a prescription medicine used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.

FARXIGA is not for people with type 1 diabetes.

FARXIGA is not for people with diabetic ketoacidosis (increased ketones in your blood or urine).

It is not known if FARXIGA is safe and effective in children younger than 18 years of age.

Who should not take FARXIGA?

Do not take FARXIGA if you:

- are allergic to dapagliflozin or any of the ingredients in FARXIGA. See the end of this Medication Guide for a list of ingredients in FARXIGA. Symptoms of a **serious** allergic reaction to FARXIGA may include:

- skin rash
- raised red patches on your skin (hives)
- swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing

If you have any of these symptoms, stop taking FARXIGA and contact your healthcare provider or go to the nearest hospital emergency room right away.

- have severe kidney problems or are on dialysis.

What should I tell my healthcare provider before taking FARXIGA?

Before you take FARXIGA, tell your healthcare provider if you:

- have type 1 diabetes or have had diabetic ketoacidosis.
- have kidney problems.
- have or have had bladder cancer.
- are pregnant or plan to become pregnant. FARXIGA may harm your unborn baby. If you are pregnant or plan to become pregnant, talk to your healthcare provider about the best way to control your blood sugar.
- are breastfeeding or plan to breastfeed. It is not known if FARXIGA passes into your breast milk. Talk with your healthcare provider about the best way to feed your baby if you are taking FARXIGA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I take FARXIGA?

- Take FARXIGA exactly as your healthcare provider tells you to take it.
- **Do not** change your dose of FARXIGA without talking to your healthcare provider.
- Take FARXIGA by mouth 1 time each day, with or without food.
- When your body is under some types of stress, such as fever, trauma (such as a car accident), infection, or surgery, the amount of diabetes medicine you need may change. Tell your healthcare provider right away if you have any of these conditions and follow your healthcare provider's instructions.
- Stay on your prescribed diet and exercise program while taking FARXIGA.
- Your healthcare provider may do certain blood tests before you start FARXIGA and during your treatment.

- Your healthcare provider will check your diabetes with regular blood tests, including your blood sugar levels and your A1c.
- Follow your healthcare provider's instructions for treating low blood sugar (hypoglycemia). Talk to your healthcare provider if low blood sugar is a problem for you.
- If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at the next regularly scheduled time. **Do not** take 2 doses of FARXIGA at the same time.
- If you take too much FARXIGA, call your healthcare provider or go to the nearest emergency room right away.

What are the possible side effects of FARXIGA?

FARXIGA may cause serious side effects, including:

See "**What is the most important information I should know about FARXIGA?**"

- **Low blood sugar (hypoglycemia).** If you take FARXIGA with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take FARXIGA. Signs and symptoms of low blood sugar may include:
  - headache
  - weakness
  - confusion
  - shaking or feeling jittery
  - drowsiness
  - dizziness
  - irritability
  - sweating
  - hunger
  - fast heartbeat
- **Kidney problems**
- **Increased fats in your blood (bad cholesterol or LDL)**

The most common side effects of FARXIGA include:

- vaginal yeast infections and yeast infections of the penis
- stuffy or runny nose and sore throat
- urinary tract infections
- changes in urination, including urgent need to urinate more often, in larger amounts, or at night

These are not all the possible side effects of FARXIGA. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FARXIGA?

Store FARXIGA at room temperature between 68°F and 77°F (20°C and 25°C).

General information about the safe and effective use of FARXIGA

This Medication Guide summarizes the most important information about FARXIGA. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about FARXIGA that is written for healthcare professionals.

For more information about FARXIGA, go to www.farxiga.com or call 1-800-321-1335.

What are the ingredients in FARXIGA?

Active ingredient: dapagliflozin.

Inactive ingredients: microcrystalline cellulose, anhydrous lactose, crospovidone, silicon dioxide, and magnesium stearate. The film coating contains: polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc, and yellow iron oxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Bristol-Myers Squibb Company
Princeton, NJ 08543 USA

Marketed by:
Bristol-Myers Squibb Company
Princeton, NJ 08543
and
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

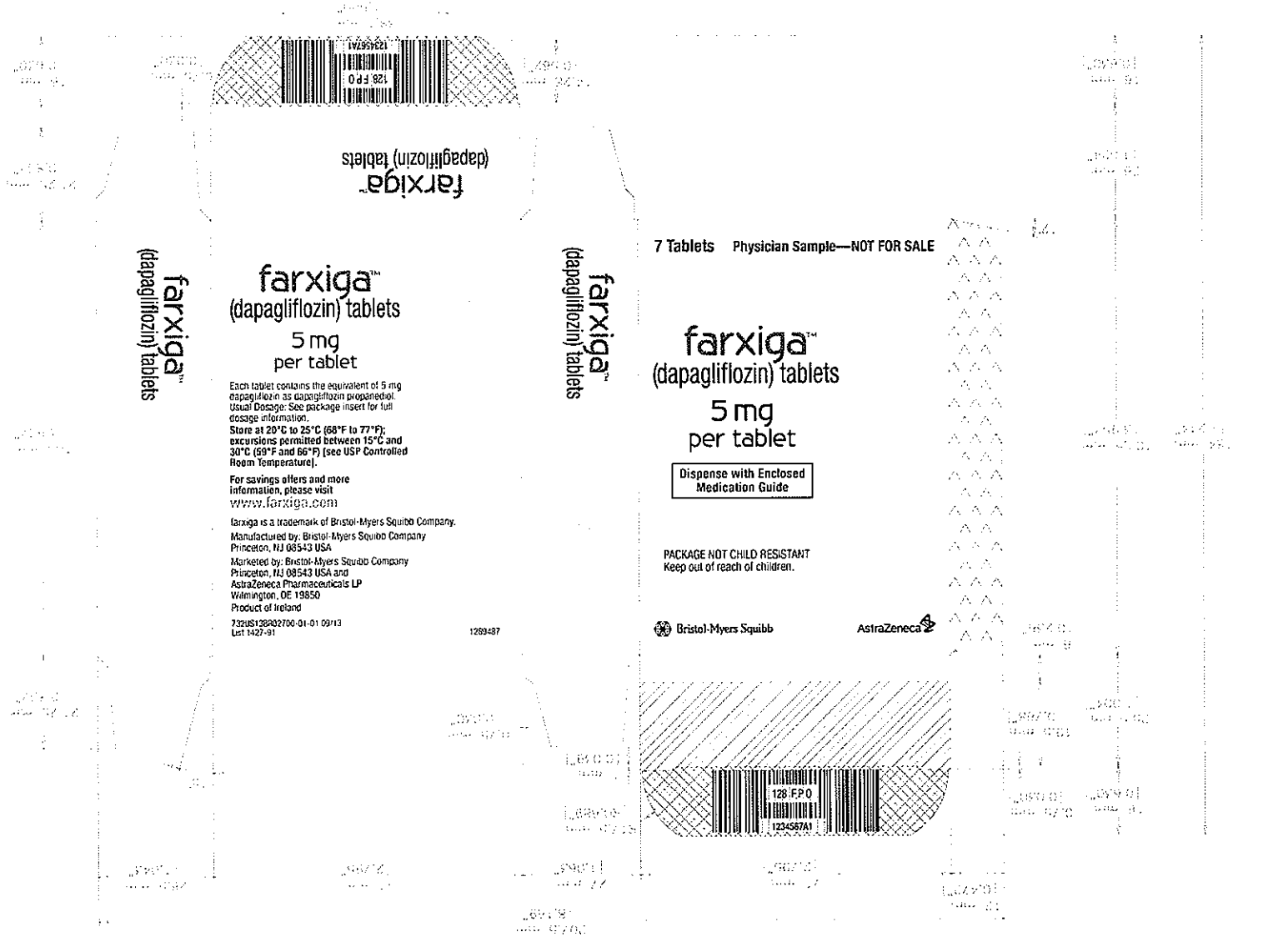
Product of Ireland

1288613 Iss January 2014

Bristol-Myers Squibb WWPT Package Design Team | New Brunswick, NJ USA

File: Farxiga_C_1289487	Global list: 142791	Local list: 1284607
Originator: Susan Stewart	Phone: 732-227-6215	Date: 12/18/13 Alpha: J
SKU Barcode: Not required (sample)		
OLV Barcode: 128 = 1289487		
Ink colors: ■ PMS Black ▩ PMS 032	PMS 382	

Barcodes marked FPO must be replaced by vendor with live code using rules supplied. Artwork may not be altered in any way without express permission from BMS Package Design Team.



Reference ID: 3433133

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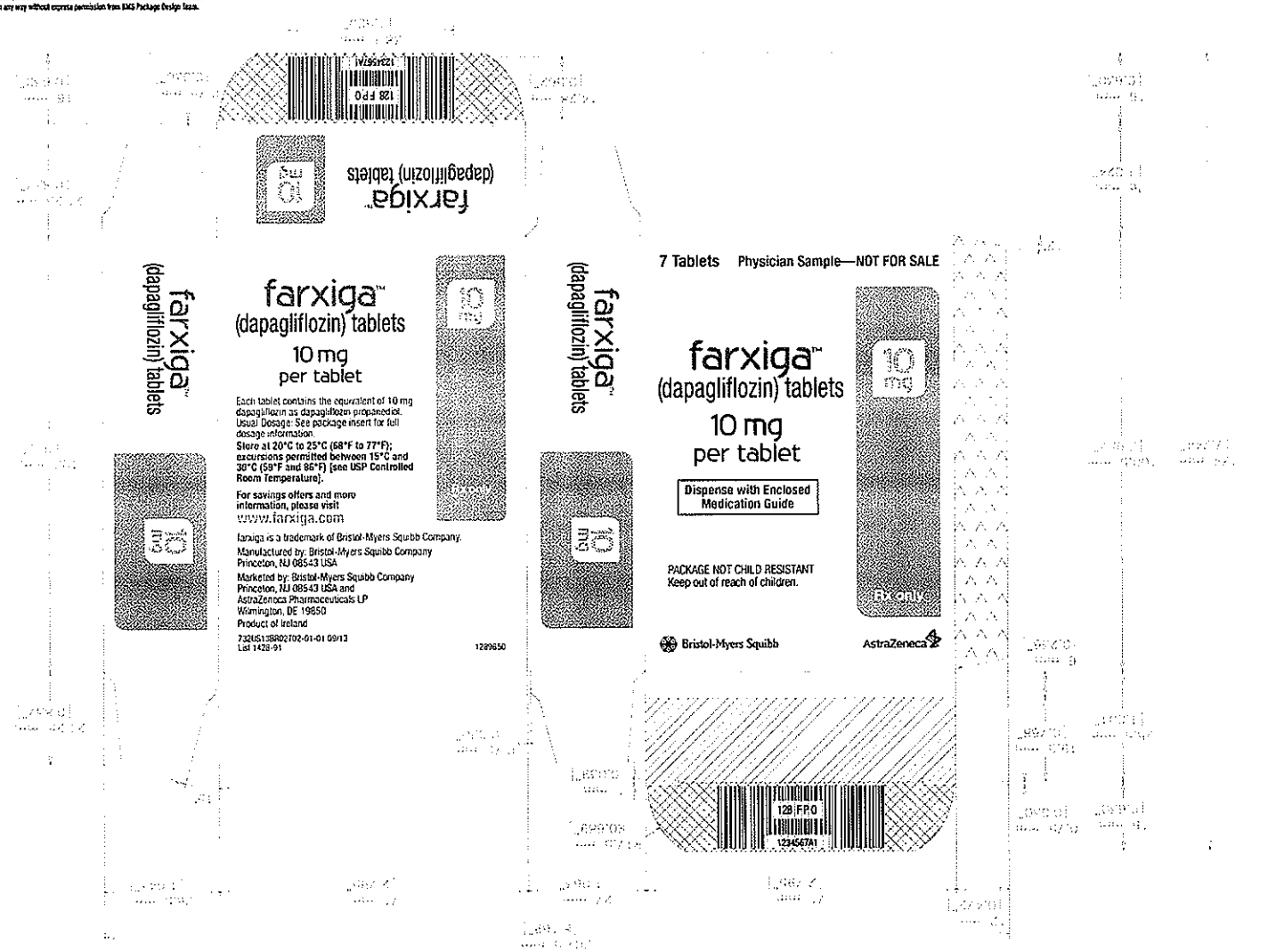
Originator: Susan Stewart	Phone: 732-227-6215	Date: 12/18/13 Alpha: K
SKU Barcode: not required - sample		
OLV Barcode: 128 = 1289650		
Ink colors: PMS Black PMS 032 PMS 7460		

Barcodes marked FPO must be replaced by vendor with live code using value supplied. Artwork may not be altered in any way without express permission from BMS Package Design Team.



5 mg

farxiga™
(dapagliflozin) tablets

100 Tablets NDC 0003-1427-14
(10 blister cards - 10 tablets in each blister card)

100 Tablets NDC 0003-1427-14
(10 blister cards - 10 tablets in each blister card)

farxiga™
(dapagliflozin) tablets

5 mg

Dispense with Medication Guide

Rx only

Bristol-Myers Squibb AstraZeneca

This unit-dose package is not child resistant. If dispensed for outpatient use, a child-resistant container should be used.

Each tablet contains the equivalent of 5 mg dapagliflozin as dapagliflozin propanediol.

Usual Dosage: See package insert for full dosage information.

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

Manufactured by:
Bristol-Myers Squibb Company
Princeton, NJ 08543 USA

Marketed by:
Bristol-Myers Squibb Company
Princeton, NJ 08543 USA and
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

Product of Ireland

Do not use if any printed blister units are open or torn.

DV_farxiga5mg100C_04

DEVELOPMENTAL ARTWORK

Bristol-Myers Squibb — WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 5mg HUB ctn — Originator: Susan Stewart — Date: 12/10/15
Filename: DV_farxiga5mg100C — PR Code: A — Developmental Copy Version: 01

- ☐ Matches correct specification (drawing)
- ☐ Panels correct per text provided
- ☐ Chip potency correct & consistent
- ☐ NDC on component verified
- ☐ Spelling OK
- ☐ Utilized correct colors
- ☐ Trim, positioning and folding shown as overlays
- ☐ Proofread by: _____

Reason for Change: Update logo and add Prestige text indicated and change direction color

Ink colors: PMS Black PMS 032 PMS 383

Artwork may not be shared in any way without express permission from BMS Package Design Team.

10 mg

farxiga™
(dapagliflozin) tablets

100 Tablets NDC 0003-1428-14
(10 blister cards - 10 tablets in each blister card)

farxiga™
(dapagliflozin) tablets

10 mg

Dispense with Medication Guide

Rx only

Bristol-Myers Squibb AstraZeneca

This unit-dose package is not child resistant. If dispensed for outpatient use, a child-resistant container should be used.

Each tablet contains the equivalent of 10 mg dapagliflozin as dapagliflozin propanediol.

Usual Dosage: See package insert for full dosage information.

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

Manufactured by:
Bristol-Myers Squibb Company
Princeton, NJ 08543 USA

Marketed by:
Bristol-Myers Squibb Company
Princeton, NJ 08543 USA and
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

Product of Ireland

Do not use if any printed blister units are open or torn.

DV_farxiga10mg100C_04

100 Tablets NDC 0003-1428-14
(10 blister cards - 10 tablets in each blister card)

farxiga™
(dapagliflozin) tablets

10 mg

Dispense with Medication Guide

Rx only

Bristol-Myers Squibb AstraZeneca

100 Tablets NDC 0003-1428-14
(10 blister cards - 10 tablets in each blister card)

farxiga™
(dapagliflozin) tablets

10 mg

Dispense with Medication Guide

Rx only

Bristol-Myers Squibb AstraZeneca

100 Tablets NDC 0003-1428-14
(10 blister cards - 10 tablets in each blister card)

farxiga™
(dapagliflozin) tablets

10 mg

DEVELOPMENTAL ARTWORK

Bristol-Myers Squibb WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 10mg HUD ctn Originator: Susan Howard Date: 12/15/11

Filename: DV_farxiga10mg100C PR Code: A Developmental Copy Version: 04

- ☐ Denotes correct specification size/range
- ☐ Spellcheck
- ☐ Pantone(s) correct per text provided
- ☐ Denotes correct colors
- ☐ Drug potency correct & consistent
- ☐ Trim, registration and colors shown as directed
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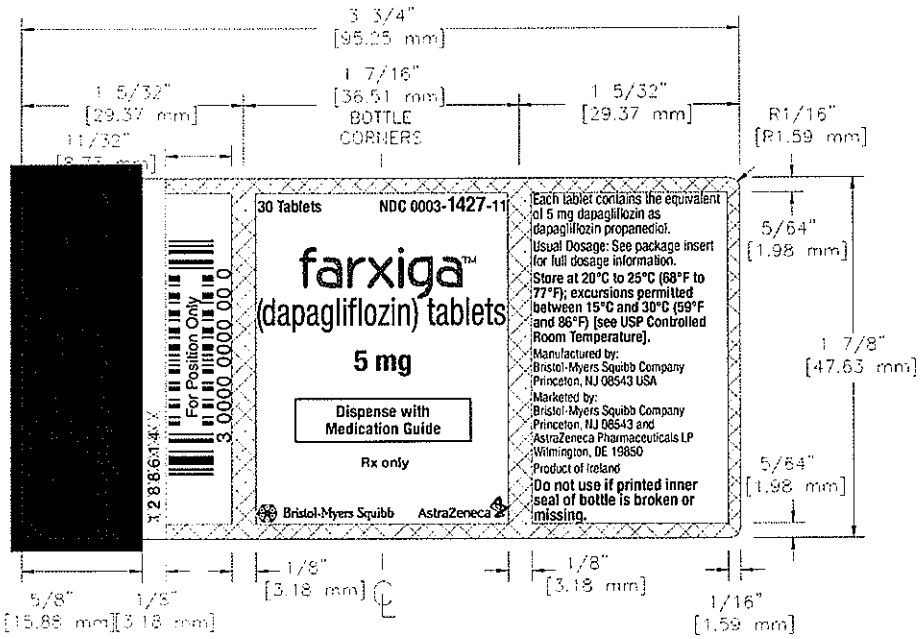
- ☐ Proofread by _____

Reason for Change: Update to approved PI and Product Information and change drug color

Ink colors: ■ PMS Black ■ PMS 032 ■ PMS 7460



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6pt. HELVETICA NEUE ROMAN
300 KERNING

NOTE: ENTIRE LABEL IS TO BE VARNISHED

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Bristol-Myers Squibb WWPT Package Design Team | New Brunswick, NJ USA

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Originator: Susan Stewart	**Phone:** 732-227-6215	**Date:** 12/18/13 **Alpha:** I
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OLV Barcode: Vision system. See art.		
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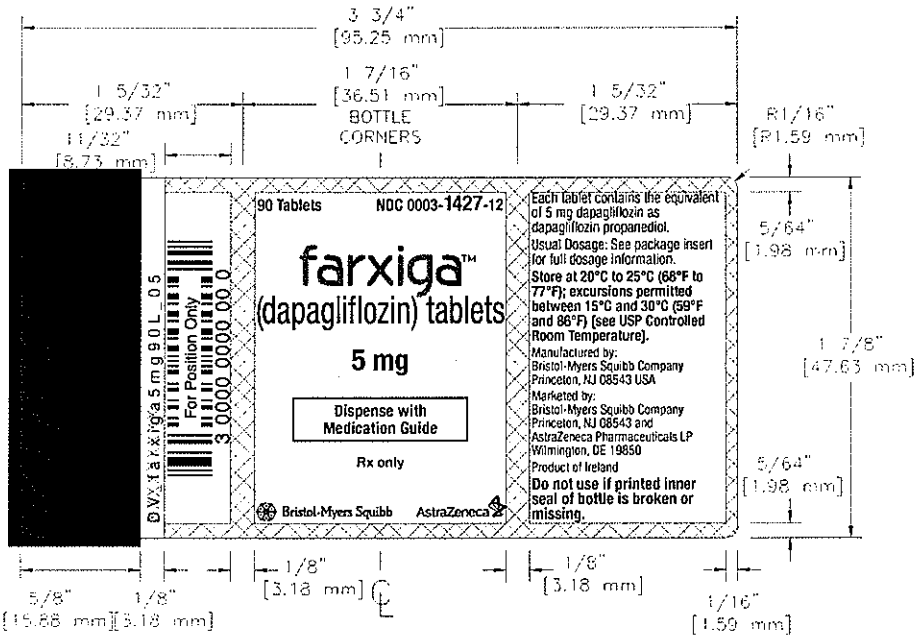

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B-MS DRAWING #: 10000091204

DEVELOPMENTAL ARTWORK

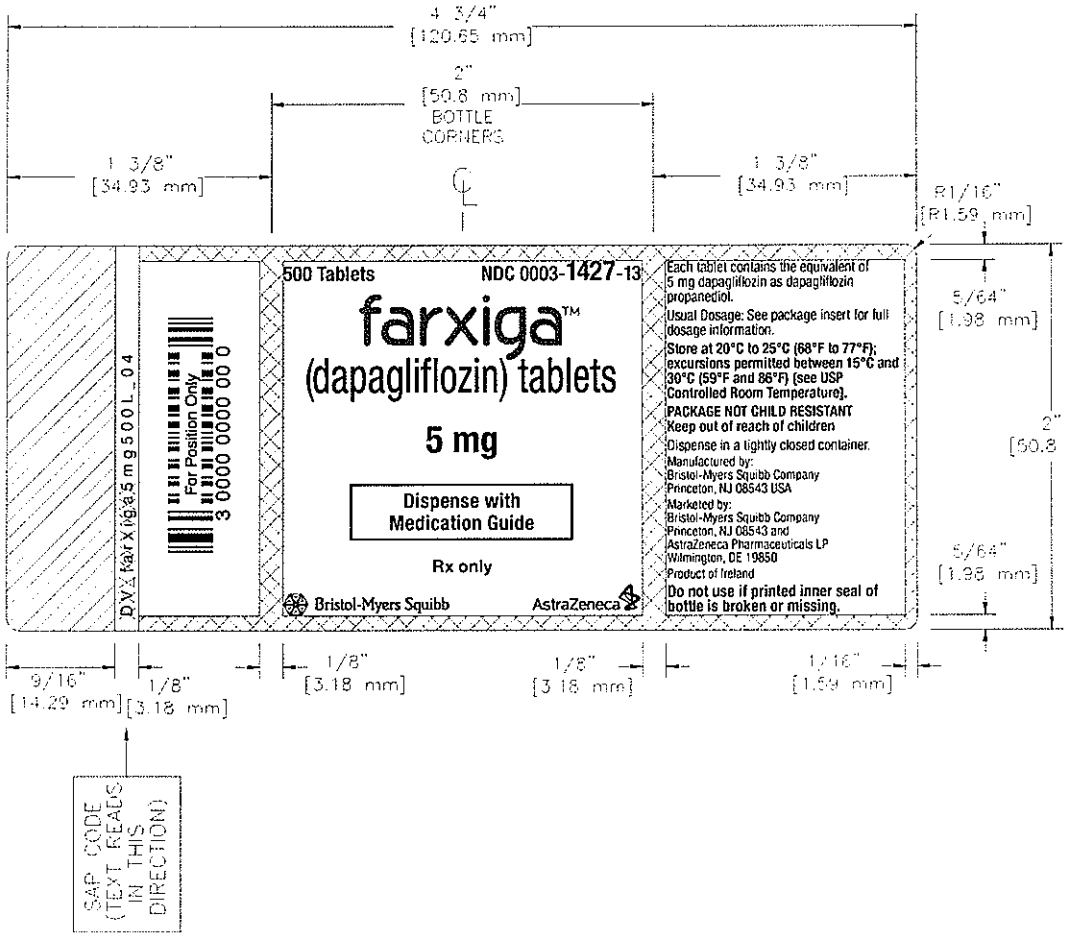
Bristol-Myers Squibb — WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 5mg trade 90 L	**Originator:** Susan Stewart	**Date:** 12/18/13
Filename: DV_farxiga5mg90L	**PR Code:** A	**Developmental Copy Version:** 05

- ☐ Utilizes correct specification (drawing)
- ☐ Revisions correct per text provided
- ☐ Drug potency correct & consistent
- ☐ NDC on component verified
- ☐ Spellcheck
- ☐ Utilizes correct colors
- ☐ Tints, gradations and colors shown as swatches
- ☐ Proofread by _____ (INITIAL HERE)

Reason for Change: Update logo and add Product of Ireland and change dosage color

Ink colors: PMS Black PMS 032 PMS 382



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B-MS DRAWING #: 026048A-00

DEVELOPMENTAL ARTWORK

Bristol-Myers Squibb — WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 5mg 500 trade L	**Originator:** Susan Stewart	**Date:** 12/18/13
Filename: DV_farxiga5mg500L	**PR Code:** A	**Developmental Copy Version:** 04

- ☐ Utilizes correct specification (drawing)
- ☐ Revisions correct per text provided
- ☐ Drug potency correct & consistent
- ☐ NDC on component verified
- ☐ Spellcheck
- ☐ Utilizes correct colors
- ☐ Tints, gradations and colors shown as swatches
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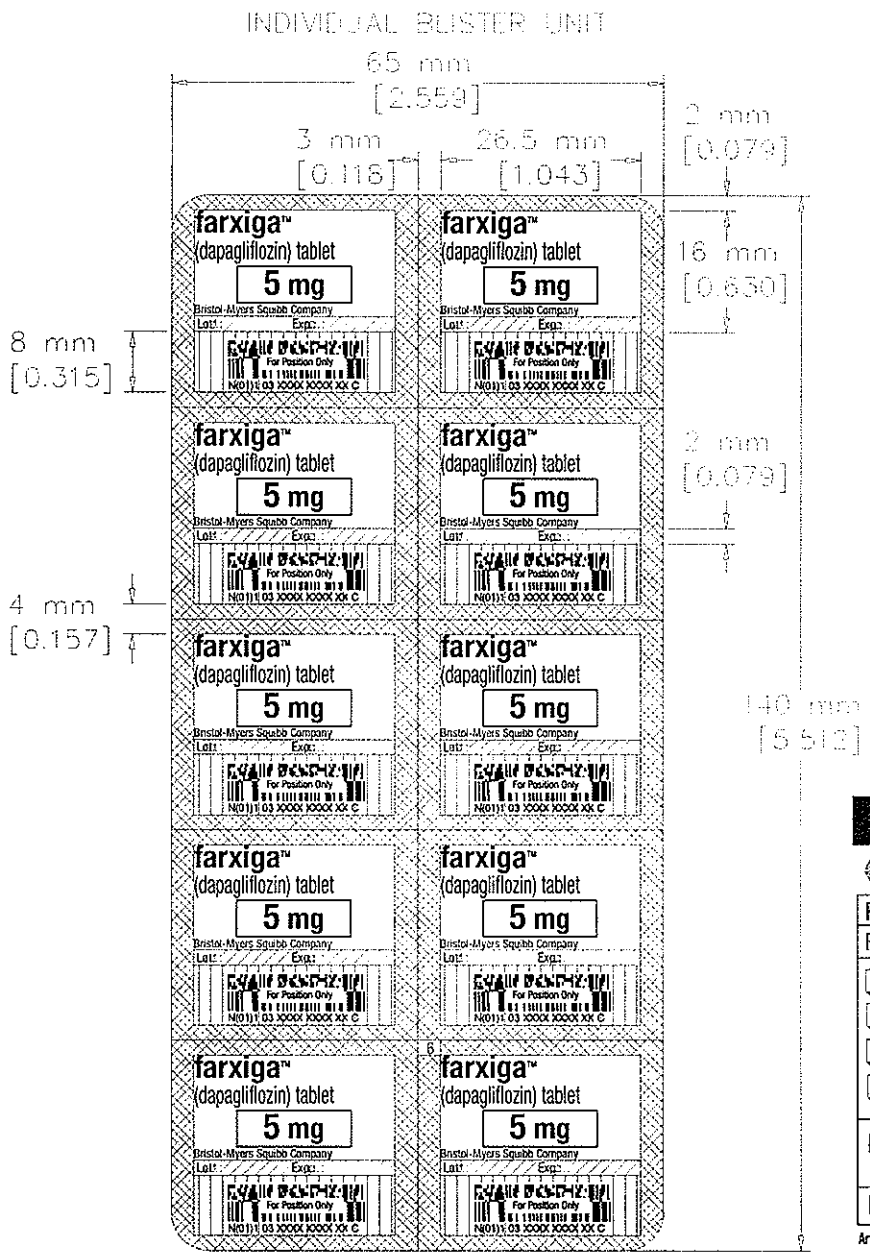
Reason for Change: Update logo and add Product of Ireland and change dosage color

Ink colors: ■ Black ▒ PMS 032 PMS 382



DEVELOPMENTAL ARTWORK

Bristol-Myers Squibb — WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 5mg HUD blister	**Originator:** Susan Stewart	**Date:** 12/12/13
Filename: DV_farxiga_5mgB	**PR Code:** A	**Developmental Copy Version:** 02

- ☐ Utilizes correct specification (drawing)
- ☐ Revisions correct per text provided
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- ☐ NDC on component verified
- ☐ Spellcheck
- ☐ Utilizes correct colors
- ☐ Tints, gradations and colors shown as swatches
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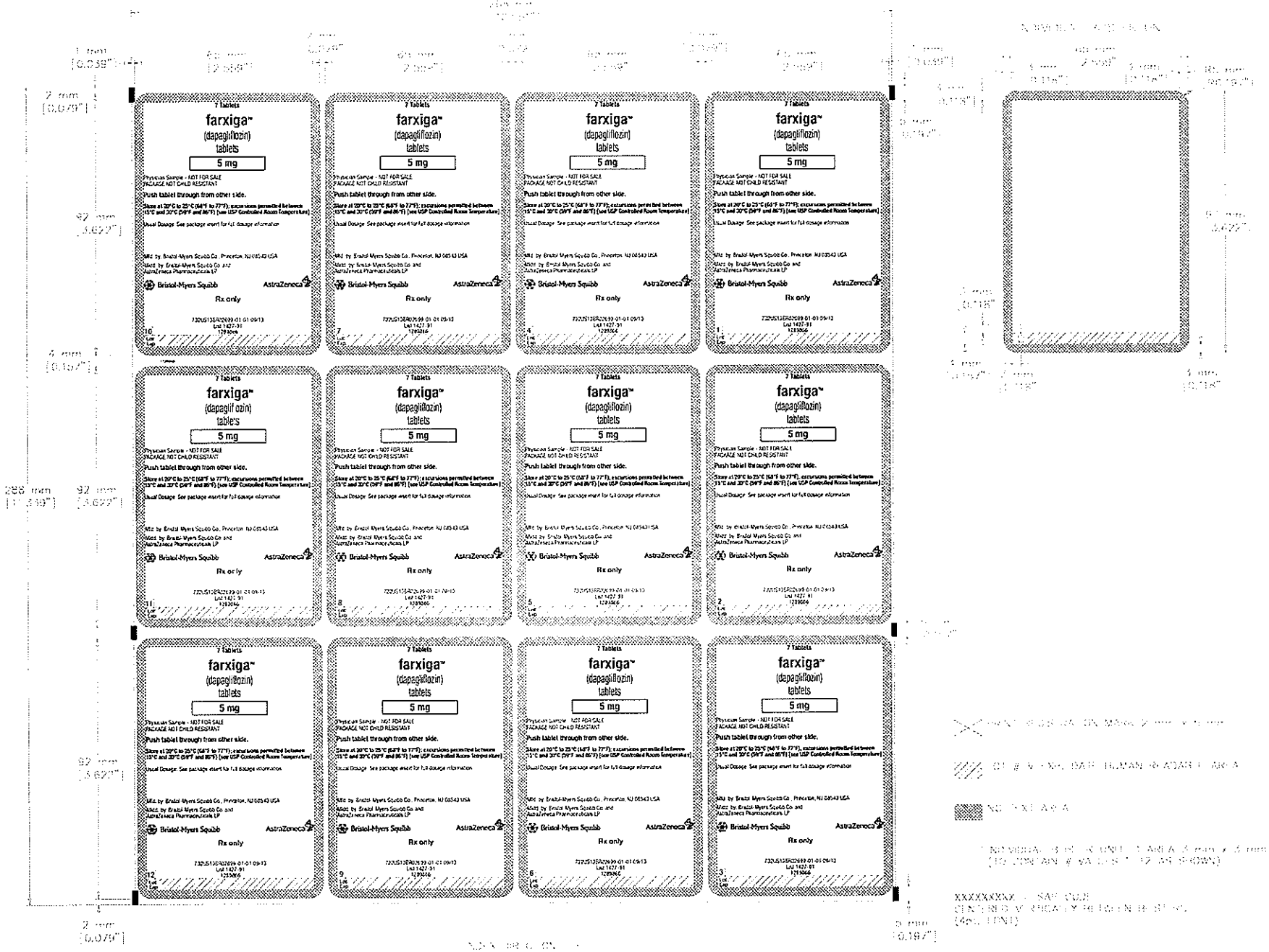
Reason for Change: Update logo and increase generic/table font size

Ink colors: ■ PMS Black



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Originator: Susan Stewart	Phone: 732-227-0215	Date: 12/18/13	Alpha: G
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OLV Barcode: Vision system. See art.			
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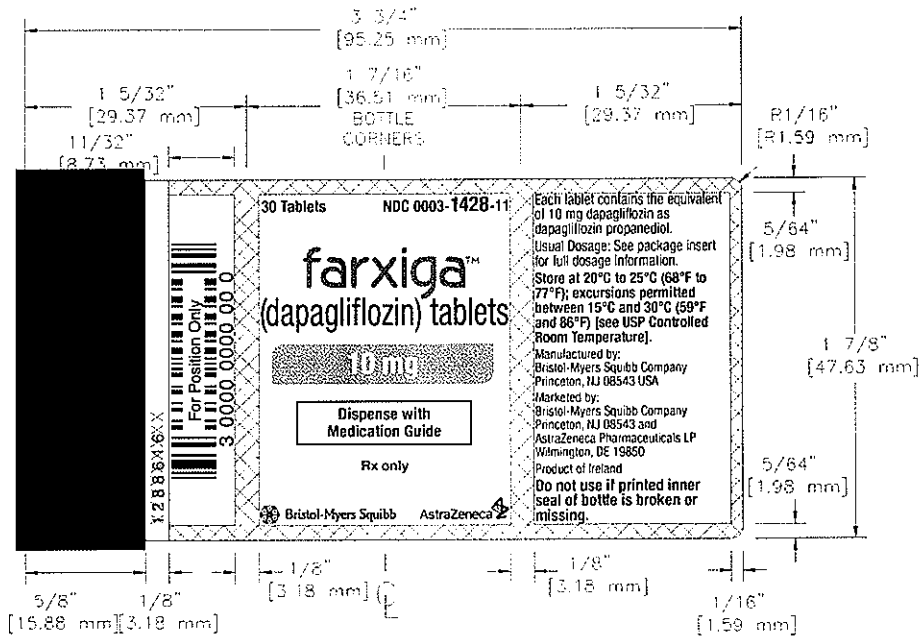

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Originator: Susan Stewart	**Phone:** 732-227-6215	**Date:** 12/18/13 **Alpha:** J
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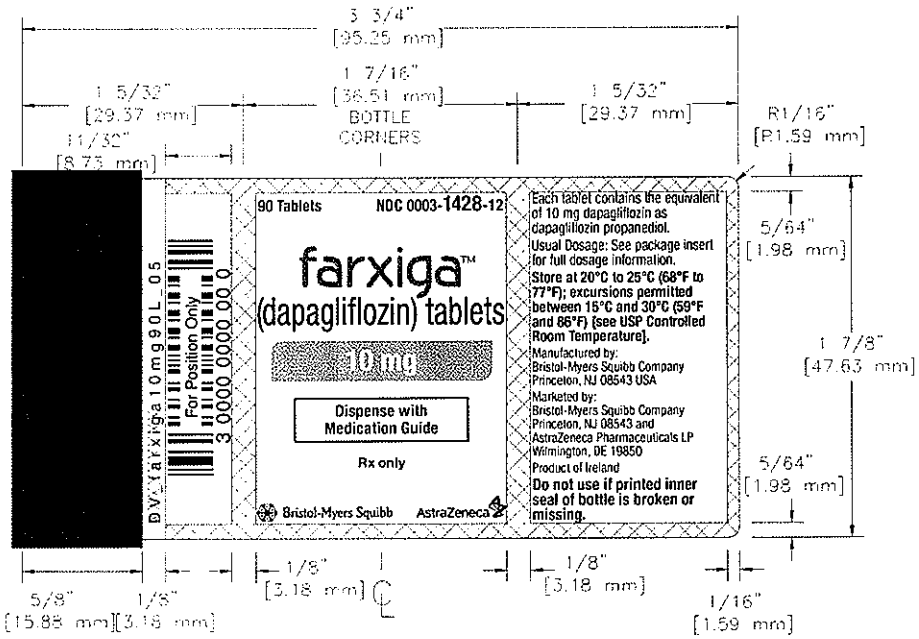

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6pt. HELVETICA NEUE ROMAN
300 KERNING

NOTE: ENTIRE LABEL IS TO BE VARNISHED

B-MS DRAWING #: 10000091204

DEVELOPMENTAL ARTWORK

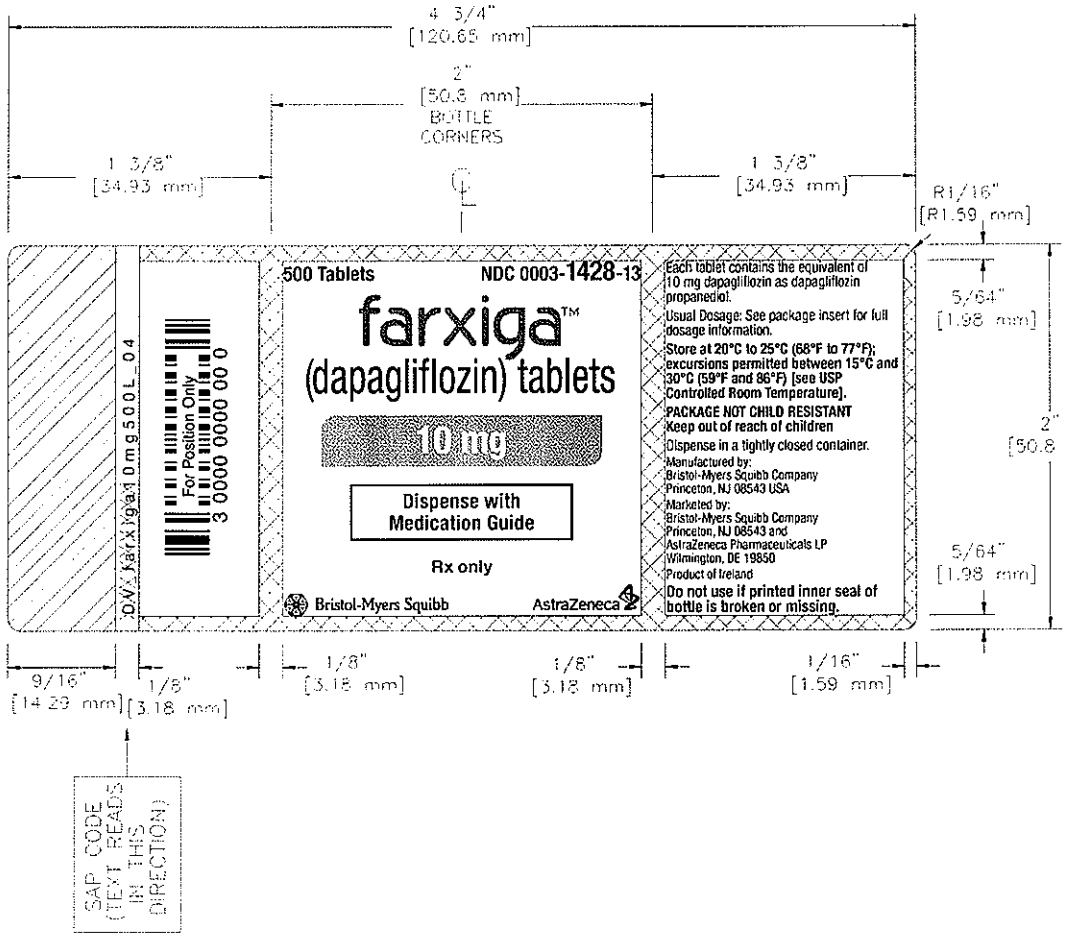
Bristol-Myers Squibb — WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 10mg trade 90	**Originator:** Susan Stewart	**Date:** 12/18/13
Filename: DV_farxiga10mg90L	**PR Code:** A	**Developmental Copy Version:** 05

- ☐ Utilizes correct specification (drawing)
- ☐ Revisions correct per text provided
- ☐ Drug potency correct & consistent
- ☐ NDC on component verified
- ☐ Spellcheck
- ☐ Utilizes correct colors
- ☐ Tints, gradations and colors shown as swatches
- ☐ Proofread by _____ INITIAL HERE

Reason for Change: Update logo and add Product of Ireland and change dosage color

Ink colors: ■ PMS Black ▩ PMS 032 ▩ PMS 7460



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B-MS DRAWING #: 026048A-00

DEVELOPMENTAL ARTWORK

Bristol-Myers Squibb — WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 10mg 500s trade L **Originator:** Susan Stewart **Date:** 12/18/13

Filename: DV_farxiga10mg500L **PR Code:** A **Developmental Copy Version:** 04

- ☐ Utilizes correct specification (drawing)
- ☐ Revisions correct per text provided
- ☐ Drug potency correct & consistent
- ☐ NDC on component verified
- ☐ Spellcheck
- ☐ Utilizes correct colors
- ☐ Tints, gradations and colors shown as swatches
- ☐ Proofread by _____ INITIAL HERE

Reason for Change: Update logo and add Product of Ireland and change dosage color

Ink colors: Black PMS 032 PMS 7460

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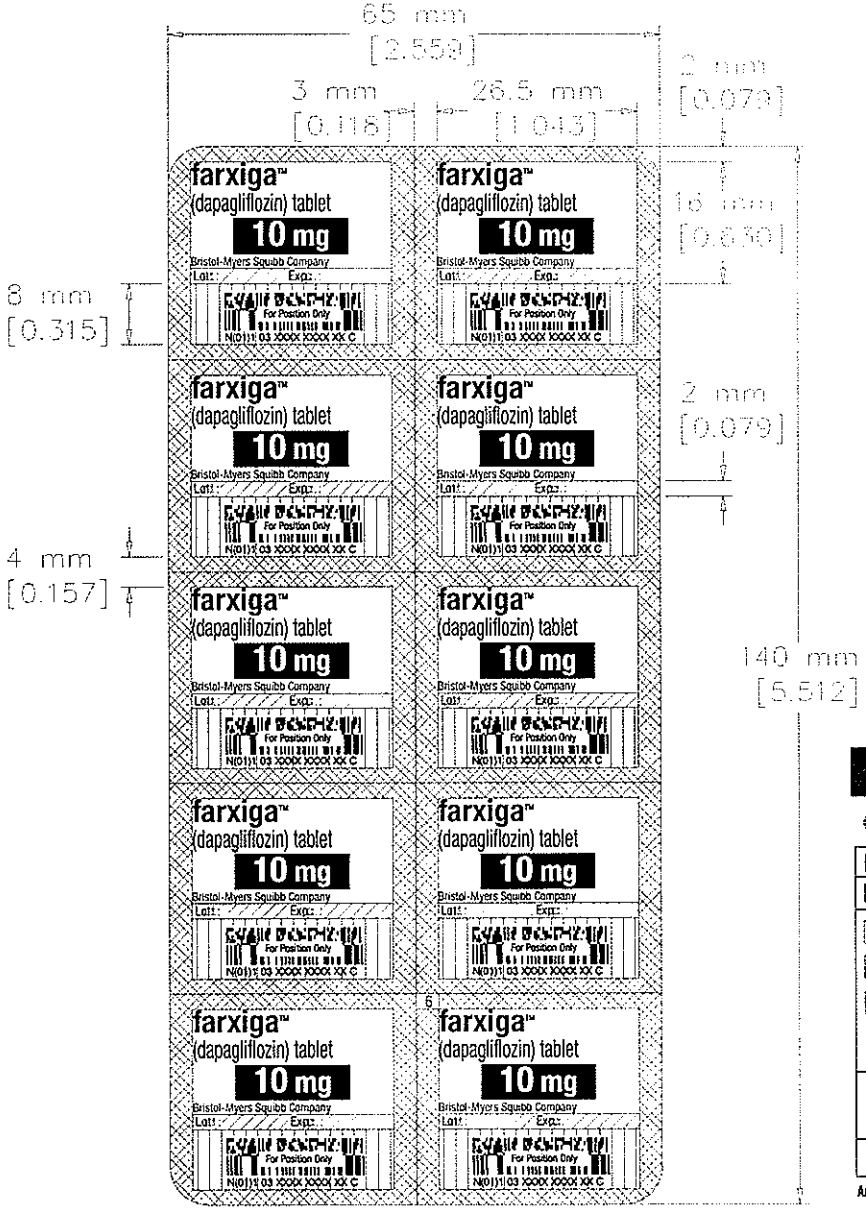

DEVELOPMENTAL ARTWORK

Bristol-Myers Squibb — WWPT Package Design Team | New Brunswick, NJ USA

Product: farxiga 10mg HUD blister	**Originator:** Susan Stewart	**Date:** 12/12/13
Filename: DV_farxiga_10mgB	**PR Code:** A	**Developmental Copy Version:** 02

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- ☐ Spellcheck
- ☐ Utilizes correct colors
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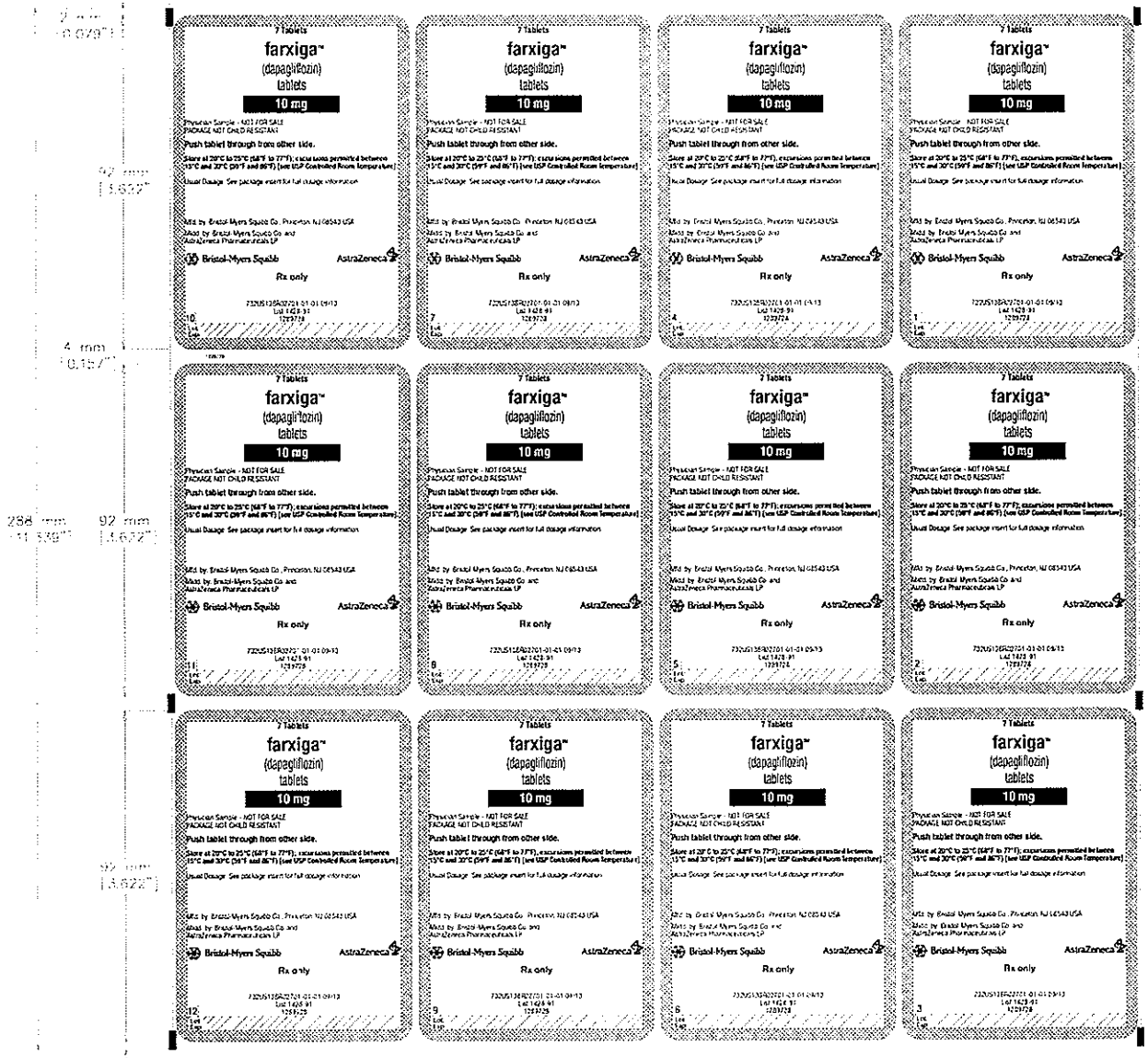
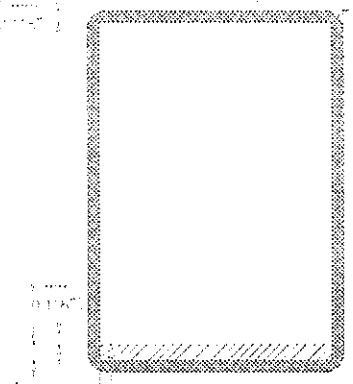
- ☐ Proofread by _____.

Reason for Change: Update logo and increase generic/tablet font size

Ink colors: ■ PMS Black





Bristol-Myers Squibb	WWPT Package Design Team | New Brunswick, NJ USA		
File: Farxiga_B_1269723	Global list: 142891	Local list: 1234812	
Originator: Susan Stewart	Phone: 732-227-6215	Date: 12.18.13	Alpha: G
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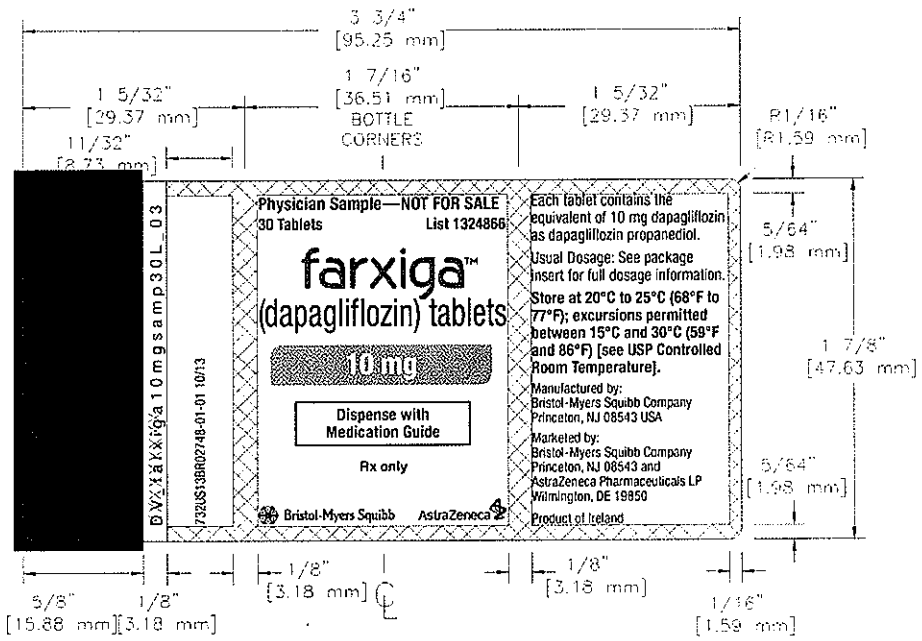
OLV Barcode: Waiver system - see art			
Ink colors: Black			

Reference ID: 3422122



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ADD COLORED BOX TO
LASER BATCH CODE AREA)

NO TEXT AREA

xxxxxxxxx = SAP CODE FOR VISION SYSTEM INSPECTION
TEXT TO BE BLACK INK.
6pt. HELVETICA NEUE ROMAN
300 KERNING

NOTE: ENTIRE LABEL IS TO BE VARNISHED

B-MS DRAWING #: 10000091204

DEVELOPMENTAL ARTWORK

Bristol-Myers Squibb | WWPT Package Design Team | New Brunswick, NJ USA

Bristol-Myers Squibb | WWPT Package Design Team | New Brunswick, NJ USA

File: Farxiga L 1288616	**Global list:** 1428[illegible]	**Local list:** 1284008	
Originator: Susan Stewart	**Phone:** 732-227-0215	**Originator:** Susan Stewart	**Date:** 7/18/13 **Alpha:** 18
SKU Barcode: Special UPC 99 00091428 30 9	**PR Code:** A	**Developmental Copy Version:** 03	
Filename: DV_farxiga 10mg sample 30s			
OLV Barcode: Vision system. See art.			
Ink colors: PMS Black PMS 032			

Barcodes marked FPO must be replaced by vendor with live code using value supplied. Artwork may not be altered in any way without express permission from BMS Package Design Team.

- ☐ Utilizes correct Specification (drawing)
- ☐ Spellcheck
- ☐ Revisions correct per text provided
- ☐ Utilizes correct colors
- ☐ Drug potency correct & consistent
- ☐ Tints, gradations and colors shown as swatches
- ☐ NDC on component verified
- ☐ Proofread by _____ INITIAL HERE

Reason for Change: Sample bottle label

Ink colors: PMS Black PMS 032 PMS 7460

Artwork may not be altered in any way without express permission from BMS Package Design Team.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CURTIS J ROSEBRAUGH
01/08/2014

EXHIBIT D

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Customer No 000000000 | ISTMT | DATE PRINTED 02/20/2014

HENRY HADAD
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON NJ 08543-4000

MAINTENANCE FEE STATEMENT

According to the records of the U.S.Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O.Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	ENTITY STATUS	ATTY DKT NUMBER
6515117	**$900.00**	**$0.00**	**07/07/06**	**10151436**	**02/04/03**	**05/20/02**	**04**	**LARGE**	**LA0049A CIP**

EXHIBIT E

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

Customer No 000000000 | ISTMT | DATE PRINTED 02/20/2014

HENRY HADAD
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON NJ 08543-4000

MAINTENANCE FEE STATEMENT

According to the records of the U.S.Patent and Trademark Office (USPTO), the maintenance fee and any necessary surcharge have been timely paid for the patent listed below. The "PYMT DATE" column indicates the payment date (i.e., the date the payment was filed).

The payment shown below is subject to actual collection. If the payment is refused or charged back by a financial institution, the payment will be void and the maintenance fee and any necessary surcharge unpaid.

Direct any questions about this statement to: Mail Stop M Correspondence, Director of the USPTO, P.O.Box 1450, Alexandria, VA 22313-1450.

PATENT NUMBER	FEE AMT	SUR CHARGE	PYMT DATE	U.S. APPLICATION NUMBER	PATENT ISSUE DATE	APPL. FILING DATE	PAYMENT YEAR	ENTITY STATUS	ATTY DKT NUMBER
6515117	**$2,480.00**	**$0.00**	**07/08/10**	**10151436**	**02/04/03**	**05/20/02**	**08**	**LARGE**	**LA0049A CIP**

EXHIBIT F

CASE LA0049A CIP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
ELLSWORTH ET AL.
APPLICATION NO: 10/151,436
FILED: MAY 20, 2002
FOR: C-ARYL GLUCOSIDE SGLT2 INHIBITORS AND METHOD

Assistant Commissioner for Patents
Washington, D.C. 20231

TERMINAL DISCLAIMER

Sir:

Bristol-Myers Squibb Company, a Delaware corporation, having a place of business at Lawrenceville-Princeton Road, Princeton, NJ 08543-4000, represents that it is the assignee and owner of the entire interest in the above-identified application by virtue of an assignment which was recorded in the United States Patent and Trademark Office on May 20, 2002 at Reel/Frame 012918/0698.

Bristol-Myers Squibb Company hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the above-identified application which would extend beyond the expiration date of the full statutory term defined in 35 USC §154-156 and §173, as presently shortened by any terminal disclaimer, of prior **Patent No. 6,414,126** issued July 2, 2002. Said Patent No. 6,414,126 is also assigned to Bristol-Myers Squibb Company by virtue of an assignment which an assignment which was recorded in the United States Patent and Trademark Office on October 4, 2000 at Reel/Frame 011206/0916.

Bristol-Myers Squibb Company hereby agrees that any patent granted on the above-identified application shall be enforceable only for and during such period that it and prior Patent No. 6,414,126 are commonly owned. This agreement runs with any patent granted on the above-identified application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, Bristol-Myers Squibb Company does not disclaim the terminal part of any patent granted on the above-identified application that would extend to the

expiration date of the full statutory term as defined in 35 USC §154-156 and §173 of prior Patent No. 6,414,126, as presently shortened by any terminal disclaimer, in the event that it later: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR §1.321, has all claims cancelled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

A terminal disclaimer fee under 37 CFR §1.20(d) is included.

Signed this 14th day of AUGUST, 2002 by the undersigned attorney of record.

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-3816

Jonathan N. Provoost
Attorney for Applicants
Reg. No. 44,292

EXHIBIT G

UNITED STATES PATENT AND TRADEMARK OFFICE
Certificate

Patent No. 6,515,117 B2 Patented: February 4, 2003

On petition requesting issuance of a certificate for correction of inventorship pursuant to 35 U.S.C. 256, it has been found that the above identified patent, through error and without any deceptive intent, improperly sets forth the inventorship.

Accordingly, it is hereby certified that the correct inventorship of this patent is: Bruce Ellsworth, Princeton, NJ (US); Wiliam N. Washburn, Titusville, NJ (US); and Wei Meng, Pennington, NJ (US).

Signed and Sealed this Twenty-fifth Day of November 2008.

S. A. JIANG
Supervisory Patent Examiner
Art Unit 1623

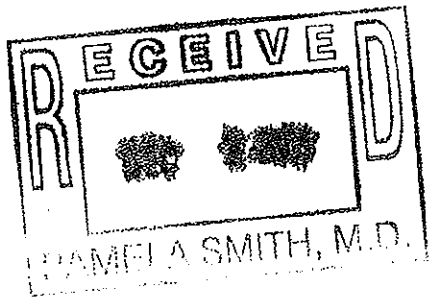
EXHIBIT H

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

IND 68,652



Bristol-Myers Squibb
Attention: Pamela Smith, M.D.
Director, Global Regulatory Strategy
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Smith:

We acknowledge receipt of your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act. Please note the following identifying data:

IND Number Assigned: 68,652

Sponsor: Bristol-Myers Squibb

Name of Drug: BMS-512148 Capsules

Date of Submission: November 20, 2003

Date of Receipt: November 21, 2003

Studies in humans may not be initiated until 30 days after the date of receipt shown above. If, on or before December 21, 2003, we identify deficiencies in the IND that require correction before human studies begin or that require restriction of human studies, we will notify you immediately that (1) clinical studies may not be initiated under this IND ("clinical hold") or that (2) certain restrictions apply to clinical studies under this IND ("partial clinical hold"). In the event of such notification, you must not initiate or you must restrict such studies until you have submitted information to correct the deficiencies, and we have notified you that the information you submitted is satisfactory.

It has not been our policy to object to a sponsor, upon receipt of this acknowledgement letter, either obtaining supplies of the investigational drug or shipping it to investigators listed in the IND. However, if the drug is shipped to investigators, they should be reminded that studies may not begin under the IND until 30 days after the IND receipt date or later if the IND is placed on clinical hold.

As sponsor of this IND, you are responsible for compliance with the Federal Food, Drug, and Cosmetic Act and the implementing regulations (Title 21 of the Code of Federal Regulations). Those responsibilities include (1) reporting any unexpected fatal or life-threatening adverse experience associated with use of the drug by telephone or fax no later than 7 calendar days after initial receipt of the information [21 CFR 312.32(c)(2)]; (2) reporting any adverse experience associated with use of the drug that is both serious and unexpected in writing no later than 15 calendar days after initial receipt of the information [21 CFR 312.32(c)(1)]; and (3) submitting annual progress reports [21 CFR 312.33].

Please forward all future communications concerning this IND in triplicate, identified by the above IND number, to the following address:

U.S. Postal Service/ Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Attention: Division Document Room, 8B-45
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, please call me at 301-827-6414.

Sincerely,

{See appended electronic signature page}

Lina AlJuburi, Pharm.D., M.S.
Regulatory Project Manager
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Lina Aljuburi
11/25/03 02:47:41 PM

EXHIBIT I

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202293

NDA ACKNOWLEDGMENT

Bristol-Myers Squibb
Attention: Amy A. Jennings, Ph.D.
Director, US/Global Regulatory Lead
5 Research Parkway
Wallingford, CT 06492-7660

Dear Dr. Jennings:

We have received your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Dapagliflozin tablet, 5mg and 10 mg

Date of Application: December 27, 2010

Date of Receipt: December 28, 2010

Our Reference Number: NDA 202293

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on **February 26, 2011** in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrinology Products
5901-B Ammendale Road

Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have any questions, call me at (301) 796-1940.

Sincerely,

{See appended electronic signature page}

Raymond Chiang, M.S.
Consumer Safety Officer
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RAYMOND S CHIANG
01/21/2011

EXHIBIT J

AS-002 Chronology Report

Common Drug Name DAPAGLIFLOZIN **From Date** 01-JAN-2003 **To Date** 10-JAN-2014
Country/Agency UNITED STATES OF AMERICA
Actual/Planned Status ACTUAL

Country/Agency UNITED STATES OF AMERICA
Initial Application Number 68,652
Initial Application Type INVES
Common Drug Name BMS-512148-05
Initial Application Title TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM)

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	20-NOV-2003	21-NOV-2003	INITIAL APPLICATION	SUBMISSION	PS TO FDA: INITIAL APPLICATION, TREATMENT OF TYPE 2 DIABETES MELLITUS (T2DM)
	21-NOV-2003	22-NOV-2003	CORRESPONDENCE	LETTER	FDA TO PS: FDA STAMP RETURN RECEIPT COPY FOR INITIAL APPLICATION.
	25-NOV-2003	02-DEC-2003	CORRESPONDENCE	LETTER	LA TO PS: FDA LTR. RE: RECEIPT OF IND68,652 ON 21-NOV-2003.
	15-DEC-2003	15-DEC-2003	CORRESPONDENCE	TELEPHONE	PL TO LA: TEL. CONT. REP. RE: IND 68,620 - STUDIES CAN PROCEED. IND 68,652 - REVIEW INCOMPLETE; 30-DAY REVIEW PERIOD ENDS 21-DEC.
	19-DEC-2003	19-DEC-2003	CORRESPONDENCE	TELEPHONE	PL TO LA: TEL. CONT. REP. RE: INITIATION OF PHASE I STUDY
	22-DEC-2003	22-DEC-2003	CORRESPONDENCE	TELEPHONE	PL TO LA: TEL. CONT. REP. RE: NO CLINICAL HOLD ISSUES, HOWEVER, QUESTIONS/COMMENTS COMING TO US FROM PHARM/TOX REVIEWER.
	23-DEC-2003	23-DEC-2003	CORRESPONDENCE	FAX	LA TO PL: FDA FAX RE: COMMENTS AND RECOMMENDATIONS AFTER COMPLETING PRECLINICAL PHARMACOLOGY REVIEW OF SUBMISSION
	23-DEC-2003	08-JAN-2004	CORRESPONDENCE	LETTER	DO TO PS: FDA LTR. RE: COMMENTS AND RECOMMENDATIONS AFTER COMPLETING PRECLINICAL PHARMACOLOGY REVIEW OF SUBMISSION
	23-FEB-2004	24-FEB-2004	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS TO DO: INFO. AMEND: PHARM/TOX., AMENDMENT.
	12-MAR-2004	13-MAR-2004	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS TO DO: PROT. AMEND.: PHARM/TOX RE: REVISED PROTOCOL 01 OF MB102001 INCORPORATING AMEND. 02.
	18-MAR-2004	19-MAR-2004	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS TO DO: INFO. AMEND.: PHARM/TOX RE: FULLY AUDITED FINAL REPORT OF ONE-MONTH TOXICITY STUDY.
	24-MAR-2004	25-MAR-2004	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS TO DO: INFO. AMEND.: PHARM/TOX RE: FINAL REPORT OF THIRTEEN-DAY ORAL RANGE-FINDING STUDY .
	20-MAY-2004	21-MAY-2004	INFO AMENDMENT -	SUBMISSION	PS TO DO: INFO. AMEND.: PHARM/TOX RE: TERMINATED STUDY REPORT DN02063.
	16-JUL-2004	17-JUL-2004	PHARM/TOX	SUBMISSION	RZ TO DO: INFO. AMEND.: CMC RE: IND amendment for a 2.5 mg capsule formulation and matching placebo
	16-JUL-2004	17-JUL-2004	INFO AMENDMENT -	SUBMISSION	PS TO DO: PROT. AMEND.: NEW PROTOCOL, NEW INVEST.; INFO. AMEND: CMC
	27-JUL-2004	03-AUG-2004	CMC	LETTER	DO TO PS: REQUEST FOR ADDITIONAL INFO. FOR AMEND. 007, DATED 16-JUL-04. PLEASE SUBMIT IRWIN SCREEN.
	23-AUG-2004	24-AUG-2004	PROT. AMEND.: NEW	SUBMISSION	PS TO DO: INFO. AMEND.: PHARM/TOX RE: DCN 930007883 AND 930007949.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	14-SEP-2004	15-SEP-2004	PROTOCOL	SUBMISSION	PS TO DO: RESPONSE TO FDA REQUEST FOR INFO. FOR AMEND. 007, DATED 16-JUL-04. RE: BMS ASSESSMENT OF NEUROTOXICITY IN LEU OF IRWIN SCREEN.
	21-SEP-2004	22-SEP-2004	CORRESPONDENCE	SUBMISSION	PS TO DO: INFO. AMEND.: PHARM/TOX, 930008139 V.1.O
	23-NOV-2004	24-NOV-2004	INFO AMENDMENT -	SUBMISSION	PS TO DO: IND SAFETY RPT.:INITIAL WRITTEN RPT., RE: NONCLINICAL IND SAFETY RPT., ADDENDUM TO INVESTIGATOR BROCHURE, STUDY DN04043.
	08-DEC-2004	09-DEC-2004	PHARM/TOX	SUBMISSION	PS TO DO: INFO. AMEND: PHARM/TOX, DN03102, DS04143.
07-FEB-2005	14-FEB-2005	15-FEB-2005	RESPONSE TO	SUBMISSION	PS TO DO: IND annual report FOR PERIOD 01-DEC-03 TO 30-NOV-04.
	23-FEB-2005	24-FEB-2005	REQUEST	SUBMISSION	PS TO DO: INFO. AMEND: PHARM/TOX, FINAL RPT'S, DN04052, DN04051.
	01-APR-2005	04-APR-2005	INFO AMENDMENT -	SUBMISSION	PS TO DO: PROTOCOL AMENDMENT - NEW PROTOCOL, NEW INVESTIGATOR; INFORMATION AMENDMENT - CHEMISTRY, MANUFACTURING & CONTROL RE: MB102-003
	25-APR-2005	25-APR-2005	PHARM/TOX	TELEPHONE	PS TO DY: TEL. CONTACT RE: INFORMATIONS REGARDING TOXCITY STUDIES.
	29-APR-2005	29-APR-2005	SAFETY REPORT:	TELEPHONE	PS TO LA: TEL. CONTACT RE: REQUEST FOR HUMAN PK DATA FOR THE SAD AND/OR THE MAD STUDIES MB102-001 AND/OR MB102-002.
	12-MAY-2005	12-MAY-2005	INITIAL/FOLLOW-UP	LETTER	DO TO PS: FDA LTR. REFER TO AMEND. DATED APRIL 1, 2005 (SERIAL#015) CONTAINING A NEW PROTOCOL, ENTITLED "A DOUBLE-BLIND, PLACEBO-CONTROLLED RANDOMIZED MULTIPLE-DOSE STUDE TO EVALUATE THE SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF BMS-512148 IN DIABETIC SUBJECTS."
	13-MAY-2005	16-MAY-2005	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS TO DO: PROTOCOL AMENDMENT - NEW INVESTIGATOR RE: MB102-003; OTHER - CHANGE OF INVESTIGATOR INFORMATION RE: MB102-001
	16-MAY-2005	17-MAY-2005	RESPONSE TO REQUEST	SUBMISSION	PS TO DO: RESPONSE TO FDA REQUEST IN REFERENCE TO INVESTIGATIONAL NEW DRUG APPLICATION FOR BMS-512148; ALSO REQUESTED HUMAN PK DATA FOR THE SAD (MB102-001) AND MAD (MB102-002) STUDIES.
	13-JUL-2005	14-JUL-2005	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS TO DO: PROTOCOL AMENDMENT - NEW INVESTIGATOR RE: MB102-003
	17-AUG-2005	18-AUG-2005	RESPONSE TO REQUEST	SUBMISSION	PS TO DO: RESPONSE TO FDA REQUEST FOR ADDITIONAL NON-CLINICAL INFORMATION AS WELL AS ALL HUMAN PK DATA FOR THE SAD (MB102-001) AND MAD (MB102-002) STUDIES.
	17-AUG-2005	18-AUG-2005	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS TO DO: PROTOCOL AMENDMENT - CHANGE IN PROTOCOL, NEW INVESTIGATOR RE: MB102-003
	01-SEP-2005	02-SEP-2005	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS TO DO: INFOR. AMEND. PHARM/TOX, 930009550, QUANTITATIVE DETERMINATION OF BMS-512148 AND ITS METABOLITES BMS-511926 IN MOUSE EDTA PLASMA BY LC/MS/MS.
	19-SEP-2005	20-SEP-2005	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS TO DO: PROTOCOL AMENDENT: NEW PROTOCOL, NEW INVESTIGATOR INFORMATION AMENDMENT:CMC RE: Amendment to IND 68,652.
	29-SEP-2005	30-SEP-2005	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS TO DO: PROTOCOL AMENDMENT: NEW PROTOCOL, NEW INVESTIGATOR INFORMATION AMENDMENT: CHEMISTRY, MANUFACTURING, AND CONTROL, Protocol MB102004.
	06-DEC-2005	07-DEC-2005	OTHER	SUBMISSION	PS TO DO: OTHER: REVISED INVESTIGATOR BROCHURE
	08-DEC-2005	09-DEC-2005	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS TO DO: Protocol Amendment: New Protocol, New Investigator Information Amendment: Chemistry, Manufacturing, and Control.
	15-DEC-2005	16-DEC-2005	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	PS TO DO: IND SAFETY REPORT: FOLLOW-UP TO A WRITTEN.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	22-DEC-2005	23-DEC-2005	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS TO DO : Protocol Amendment: New Protocol, NewInvestigator Information Amendment: Chemistry, Manufacturing, and Control.
	05-JAN-2006	06-JAN-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS TO DO: Protocol Amendment: New Investigator
	05-JAN-2006	06-JAN-2006	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS TO DO: INFORMATION AMENDMENT: PHARMACOLOGY/TOXICOLOGY
	03-FEB-2006	06-FEB-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS TO MP: PROTOCOL AMENDMENT: NEW INVESTIGATOR
	15-FEB-2006	16-MAR-2006	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Info Amend: Pharm/Toxi: Reference to Investigation New Drug for BMS-512148.
	16-FEB-2006	17-FEB-2006	ANNUAL REPORT	SUBMISSION	PS TO MP: ANNUAL REPORT for period 01-DEC-04 TO 30-NOV-05.
	21-FEB-2006	22-FEB-2006	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amendment - Change in Protocol re: MB102-008
	06-MAR-2006	07-MAR-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amend: New Investi., Other: Change of Investi. Info: MB102-008.
	15-MAR-2006	16-MAR-2006	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Information Amendment: Pharma/Toxic: Reference to Investigational New Drug Appl for BMS-512148.
	28-MAR-2006	29-MAR-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amendment: New Investigator, Other:Change of Investigator Info. Re: MB102008 and MB102004.
	07-APR-2006	10-APR-2006	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS to MP: Protocol Amendment: New Protocol, New Investigator Info Amend: CMC re: MB102007.
	19-APR-2006	20-APR-2006	OTHER	SUBMISSION	CL to MP: Other: Change in BMS Correspondent
	24-APR-2006	25-APR-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	CL to MP: Protocol Amendment: New Investigator re: Protocol MB102007 & MB102008.
	24-APR-2006	03-MAY-2006	CORRESPONDENCE	LETTER	MP to PS: FDA Ltr re: BMS-512148 Oral and reference to amendment submission dated 5-Jan-06/S#029 completed review with comments and recommendations.
	08-MAY-2006	09-MAY-2006	INFO AMENDMENT - PHARM/TOX	SUBMISSION	CL to MP: Information Amendment: Pharmacology/Toxicology re: Determination, Validation of Method for the Determination, and Quantitiative/Metabolite of BMS-512148 (SGLT2) and BMS-511926:
	16-MAY-2006	17-MAY-2006	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	CL to MP: Protocol Amendment: Change in Protocol re: Protocol MB102008
	17-MAY-2006	18-MAY-2006	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	CL to MP: Protocol Amendment: Change in Protocol re: Protocol MB102007
	01-JUN-2006	02-JUN-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	CL to MP: Protocol Amendment: New Investigator; Other: Change of Investigator Information re: BMS-512148 and Protocol MB102008.
	05-JUN-2006	06-JUN-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	CL to MP: Protocol Amendment 3: Change in Protocol re: Protocol MB102007: Amendment 3 is to correct a stmt incorporated into Amendment 2.
	10-JUL-2006	11-JUL-2006	CORRESPONDENCE	TELEPHONE	CL to LA: BMS Telephone Contact re: The time needed for the Agency to review Protocol MB102009 for the pilot study.
	12-JUL-2006	13-JUL-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	CL to MP: Protocol Amendment: New Investigator; Other: Change of Investigtor Information re: Protocol Study MB102008.
	26-JUL-2006	27-JUL-2006	OTHER	SUBMISSION	CL to MP: Other: Request for Protocol Review re: BMS wish to submit the following draft clinical protocol for review and comment by the FDA. Protocol MB102009.
	26-JUL-2006	27-JUL-2006	CORRESPONDENCE	TELEPHONE	CL to LA: BMS Telephone Contact re: A draft protocol for the pilot study MB102009 is on the way to the FDA.
	15-AUG-2006	16-AUG-2006	OTHER	SUBMISSION	PS to MP: Other: Change in Correspondent.
	23-AUG-2006	24-AUG-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amendment: New Investigator; Other: Change of Investigator Information re: Protocol MB102008.
	18-SEP-2006	19-SEP-2006	INFO AMENDMENT - CLINICAL	SUBMISSION	PS to MP: Information Amendment: Clinical for MB102-001.
	22-SEP-2006	22-SEP-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amendment: New Investigator; Other: Change of Investigator Information re: Protocol MB102008.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	25-SEP-2006	26-SEP-2006	OTHER	SUBMISSION	PS to MP: Other: Responses to FDA Review; Protocol Amendment: New Protocol, New Investigator; Information Amendment: CMC re: The response to the Agency's review of Protocol MB102-009.
	06-OCT-2006	09-OCT-2006	GENERAL CORRESPONDENCE	SUBMISSION	PS to MP: General Correspondence re: BMS is notifying the Division of our plans to submit carcinogenicity protocols for BMS-512148 for review.
	25-OCT-2006	26-OCT-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amendment: New Investigator re: Protocol Study MB102009.
	02-NOV-2006	02-NOV-2006	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amendment: Change in Protocol re: Amendment #2, dated 17-Oct-06 and Revised Protocol 1, dated 24-Oct-06, for Protocol MB102009.
	06-NOV-2006	07-NOV-2006	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Information Amendment: Pharmacology/Toxicology re: BMS-512148, BMS-512148, and BMS-512148.
	06-NOV-2006	07-NOV-2006	OTHER	SUBMISSION	PS to MP: Other: Request for Special Protocol Assessment.
	06-NOV-2006	07-NOV-2006	OTHER	SUBMISSION	PS to MP: Other: Request for Special Protocol Assessment re: BMS-512148.
	15-NOV-2006	16-NOV-2006	CORRESPONDENCE	LETTER	LA to PS: FDA ltr. re: acknowledgement of receipt of November 6, 2006 requests, serial numbers 056 & 057, on November 7, 2006. Upon completion of FDA review of these submissions, a written response will be provided within 45 days of receipt.
	27-NOV-2006	28-NOV-2006	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amend.: New Investigator for MB102009
	27-NOV-2006	28-NOV-2006	RESPONSE TO REQUEST	SUBMISSION	PS to MP: Response to FDA Request for Info. in ref. to comments and recommendations
	06-DEC-2006	07-DEC-2006	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Info. Amend.: Pharm/Tox; in ref. to IND app. for BMS-512148 IND 68,652 wishing to amend final reports of study no. MBA00131 (doc. control # 930014671), MBA00132 (doc. control # 930016284), 930016600, & MBA00133 (doc. control # 930015706
	14-DEC-2006	15-DEC-2006	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Info. Amend.: Pharm./Tox.; in re. to BMS-512148 (Study # 1212/0246) DCN # 930017980
	15-DEC-2006	18-DEC-2006	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amed.: Change in Protocol in ref. to BMS-512148 IND 68,652; MB102007 "The Pharmacodynamics, pharmacokinetics and safety of BMS-512148
	21-DEC-2006	22-DEC-2006	TRANSFER OF OBLIGATIONS	SUBMISSION	PS to MP: Other: Transfer of Obligations to a CRO; re BMS-512148; in accordance with 21CFR & 312.52(a), notification provided that part of the sponser obligations have been transferred to a CRO for studies conducted under 68,652; refer to attachment 1
	02-JAN-2007	03-JAN-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amend.: Change in Protocol; re: IND app. for BMS-512148; Providing Amend. 3 dated 6-Dec.-06 and revised protocol 2 dated 7-Dec.-06 for MB102009
	03-JAN-2007	04-JAN-2007	INFO AMENDMENT - CLINICAL	SUBMISSION	PS to MP: Info. Amend.: Clinical; re: IND app. for BMS-512148 study # MB102006 dated 13-Nov.-06 DCN # 930018203
	04-JAN-2007	05-JAN-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amend.: New Investigator/Other: COI Info.: re: IND app. for BMS-512148, protocol # MB102009 & MB102008
	11-JAN-2007	12-JAN-2007	OTHER	SUBMISSION	PS to MP: Other - Revised Investigator Brochure
	25-JAN-2007	26-JAN-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amend.: Change in Protocol; re: IND app. for BMS-512148, protocol MB102007 originally submitted 7-April-06 (serial # 0037) revised 15-Dec.-06 (serial # 0062)
	25-JAN-2007	26-JAN-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amend.: Change in Protocol; re: IND app. for BMS-512148, protocol MB102009 originally submitted 25-Sept.-06 (serial # 0051) & revised 2-Jan.-07 (serial # 0064)
	29-JAN-2007	30-JAN-2007	INFO AMENDMENT - CLINICAL	SUBMISSION	PS to MP: Information Amendment - Clinical re: Bristol Myers Squibb Final Clinical Study Report (MB102002), dated Dec 05, 2006.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	31-JAN-2007	01-FEB-2007	INFO AMENDMENT - CLINICAL	SUBMISSION	PS to MP: Info. Amend.: Clincial; re: IND app. for BMS-512148; study MB102003 dates 12/21/06, 2/22/06, 6/13/06, & 9/15/06
	01-FEB-2007	02-FEB-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amend.: New Investigator/Other: Change of Investigator Info; re: IND app. for BMS-512148, study MB102008 & MB102009
	13-FEB-2007	14-FEB-2007	INFO AMENDMENT - CLINICAL	SUBMISSION	PS to MP: Info. Amend.: Clinical; re: IND app. for BMS-512148; study MB102004 (10-Jan.-07) DCN 930019215; MB102004 (19-Sept.-06) DCN 930017835; & 6108-534 (11-Sept.-06) DCN 930017657
	13-FEB-2007	14-FEB-2007	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Info. Amend.: Pharm/Tox; re: IND app. for BMS-512148; study MBA00260 (DCN 930018804) & BMS-511926 (DCN 930016600)
	15-FEB-2007	16-FEB-2007	ANNUAL REPORT	SUBMISSION	PS to MP: Annual Report covers the period 1-Dec.05 to 30-Nov.-06
	28-FEB-2007	01-MAR-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amendment: New Investigator; Other: Change of Investigator Information re: Protocol MB102009 and MB102008.
	28-FEB-2007	01-MAR-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amendment: Change in Protocol re: Administrative Ltr. for the following Protocol MB102008.
	09-MAR-2007	12-MAR-2007	INFO AMENDMENT - CLINICAL	SUBMISSION	PS to MP: Info. Amend.: Clinical; re: IND app. for BMS-512148; study MB102005 (DCN 930020173) & study 6108-529 (DCN 930016101)
	26-MAR-2007	26-MAR-2007	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Info. Amend.: Pharm/Tox; re: IND app. for BMS-512148, study #DN05081 (7-March-07) DCN #930018536
	29-MAR-2007	29-MAR-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amendment: New Investigator will be participating in the following study: MB102009.
	11-MAY-2007	14-MAY-2007	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS to MP: Protocol Amendment: New Protocol, New Investigator; Information Amendment: CMC re: Protocol MB102017 and Amendment 1, dated 17-Apr-07.
	06-JUN-2007	07-JUN-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amend.: Change in Protocol; re: IND app. for BMS-512148, protocol MB102009; DCN # 930021815 & 930016810
	14-JUN-2007	15-JUN-2007	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	PS to MP: Other: Change of Investigator Info.; re: IND app. for BMS-512148, protocol MB102009
	02-JUL-2007	03-JUL-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amend.: Change in Protocol; re: IND app. for BMS-512148, protocol MB102007, DCN #'s 930022238 & 930014094
	03-JUL-2007	05-JUL-2007	OTHER	SUBMISSION	PS to MP: Other: Request for Info.; re: IND app. for BMS-512148
	12-JUL-2007	13-JUL-2007	OTHER	SUBMISSION	PS to MP: Other: Request End of Phase 2 Mtg.; re: IND app. for BMS-512148, to review the results of completed clinical trials & relevant preclinical studies supporting the proposed Phase 3 clinical dev. program
	16-JUL-2007	17-JUL-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PS to MP: Protocol Amend.: Change in Protocol; re: providing admin. letter dated 20-June-07 for protocol MB102017 address purpose to the change in Medical Monitor
	18-JUL-2007	19-JUL-2007	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	PS to MP: Other: Change of Investigator Info.; re: protocol MB102007 & MB102009
	19-JUL-2007	20-JUL-2007	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS to MP: Protocol Amend.: New Protocol, New Investigator/Info. Amend.: CMC; re: protocol MB102018 (DCN #930022701)
	24-JUL-2007	25-JUL-2007	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Info. Amend.: Pharm/Tox; re: Study DN04103 (DCN 930020221) study DN06019 (DCN 930021868)
	01-AUG-2007	26-JUL-2007	CORRESPONDENCE	SUBMISSION	JM To PS.Correspondence:Letter. FDA is encouraging BMS to submit another End-of-Phase 2 meeting request after BMS submits the study report for study MB102-008.
	06-AUG-2007	07-AUG-2007	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PS to MP: Info. Amend.: Pharm/Tox; re: study 930005313 & 93017615
	06-AUG-2007	07-AUG-2007	OTHER	SUBMISSION	PS to MP: Other: Request End of Phase 2 Mtg.; re: resubmitting the Type B end-of-phase 2 mtg. request to review the results of completed clin. trials & relevant nonclin. studies supporting the proposed phase 3 clin. dev. program with BMS-512148

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	09-AUG-2007	10-AUG-2007	OTHER	SUBMISSION	PS to MP: General Correspondence: End of Phase 2 Briefing Package; re: mtg for Sept. 11, 2007 in add. to the formal submission of 3 copies to the FDA's CDR, BMS is also providing 15 desk copies directly to the att. of JM
	15-AUG-2007	16-AUG-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	PS to MP: Protocol Amend.: New Investigator/Other: Change of Investigator Info.; re: protocol MB102009 & MB102007
	31-AUG-2007	30-AUG-2007	INFO AMENDMENT - CLINICAL	SUBMISSION	PS to MP: Info. Amend: Clinical: Included in this submission is a TRANSFER OF OBLIGATION to a contract research organization for the following ongoing studies: MB102-007, MB102-008, MB102-009, MB102-017, and MB102-018. CRO/Vendor Accenture Services Pvt. Ltd
	05-SEP-2007	06-SEP-2007	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	PS to MP: IND Safety Report: Initial Written Report; re: report #13882857/loss of consciousness; study MB102009
	07-SEP-2007	07-SEP-2007	CORRESPONDENCE	EMAIL	MP to PS: Corres. E-mail. Email containing Pre-Meeting Minutes, and an attached letter that provides extensive comments on the QTc Study.
	07-SEP-2007	14-SEP-2007	CORRESPONDENCE	LETTER	PS to MP. Corres. Letter.Refering to the BMS Amendment dated 19-July-2007 containing a new protocol MB102-018. FDA has completed the review of BMS submission and has the following comments and request for additional Information.
	10-SEP-2007	11-SEP-2007	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	PS to MP: Prot.Amend: New Protocol, New Investigator, Info Amend CMC, and Info Amend: Clinical. We now wish to Amend our IND with the following info for study MB102-013 (DCN # 930022086 v.1.0 & 930022071 v.1.0) New Investigator at site (019) CMC INFO. Study MB102-013 (DCN 930023389 v 2.0) Info Amend:Clincal Included in this submission is a TRANSFER OF OBLIGATION to a contract research organization. CRO/Vendor Accenture Services Pvt. Ltd.
	13-SEP-2007	14-SEP-2007	OTHER	SUBMISSION	MW to MP: Other Change in Correspondent.
	14-SEP-2007	17-SEP-2007	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP: Prot. Amend: New Protocol, we are providing Amendment 1 dated 11-July-2007 (DCN 930022045 v1.0). New Invest: for MB102-014. Info Amend CMC. BMS will provide the following clinical supplies to be used in the conduct of Protocol MB102-014. Info Amend: Clinical. Included in this submission is a TRANSFER OF OBLIGATION to a contract research Org.
	19-SEP-2007	20-SEP-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP:Prot. Amend: New Invetigator & Other: Change of Investogator Info. Documentation is attached for the new investigators who will be participating in the following studies MB102-013, MB102-014. Other Change: Changes to previously submitted investigator info are provided in a summary table for the following protocol: MB102-008.
	25-SEP-2007	26-SEP-2007	INFO AMENDMENT - PHARM/TOX	SUBMISSION	MW to MP: Info Amend: Pharm/Tox. We now wish to Amend our IND with the following two final Reports. Study DN05030 and DN05031 (DCN # 930023449 v1.0 & 930023450 v1.0)
	25-SEP-2007	26-SEP-2007	OTHER	SUBMISSION	MW to MP: Other: Meeting Minutes. Enclosed within is a copy of BMS minutes and slides from the meeting held 11-Sept-2007.
	27-SEP-2007	28-SEP-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW to MP. Prot. Amend: Change in Prot. We are now providing an Administrative Letter for the following protocol MB102-009. The Administrative letter dated 06-Sept-07 informs all investigators currently participating in MB102-009 of a change in protocol Manager.
	11-OCT-2007	18-OCT-2007	CORRESPONDENCE	SUBMISSION	JM to PS. Correspondence: Letter. We also refer to the End-Of-Phase 2 meeting between representatives of BMS and AstraZeneca and the FDA 11-Sept-2007. Included in this letter are the offical minutes of that meeting held on 11-Sept-2007.
	17-OCT-2007	18-OCT-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP:Prot Amend: New Investigator. Documentation is attached for the new investigators who will be participating in the following studies: MB102-009, MB102-013,and MB102-014.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	31-OCT-2007	01-NOV-2007	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP. Protocol Amend: New Protocol and Investigator. Info Amend: CMC.We now wish to Amend our IND with the following protocols (DCN 930023471 v1.0) and Investigator Info for MB102-019. Info Amend: CMC concerning Dapagliflozin Flim Coated Tablets 10 mg.
	07-NOV-2007	08-NOV-2007	OTHER	SUBMISSION	MW ro MP. Other: Revised Investigator Brochure. We are now providing and updated Investogator's Brochure dated 23-Oct-2007.
	15-NOV-2007	16-NOV-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP. Prot:Amend: New Investigator. Documentation is attached for the new investigators who will be participating in the following studies: MB102-013 and MB102-014.
	21-NOV-2007	22-NOV-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW to MP. Prot Amend: Change in Protocol. BMS is now providing site specific amendments for the following protocols: MB102-013(DCN 930023641 v1.0), MB102-014,(DCN 930023644 v1.0).
	21-NOV-2007	22-NOV-2007	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP. Prot Amend: New Protocol and New Investigator. Info Amend: CMC. We now wish to amend our IND with the following information on protocol MB102-026. Also providing investigator info for conducting the following studies MB102-026. BMS is now providing clinical supplies to be used in the conduct of protocol MB102-026.
	05-DEC-2007	06-DEC-2007	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW to MP. Prot Amend: Change in Protocol. We are now providing Amendment 6, dated 17-Oct-2007(DCN 930024515 v1.0) and Revised Protocol 4, dated 17-Oct-2007.(DCN 930014094 v6.0)
	11-DEC-2007	12-DEC-2007	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP. Prot Amend: New Investigator and Other: Change of Investigator Info. Documentation is provided for the New Investigators participating in the following studies MB102-013 and MB102-014, Other Changes submitted for investigators participating in the following protocols: MB102-007 and MB102-013.
	13-DEC-2007	14-DEC-2007	INFO AMENDMENT - CLINICAL	SUBMISSION	MW to MP: Information Amendment - Clinical re: transfer of obligations to a CRO for the protocols - MB102004, MB102005, MB102007 and MB102008, MB102009, MB102013, MB102014, MB102017, MB102018, MB12019 and MB102026.
	17-DEC-2007	18-DEC-2007	OTHER	SUBMISSION	MW to MP: Other - Request for meeting/background document to follow-up to the 11 Sep 2007 end-f-phase 2 (EoP2) mtg. held w/ the Division to discuss the proposed development program for dapagliflozin and to the Division's meeting minutes dated 11 October 2007.
	20-DEC-2007	21-DEC-2007	OTHER	SUBMISSION	MW to MP. Other Response to FDA Comments. Provied with in are responses to the Division's comments dated 7-Sept-2007. We have revised the protocol for Study MB102-018. Protocol Amend: Change in Investigator and New Investigator Info is being submitted for Protocol MB102-018. Info Amend: CMC. Info Amend: Clinical. We are now providing notification that part of the sponsor obligations have been transferred to a CRO for the Protocol MB102-018.
	27-DEC-2007	08-JAN-2008	CORRESPONDENCE	LETTER	JM to MW. Corres. Letter. FDA has concluded that the meeting is unnecessary.
	07-JAN-2008	08-JAN-2008	INFO AMENDMENT - CLINICAL	SUBMISSION	MW TO MP: PROVIDING INFO. FOR CLINICAL PROT'S MB102013, 930033171 & MB102014, 930033195.
	07-JAN-2008	08-JAN-2008	INFO AMENDMENT - CLINICAL	SUBMISSION	MW TO MP: PROVIDING INFO. FOR PROT'S MB102013, 930033171 & MB102014, 930033195.
	09-JAN-2008	10-JAN-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP. Prot Amend: New Investigator. Documentation is attached for the new investigators who will be participating in the following studies: Protocol MB102-013 and MB102-014.
	16-JAN-2008	17-JAN-2008	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW TO MP: F/U SAFETY RPT. # 14437453.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	18-JAN-2008	22-JAN-2008	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW to MP. Protocol Amend: Change in Prtotocol. We are now providing Amendment 03 both dated 20-Dec-2007 (DCN 930025259 v1.0 930025378 v1.0) and Revised Protocols 01 both also dated 20-Dec-2007 for the following studies: Protocol MB102-013 and MB102-014.
	08-FEB-2008	11-FEB-2008	INFO AMENDMENT - PHARM/TOX	SUBMISSION	MW to MP. Info Amend: Pharm/Tox.We wish to amend our IND with the following final report: During a routine Data Clean-Up, it was discovered that Study DN06059 was inadvertently not submitted to the Agency. We are now providing the report contained here with in. (DCN 930019585v.1.0)
	14-FEB-2008	15-FEB-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP. Prot Amend: New Investigator. Other: Change in Investigator Info. Documentation is attached for New Investigators and changes in previously submitted investigators who are participating in the following studies: Protocol MB102-013 and MB102-014.
	15-FEB-2008	19-FEB-2008	ANNUAL REPORT	SUBMISSION	MW to MP. Annual Report. The reporting interval for this IND is 1-Dec-200 6 through 30-Nov-2007.
	27-FEB-2008	28-FEB-2008	OTHER	SUBMISSION	MW to MP. Other: Clinical, NON IND Protocols. We now wish to provide copies of the following Phase 3 clinical protocols for informational purpose. Protocol MB102-022 (AZ study Number D1690C0004)(DCN 930026471 v2.0), Protocol MB102-028 (AZ study Number D1690C00005)(DCN 930025945 v1.0), and Protocol MB102-033 (AZ Study Number D1690C00006).(DCN 930025956 2.0)
	29-FEB-2008	05-MAR-2008	CORRESPONDENCE	LETTER	FDA to MW. Corres. Referring to BMS Amendment dated 17-Dec-2007, containing a request for a meeting to discuss dapagliflozin. Request for meeting is denied but a written respose to questions is now being provided.
	29-FEB-2008	07-MAR-2008	CORRESPONDENCE	LETTER	FDA PROVIDING WRITTEN RESPONSE TO QUESTIONS IN AMEND. DATED 17-DEC-07.
	07-MAR-2008	10-MAR-2008	GENERAL CORRESPONDENCE	SUBMISSION	MW to MP. General Corres: Request for Concurrence. Upon further reflection, the sponsor now wishes to take the oppurtunity to share with the FDA, its current views regarding the responses provided by the division in relation to two topics contained within the responses to Question 4 of the EoP2 Breifing Document.
	13-MAR-2008	14-MAR-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP. Prot Amend New Investigator. Other: Change of Investigator Info. Documentation is attached for new investigators and previously submitted investigators who will be participating in the following studies: MB102-013 and MB102-014.
	04-APR-2008	07-APR-2008	INFO AMENDMENT - CLINICAL	SUBMISSION	BMS PROVIDING REPORT OF MODELING AND SIMULAION DATA PER DOP2 MTG. RE: 2.5,5 & 10 MG DOSES CHOSEN IN PHASE 3 PROGRAM. 930026100, 1.0.
	04-APR-2008	07-APR-2008	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MB102-027; NEW INVESTIGATOR; INFO. AMEND: CMC. 930025772, 1.0.
	09-APR-2008	10-APR-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	INCLUDES MB102007, 013, 014, 009
	24-APR-2008	25-APR-2008	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP: Protocol Amendment: New protocol, New Investigator re: MB102021, Info. Amendment: CMC - re: teh clinical supplies to be used in the conduct of Protocol MB102021, Info Amendment: Clinical re: Transfer of obligations to a CRO (Accenture Services Pvt. Ltd.) for this study.
	30-APR-2008	01-MAY-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	NEW & COI MB102007, 013, 014.
	21-MAY-2008	22-MAY-2008	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW to MP: Protocol Amendment - Change in protocol re: MB102013 & MB102014. Other - Transfer of obligations to a CRO for the protocols MB102013 &B102014
	30-MAY-2008	02-JUN-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MB102013, 021
	18-JUN-2008	19-JUN-2008	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP: Protocol Amend.: New Protocol, New Inv, Info Amend.: CMC & Info Amend. Clinical for MB102029
	02-JUL-2008	03-JUL-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW TO MP: NEW INVESTIGATOR INFO. MB102-021, 029.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	15-JUL-2008	16-JUL-2008	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW TO MP: NEW PROT., NEW INVESTIGATOR; INFO. AMEND: CMC, INFO. AMEND: CLINICAL; MB102030, DCN 930027721, 930027707.
	30-JUL-2008	31-JUL-2008	GENERAL CORRESPONDENCE	SUBMISSION	MW to MP: General Correspondence to ensure the Division that an evaluation of available blinded & unblinded safety data was conducted in order to support the conduct of Study MB102021.
	31-JUL-2008	01-AUG-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW TO MP: MB102021, 029, 030.
	06-AUG-2008	07-AUG-2008	OTHER	SUBMISSION	PC TO MP: CMC-TYPE B MTG. REQUEST FOR OCT. 7,8, OR 9, 2008.
	08-AUG-2008	11-AUG-2008	INFO AMENDMENT - CLINICAL	SUBMISSION	MW TO MP: NOTIFICATION THAT PART OF SPONSOR OBLIGATIONS TRANSFERRED TO CRO FOR PROTOCOLS MB102021, 029, 030.
	13-AUG-2008	14-AUG-2008	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW TO MP: MB102007, ADMIN. LTR. 04, 930026400; AMEND. 08, 930027929; AMEND. 09, 930029026; AND REVISED PROT. 06, 930014094.
	19-AUG-2008	20-AUG-2008	OTHER	SUBMISSION	MW to MP: SAP re: clinical study MB102009. The database lock for Study MB102009 is targeted to occur by Aug 22, 2008.
	22-AUG-2008	25-AUG-2008	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW TO MP: MB102033, NEW INVESTIGATOR, INFO. AMEND: CMC; 930025956.
	28-AUG-2008	29-AUG-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW TO MP: NEW & COI - MB102-007, 014, 029, 030.
	29-AUG-2008	01-SEP-2008	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW TO MP: MB102032, INFO. AMEND: CMC, INFO. AMEND: CLINICAL; 930029252, 930028992 & 930030071.
	02-SEP-2008	03-SEP-2008	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW TO MP: INITIAL WRITTEN RPT. # 14306955.
	03-SEP-2008	04-SEP-2008	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW TO MP: MB102020, INFO. AMEND: CMC, INFO. AMEND: CLINICAL, 930029300.
	05-SEP-2008	08-SEP-2008	OTHER	SUBMISSION	PC to MP: Briefing doc. for the CMC End-of-Phase II mtg. scheduled for Oct 9, 2008.
	25-SEP-2008	26-SEP-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP: Prot. Amendment: New Inv. re: MB102029, MB102030; COI re: MB102007, MB102013, MB102014, MB102027 & MB102030.
	03-OCT-2008	06-OCT-2008	OTHER	SUBMISSION	MW to MP: Letter authorizing DMEP to reference BMS ' IND 68,652 for Dapagliflozin (BMS-512148) in support of the clinical protocol, IND 102,811; that will be submitted by Dr.Ralph DeFronzo from University of Texas Health Center.
	07-OCT-2008	07-OCT-2008	CORRESPONDENCE	EMAIL	JM to MW: FDA email re: comments on protocols MB102030 & MB102033.
	07-OCT-2008	07-OCT-2008	CORRESPONDENCE	EMAIL	MW to JM: FDA email re: request for ECAC comment , in order to obtain a rapid agreement for the ongoing 104-week carcinogenicity study (DN06073).
	08-OCT-2008	08-OCT-2008	CORRESPONDENCE	EMAIL	MW to JM: FDA email re: ECAC recommendations on BMS' proposal for changes to the ongoing carcinogenecity study under IND 68,652.
	15-OCT-2008	16-OCT-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP: Inv.documentation for new investigators particpating in the protocols - MB102029, MB102030, MB102032 & changes to previously submitted inv info for the protocol MB102009.
	16-OCT-2008	17-OCT-2008	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW to MP: Initial written rpt. for Urinary tract infection, Rpt. No. 14358089.
	22-OCT-2008	23-OCT-2008	OTHER	SUBMISSION	MW to MP: Response to the Agency's comments received Oct 7, 2008. Also included for the Agency's review & comment is the Core Statistical Analysis Plan for the dapagliflozin clinical program.
	07-NOV-2008	10-NOV-2008	OTHER	SUBMISSION	MW to MP: Response to the Agency's comments received on Oct 24, 2008. The core SAP for dapagliflozin clinical program is referenced in this response & was previously provided on OCt 22, 2008.
	12-NOV-2008	13-NOV-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	NEW & COI - MB102029, 030, 032, 021.
	21-NOV-2008	24-NOV-2008	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW TO MPI INITIAL SAFETY RPT. # 14408983.
	25-NOV-2008	26-NOV-2008	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW to MP: Initial written rpt. re: Rpt. No. 14404388.
	25-NOV-2008	26-NOV-2008	GENERAL CORRESPONDENCE	SUBMISSION	MW to MP: General correspondence submitted for transparency in regard to a recently discovered error in a specific packaging order of the randomized treatment for study D1690C00006.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	26-NOV-2008	27-NOV-2008	OTHER	SUBMISSION	PC to MP: CMC request for FDA comment on the modified dissolution method to support development of dapagliflozin products.
	01-DEC-2008	03-DEC-2008	CORRESPONDENCE	EMAIL	MULTI. EMAIL CONTACT (DEC. 1 & 3) RE: STATUS ON REVIEW OF PROPOSED CORE STATISTICAL ANALYSIS PLAN (CORE SAP)
	03-DEC-2008	04-DEC-2008	INFO AMENDMENT - PHARM/TOX	SUBMISSION	PROVIDING FINAL RPT. 930032019.
	05-DEC-2008	08-DEC-2008	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW TO MP: PROVIDING DOCUMENTATION FOR PROT. MB102029, 930032307, 930014094.
	08-DEC-2008	09-DEC-2008	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	PROVIDING DOCUMENTATION FOR PROT. MB102030, 930031588, 930027721.
	10-DEC-2008	11-DEC-2008	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW TO MP: NEW & COI - MB102029, 032.
	15-DEC-2008	16-DEC-2008	INFO AMENDMENT - CLINICAL	SUBMISSION	MW TO MP: PROVIDING DOCUMENTATION FOR IB 930005487.
	19-DEC-2008	22-DEC-2008	INFO AMENDMENT - CLINICAL	SUBMISSION	MW TO MP: PROVIDING INFO. RE: CONDUCT OF PROT. MB102029, 930031482.
	19-DEC-2008	22-DEC-2008	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW TO MP: PROVIDING DOCUMENTATION FOR PROT. MB102021, 930030893, 930025907.
	22-DEC-2008	23-DEC-2008	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW TO MP: INITIAL SAFETY RPT. # 14437453.
	06-JAN-2009	07-JAN-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW TO MP: F/U SAFETY RPT. # 14437453
	15-JAN-2009	16-JAN-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW TO MP: MB102-029, 032.
	05-FEB-2009	06-FEB-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP: Investigator documentation for new investigators particpating in the protocols MB102020, MB102029, MB102032.
	11-FEB-2009	12-FEB-2009	INFO AMENDMENT - PHARM/TOX	SUBMISSION	MW to MP: Final report for Study DN08040, DCN 930032339
	12-FEB-2009	19-FEB-2009	CORRESPONDENCE	LETTER	MP to MW: FDA letter re: confirmation of receipt of safety reports. FDA requested BMS to submit additional information within 3 weeks of receipt of this letter.
	13-FEB-2009	13-FEB-2009	CORRESPONDENCE	EMAIL	MW to JM: FDA email re: IND 68652 SN0173 - current adjudication charter for Dapa
	13-FEB-2009	16-FEB-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW to MP: Initial written rpt. re: Rpt. No. 14499750.
	13-FEB-2009	16-FEB-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	MW to MP: Includes currently active version (v 2.1) of the CEC, Charter/Manual of Operations Dapaglifozin pgm, Adjudication charter, Request for comment.
	13-FEB-2009	16-FEB-2009	ANNUAL REPORT	SUBMISSION	MW to MP: IND Annual Report for the period 12/1/2007 to 11/30/2008.
	19-FEB-2009	20-FEB-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP: Revised protocol 1 to MB102036. Info. Amendment: CMC for the protocol MB102036, Info. Amendment: Clinical - transfer of obligations to a CRO.
	23-FEB-2009	24-FEB-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW to MP: F/U #1 to a written rpt. re: Rpt. No. 14499750.
	24-FEB-2009	25-FEB-2009	CORRESPONDENCE	EMAIL	MW to JM: FDA email re: DMEP's request for information.
	26-FEB-2009	26-FEB-2009	CORRESPONDENCE	EMAIL	MW to JM: F/U on DMEP's request for information on serious adverse events
	26-FEB-2009	27-FEB-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	MW to MP: Completed clinical study report re: MB102026 dated Feb. 9, 2009.
	27-FEB-2009	28-FEB-2009	GENERAL CORRESPONDENCE	SUBMISSION	MW to MP: Request for waiver from requirements of 21 CFR 312.120 (b). Final clinical study report for protocol MB102008.
	02-MAR-2009	03-MAR-2009	CORRESPONDENCE	EMAIL	JM to MW: FDA confirmation to update BMS on the status of FDA review.
	03-MAR-2009	04-MAR-2009	CORRESPONDENCE	EMAIL	MW to JM: FDA email. BMS sent a thank you email for the confirmation
	04-MAR-2009	04-MAR-2009	CORRESPONDENCE	EMAIL	JM to MW: IND 68,652 Dapagliflozin - Revised Dissolution method.
	04-MAR-2009	05-MAR-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	MW to MP: Completed clinical study report MB102019 dated Nov 18, 2008.
	06-MAR-2009	09-MAR-2009	GENERAL CORRESPONDENCE	SUBMISSION	MW to MP: General correspondence re: the protocol AZ Study D1690C00006, this study is being conducted by our development partner, AZ
	09-MAR-2009	19-MAR-2009	CORRESPONDENCE	SUBMISSION	MP to MW: FDA letter requesting a written response with additional information on the Amendment dated Feb. 26, 2009 containing the report for Study MB102026.
	11-MAR-2009	12-MAR-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW to MP: Initial written rpt. re: Balanoposthitis, Rpt. No. 14524623.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	12-MAR-2009	13-MAR-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP: Investigator documentation for the new investigators participating in the protocols MB102029, MB102032. Updates to investigator information for the protocols MB102013, MB102021, MB102029, MB102030, MB102032, MB102036.
	12-MAR-2009	13-MAR-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW to MP: Initial written rpt. re: Report No. 14526917.
	13-MAR-2009	16-MAR-2009	RESPONSE TO REQUEST	SUBMISSION	MW to MP: Response to FDA request for a summary of the safety information.
	16-MAR-2009	17-MAR-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP: New protocol and New investigator info. re: MB102034. Info. on clinical supplies to be used in the conduct of protocol MB102034.
	20-MAR-2009	23-MAR-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP: New Protocol and New Investigator information for MB102045. Clinical supplies to be used in the conduct of protocol MB102045.. Transfer of obligations to a CRO for the conduct of protocol MB102045.
	25-MAR-2009	26-MAR-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	MW to MP: New Protocol and New Investigator information for MB102037, Info. on clinical supplies to be used in the conduct of protocol MB102037, transfer of obligations to a CRO for the conduct of protocol MB102037.
	30-MAR-2009	31-MAR-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW to MP: F/U#1 to a written report re: Pneumonia, Rpt. No.14526917.
	14-APR-2009	21-APR-2009	CORRESPONDENCE	LETTER	MP to MW: Letter from the FDA granting waiver to the specific sections of the CFR requirements (312.120(b)(2) and 312.120(b)(7)) and limited to the single completed study for the protocol MB102008.
	17-APR-2009	20-APR-2009	GENERAL CORRESPONDENCE	SUBMISSION	MW to MP: Correspondence in regard to recently acquired info. re: clinical investigator, Christopher Chappel, MD, who has been involved with 2 BMS-sponsored studies in the clinical devlopment program for Dapagliflozin.
	21-APR-2009	21-APR-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW to MP: Inv. documentation for new investigators particpating in the protocols - MB102029, MB102030, MB102034. Updates to inv. info. for the protocols - MB102013, MB102014, MB102021, MB1020298, MB102030, MB102034.
	22-APR-2009	23-APR-2009	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	MW to MP: Amendment 02 dated 20-Feb-2009 (DCN 930035639) & Revised Protocol 02 dated 20-Feb-2009 (DCN 930025956)
	01-MAY-2009	01-MAY-2009	GENERAL CORRESPONDENCE	SUBMISSION	MW TO MP: BMS PROVIDING CLINICAL INFO. IN SUPPORT OF AMENDED STUDY MB102020, INCLUDING PROD. CHARACTERISTICS, PKG. LBL'G, CERT. OF ANALYSIS AND PO FOR INUTEST.
	04-MAY-2009	04-MAY-2009	CORRESPONDENCE	SUBMISSION	MW TO JM: BMS PROVIDING ELECTRONIC VERSION OF SUBMISSION IN SUPPORT OF MB102020, DATED 01-MAY-09 (SN0192) IN PDF. TO HELP FACILITATE REVIEW.
	05-MAY-2009	05-MAY-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	MW TO MP: INITIAL SAFETY REPORT # 14599468
	06-MAY-2009	06-MAY-2009	OTHER	SUBMISSION	MW TO MP: AMENDED CORE STATISTICAL ANALYSIS PLAN (930031482) ORIGINALLY SENT 22-OCT-2008
	14-MAY-2009	14-MAY-2009	GENERAL CORRESPONDENCE	SUBMISSION	MW TO MP: RESPONSE TO FDA REQUEST FOR INFORMATION DATED 09-MAR-2009 RE: STUDY MB102026.
	15-MAY-2009	15-MAY-2009	CORRESPONDENCE	EMAIL	MW TO JM: BMS PROVIDING ELECTRONIC COPY OF RESPONSE TO FDA RE: CK LEVEL FILED 14-MAY-09, IN PDF. FORMAT.
	15-MAY-2009	22-MAY-2009	CORRESPONDENCE	LETTER	MP TO MW: FDA PROVIDING COMMENTS AND REQUESTS FOR ADD'L INFO. RE: AMENDMENT DATED 01-MAY-09, FOR STUDY MB102020.
	19-MAY-2009	19-MAY-2009	CORRESPONDENCE	EMAIL	JM TO MW: FDA INDICATES REVIEWERS DO NOT OBJECT TO START OF PROTOCOL MB102020. ADDITIONAL INVESTIGATORS ADDED TO STUDY NOT CONSIDERED TO BE "BRODER USE."
	20-MAY-2009	20-MAY-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MW TO MP: MB102013, 014, 021, 029 & 034.
	28-MAY-2009	28-MAY-2009	OTHER	SUBMISSION	AJ to MP:Change in correspondent
	29-MAY-2009	29-MAY-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	MW TO MP: ADDENDUM 1 TO IB, 930035630.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	02-JUN-2009	03-JUN-2009	INFO AMENDMENT - CMC	SUBMISSION	PC to MP: Response to FDA request for additional supporting data on the revised dissolution method. Also includes information amendment on the slightly modified drug substance manufacturing process.
	08-JUN-2009	08-JUN-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	MW TO MP: NOTIFICATION TO FDA OF BMS' TERMINATION OF CLIN. TRIAL AGREEMENT WITH EMERALD COAST RESEARCH GRP. RE: STUDIES MB102013, 029, 030 & 32.
	10-JUN-2009	10-JUN-2009	CORRESPONDENCE	EMAIL	AJ TO JM: EMAIL RE: INTENT TO REQUEST TYPE A MTG. TO DISCUSS CV ANALYSIS PLANS FOR DAPAGLIFLOZIN.
	10-JUN-2009	10-JUN-2009	CORRESPONDENCE	EMAIL	MW TO JM: MUTLI. EMAIL CONTACTS (JUNE 10, 11, 18, 2009) RE: CHANGE INCORRESPONDENT AND TYPE A MTG. REQUEST.
	15-JUN-2009	15-JUN-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI MB102013, 014, 030, 034.
	16-JUN-2009	16-JUN-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: New protocol, New Investigator, CMC and Clinical information re: MB102058.
	18-JUN-2009	18-JUN-2009	OTHER	SUBMISSION	AJ to MP: Req. for a Type A mtg. w/FDA to discuss the proposed CV-analysis plan in support of Dapagliflozin as a trt. for type 2 diabetes mellitus.
	18-JUN-2009	18-JUN-2009	CORRESPONDENCE	LETTER	MP TO MW: FDA REQUEST FOR ADD'L INFO. TO PROVIDE DESCRIPTION OF MICROBIAL LIMITS TESTING AND PROVIDE DESCRIPTION OF WATER ACTIVITY IN TABLET FORM OF DRUG PRODUCT.
	23-JUN-2009	23-JUN-2009	OTHER	SUBMISSION	AJ to MP: SAP for the clinical study AZ protocol D1690C00006(BMS Study no. MB102033), dated Aug. 22, 2008. Database lock for MB102033 is targeted to occur by June 24, 2009.
	23-JUN-2009	23-JUN-2009	OTHER	SUBMISSION	AJ TO MP: RESPONSE TO REQUEST FOR INFO. PROVIDING UPDATED INFORMED CONSENT FORM FOR STUDY MB102020.
	23-JUN-2009	23-JUN-2009	CORRESPONDENCE	EMAIL	JM TO AJ: FDA FORWARDING COPY OF MICRO REQUEST LTR.
	23-JUN-2009	23-JUN-2009	CORRESPONDENCE	EMAIL	MJ TO AJ: FDA EMAIL STATING MTG. REQUEST DATED 18-JUN-09, IS DENIED. FDA WILL PROVIDE WRITTEN RESPONSE TO BMS QUESTIONS.
	23-JUN-2009	23-JUN-2009	CORRESPONDENCE	LETTER	JM TO AJ: FDA LTR. STATING MTG. REQUEST DATED 18-JUN-09, IS DENIED. FDA WILL PROVIDE WRITTEN RESPONSE TO BMS QUESTIONS.
	25-JUN-2009	25-JUN-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW D1690C00006 (MB102033).
	25-JUN-2009	25-JUN-2009	CORRESPONDENCE	EMAIL	AJ TO JM: MTG. REQUEST FOR TELECONF., IF NEEDED FOR CLARIFICIATION, POSSIBLY IN SEPTEMBER.
	26-JUN-2009	26-JUN-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 14668792.
	26-JUN-2009	26-JUN-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 14662340.
	01-JUL-2009	01-JUL-2009	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: MB102045.
	02-JUL-2009	02-JUL-2009	RESPONSE TO REQUEST	SUBMISSION	PC TO MP: RESPONSE TO FDA REQUEST FOR INFO. PROVIDING MICROBIAL TESTING METHOD FOR PRODUCTS PLACED ON LONG-TERM STABILITY PROGRAM.
	08-JUL-2009	08-JUL-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: CLINICAL RPTS. 930032755, 930027515.
	08-JUL-2009	08-JUL-2009	CORRESPONDENCE	EMAIL	AJ TO JM: BMS CONFIRMING FAX COPIES OF 2 IND SAFETY RPTS. SAME AS RPTS. FILED TO SUBMISSION.
	13-JUL-2009	13-JUL-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI MB102014, 021, 029, 030, 34, 045.
	15-JUL-2009	15-JUL-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 14557383.
	22-JUL-2009	22-JUL-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: MB012059, 930035262, 930037624, 930036989, NEW INVESTIGATOR, INFO. AMEND: CMC - CLINICAL SUPPLIES IN CONDUCT OF MB102059.
	22-JUL-2009	22-JUL-2009	CORRESPONDENCE	EMAIL	JM TO AJ: FDA CONFIRMING NON-REQUIREMENT OF STUDY MB102020 FOR NDA SUBMISSION.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	23-JUL-2009	23-JUL-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: MB102057, 930036479; INFO. AMEND: CMC - CLINICAL SUPPLIES FOR CONDUCT OF STUDY, INFO. AMEND: CLINICAL - PART OF OBLIGATIONS TRANSFERRED TO CRO.
	28-JUL-2009	28-JUL-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 14705156.
	03-AUG-2009	03-AUG-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 14708234.
	04-AUG-2009	04-AUG-2009	CORRESPONDENCE	EMAIL	JM TO JA: MULTI. CONTACTS (JULY 23-AUG.4) RE: DENIAL OF DAPA. MTG. REQUEST. FDA WILL PROVIDE WRITTEN RESONSES TO BMS QUESTIONS.
	05-AUG-2009	05-AUG-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: GEN. ADDENDUM 2 TO IB, 930037698.
	17-AUG-2009	17-AUG-2009	CORRESPONDENCE	SUBMISSION	MP to AJ: FDA's request for a written response re: the comments and requests for additional info. on the amendments dated Nov. 26, 2008 and June 2, 2009.
	18-AUG-2009	18-AUG-2009	CORRESPONDENCE	LETTER	MP TO AJ: FDA REPSONSES TO BRIEFING DOCUMENT DATED 18-JUN-09.
	19-AUG-2009	19-AUG-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI MB102013, 029, 030, 032, 034 & 057.
	20-AUG-2009	20-AUG-2009	CORRESPONDENCE	EMAIL	AJ TO JM: BMS REQUEST TO MEET AND DISCUSS FDA RESPONSE TO CV ASSESSMENT PLAN.
	24-AUG-2009	24-AUG-2009	CORRESPONDENCE	EMAIL	AJ TO JM: BMS NOTIFICATION OF PENDING IND FOR DAPA. FIXED-DOSE COMBO (FDC). PILOT STUDY PLANNED FOR 2010 FOR TYPE 1 DIABETIES.
	24-AUG-2009	24-AUG-2009	CORRESPONDENCE	EMAIL	JM TO AJ: FDA INDICATES TELECONF. POSSIBLE TO DISCUSS QUESTION # 5, PER FDA RESPONSE TO CV ASSESSMENT PLAN.
	25-AUG-2009	25-AUG-2009	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: PROTOCOL MB102029, 930036996 & 930026378.
	27-AUG-2009	27-AUG-2009	OTHER	SUBMISSION	AJ TO MP: STATISTICAL ANALYSIS PLAN, 930033171, MB102013; 930036472, MB102021; 930036844, MB102032; 930036694, MB102034 & 930038159, MB102045.
	27-AUG-2009	27-AUG-2009	CORRESPONDENCE	EMAIL	JM TO AJ: FDA CONFIRMS PIP CAN BE SUBMITTED WITH THE NDA.
	02-SEP-2009	02-SEP-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written report re: Rpt. 14750855.
	16-SEP-2009	16-SEP-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI - MB102013, 014, 029, 030 & 034.
	01-OCT-2009	01-OCT-2009	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Documentation for protocol MB102013, Amendment 05 dated 24-Aug-09 (DCN 930038422), Revised protocol 03 dated 24-Aug-09 (DCN 930022086).
	01-OCT-2009	01-OCT-2009	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/Tox reports on study 3210-0472-6100 (DCN 930022078), Study 930018488 (DCN 930018488), Study 930020296 (DCN 930020296)...
	02-OCT-2009	02-OCT-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for new inv. participating in the protocol MB102030. Updated inv. documentation for the protocols MB102009, MB102013, MB102014, MB102021, MB102030, MB102032.
	02-OCT-2009	02-OCT-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: Protocol D1690C00010 (BMS protocol no. MB102061, DCN 930036839), new Inv documentation for protocol D1690C00010 (BMS Protocol MB102061), info. on the list of clinical supplies to be supplied by BMS & AZ for use in the conduct of Protocol D1690C00010. AZ will maintain sponsorship of this protocol with the exception of IND submissions which BMS will provide to the Agency.
	05-OCT-2009	05-OCT-2009	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/Tox reports for Study DN02063, dated Apr. 30, 2009 (DCN 930005621), Addendum 01 for study reports DN02063 (930005621), DN02064 (930004470).....
	06-OCT-2009	06-OCT-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Study MB102029 Data Monitoring Committee Charter dated Aug 10, 2009 (DCN 930039227) and Letters & minutes from Data Monitoring Committee.
	08-OCT-2009	08-OCT-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical report for Study MB102017, dated Feb. 6, 2008, DCN 930026239.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	09-OCT-2009	09-OCT-2009	CORRESPONDENCE	EMAIL	AJ TO MH: CONTACT RE: RESPONSE TO CV QUESTIONS.
	13-OCT-2009	13-OCT-2009	RESPONSE TO REQUEST	SUBMISSION	AJ TO MP: RESPONSE TO FDA FEEDBACK RE: CV ANALYSIS PLAN.
	16-OCT-2009	16-OCT-2009	CORRESPONDENCE	TELEPHONE	AJ TO MH: CONTACT RE: BMS MTG. REQUEST TO DISCUSS/CLARIFY FDA FEEDBACK RE: CV ANALYSIS PLAN.
	19-OCT-2009	19-OCT-2009	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: MB102035, NEW INVESTIGATOR, INFO. AMEND: CMC; CLINICAL; 930036971, 930036966 & 930039441.
	19-OCT-2009	19-OCT-2009	OTHER	SUBMISSION	AJ to MP: Request for a Type A meeting with the FDA to discuss the proposed CV analysis plan in support of dapagliflozin as a treatment for type 2 diabetes mellitus.
	21-OCT-2009	21-OCT-2009	CORRESPONDENCE	LETTER	MH TO AJ: FDA GRANTING TYPE C MTG. TO DISCUSS CV ANALYSIS PLAN SCHEDULED FOR 09-NOV-09.
	22-OCT-2009	22-OCT-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI - MB102-014, 021, 029, 034, 045 & 058.
	28-OCT-2009	28-OCT-2009	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING TELECONF. CALL IN INFO. FOR RESCHEDULED MTG. FOR 04-DEC-09.
	02-NOV-2009	02-NOV-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#1 to a written report re: Report#14750855.
	10-NOV-2009	10-NOV-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: IB ver. 06 dated Nov. 4, 2009 (DCN 930005487). X-Ref INDs 68,652 & 106,890.
	10-NOV-2009	10-NOV-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#1 to a written rpt. re: Rpt. No. 14705156. XRef INDs 68,652 & 106,890.
	12-NOV-2009	12-NOV-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical rpt. for the study MB102014, dated Oct. 22, 2009, DCN 930035479.
	17-NOV-2009	17-NOV-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical rpt. for the study MB102027, dated Oct. 18, 2009, DCN 930035435.
	19-NOV-2009	19-NOV-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI - MB102-029, 030, 032, 034 & 035.
	20-NOV-2009	20-NOV-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Investigator documentation for new investigators participating in the AZ protocol D1690C00010.
	20-NOV-2009	20-NOV-2009	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Amendment 03 dated 16-Oct-09 (DCN 930040464) and Revised protocol dated 16-Oct-09 (DCN 930025956).
	30-NOV-2009	30-NOV-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U SAFETY RPT. # 14750855.
	02-DEC-2009	02-DEC-2009	OTHER	SUBMISSION	AJ TO MP: MB102029 - DATA MONITORING COMMITTEE MINUTES.
	03-DEC-2009	03-DEC-2009	CORRESPONDENCE	SUBMISSION	AJ to MH: IND 68,652 Dapagliflozin meeting 04-Dec-09.
	09-DEC-2009	09-DEC-2009	OTHER	SUBMISSION	AJ to MP: Statistical Analysis Plan for the protocols MB102021, MB102032.
	15-DEC-2009	15-DEC-2009	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Termination of site 001 (The University of Texas Health Sciences Center at San Antonio) for Study MB102020.
	15-DEC-2009	15-DEC-2009	OTHER	SUBMISSION	AJ to MP: Mtg. Mts. from the 4-Dec-09 mtg. b/w the Division and BMS/AZ.
	17-DEC-2009	17-DEC-2009	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Investigator documentation for new investigators participating in the protocol MB102035. Updated 1572s for the protocols MB102032, MB102034, MB102045.
	18-DEC-2009	18-DEC-2009	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#3 to a written rpt. re: Rpt. No. 14750855.
	21-DEC-2009	21-DEC-2009	CORRESPONDENCE	EMAIL	AJ to MH: Question re: planning for a dapa pre-NDA mtg. in 2010.
	22-DEC-2009	22-DEC-2009	CORRESPONDENCE	LETTER	MP to AJ: FDA ltr. re: request for a wriiten response within 30 days of the date of the FDA letter including comments on the IND.
	04-JAN-2010	04-JAN-2010	CORRESPONDENCE	EMAIL	AJ to MH: IND 68652 FDA Request for bone marker data for dapagliflozin.
	05-JAN-2010	05-JAN-2010	OTHER	SUBMISSION	AJ to MP: Core Statistical Analysis Plan (DCN 930040742) & SAP for protocol MB102035 (DCN 930040903).
	06-JAN-2010	06-JAN-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: New protocol D1690C00018, dated Nov. 17, 2009, DCN 930041049 (NCT01031680)
	07-JAN-2010	07-JAN-2010	CORRESPONDENCE	EMAIL	AJ to MH: Thank you email to the FDA for the quick f/u confirming that there will not be a separate CMC mtg.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	07-JAN-2010	07-JAN-2010	CORRESPONDENCE	TELEPHONE	AJ to MH: Teleconference w/FDA re: the timing for BMS to respond to FDA's request for bone marker data, the timing for the pre-NDA mtg, and the possibility for a separate CMC pre-NDA mtg.
	12-JAN-2010	12-JAN-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: New protocol D1690C00019 dated Dec. 21, 2009, DCN 930041323, list of clinical supplies to be used in the conduct of Protocol D1690C00019.
	13-JAN-2010	13-JAN-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Administrative ltr. 01 dated 02-Dec-2009 to MB102013 (DCN 930040708).
	13-JAN-2010	13-JAN-2010	CORRESPONDENCE	EMAIL	AJ to MH: Request for clarification on part of the FDA minutes for the 4-Dec-09 mtg.
	13-JAN-2010	13-JAN-2010	CORRESPONDENCE	LETTER	MH to AJ: FDA ltr. re: copy of the official meeting minutes for the Dec. 4, 2009 teleconference.
	20-JAN-2010	20-JAN-2010	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Updates to Inv. info. for the protocol MB102021.
	25-JAN-2010	25-JAN-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New Inv. documentation for the protocol MB102035. Updates to inv. info. for MB102029, MB102030, MB102032, MB102034 & MB102035.
	02-FEB-2010	02-FEB-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Study DN09023 dated Nov. 3, 2009 (DCN 930039894). X-Ref INDs 68,652 & 106,890.
	04-FEB-2010	04-FEB-2010	CORRESPONDENCE	EMAIL	AJ to MH: Plan to submit Dapagliflozin NDA ~Dec 10, and ques. to the FDA on cDISC dataset requirements.
	08-FEB-2010	08-FEB-2010	RESPONSE TO REQUEST	SUBMISSION	AJ to MP: Response to the FDA's letter dated 19-Dec-08.
	11-FEB-2010	11-FEB-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written rpt. re: Rpt. No. 14807564.
	16-FEB-2010	16-FEB-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written rpt. re: Rpt. No. 14933246. X-Ref INDs 68,652 & 106,890.
	16-FEB-2010	16-FEB-2010	ANNUAL REPORT	SUBMISSION	AJ to MP: IND Annual rpt. for the period 12/01/2008 - 11/30/2009.
	17-FEB-2010	17-FEB-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#2 to a written rpt., re: Rpt. No. 14705156. XRef INDs 68,652 & 106,890.
	18-FEB-2010	18-FEB-2010	RESPONSE TO REQUEST	SUBMISSION	PC to MP: Response to FDA request for the info, which includes the full development data package concerning the revised dissolution method. Request for a teleconference with the reviewer for a discussion on the revised dissolution method during the week of March 12th.
	18-FEB-2010	18-FEB-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical report for the study MB102013 dated Feb. 2, 2010 (DCN 930038052)
	24-FEB-2010	24-FEB-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for the protocol D1690C00019. Part of the sponsor obligations have been transsferred from AZ to External Service Providers for study no. D1690C00019.
	01-MAR-2010	01-MAR-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical Report for MB102007 dated Feb. 5, 2010, DCN 930038582.
	03-MAR-2010	03-MAR-2010	OTHER	SUBMISSION	AJ to MP: SAP for the protocols MB102029, MB102030, MB102032, MB102045.
	08-MAR-2010	08-MAR-2010	OTHER	SUBMISSION	AJ to MP: Transfer of obligations for the protocol D1690C00010.
	08-MAR-2010	08-MAR-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#1 to a written rpt. re: Rpt. No. 14557383. X-Ref INDs 68,652 & 106,890.
	11-MAR-2010	11-MAR-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for inv.s participating in the AZ protocol D1690C00018.
	15-MAR-2010	15-MAR-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: New protocol MB102074, dated Dec 17, 2009, DCN 930041337. New inv. info. for MB102074. Transfer of obligations to a CRO for MB102074.
	16-MAR-2010	16-MAR-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical report for study MB102036 dated Mar. 1, 2010, DCN 930038101.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	16-MAR-2010	16-MAR-2010	CORRESPONDENCE	EMAIL	MH TO PC: FDA IN PROCESS OF REVIEWING REVISED DISSOLUTION METHOD. REQUEST FOR MTG. DENIED UNLESS OTHERWISE LATER DETERMINED.
	17-MAR-2010	17-MAR-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for new inv.s participating in the protocol MB102029, MB102035. Updates to inv. info. for MB102029, MB102030, MB102034, MB102035.
	25-MAR-2010	25-MAR-2010	RESPONSE TO REQUEST	SUBMISSION	AJ to MP: Bone marker data as requested by FDA in the 22-Dec-09 letter.
	25-MAR-2010	25-MAR-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Revised CV SAP (version 1.6 DCN 930042827) & request for feedback from the Division.
	30-MAR-2010	30-MAR-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Admin. ltr. 03 dated 22-Dec-09 (DCN 930041111), Amendment 03 dated 15-Mar-10 n(DCN 930042773) & Revised protocol 02 dated 15-Mar-10 (DCN 930032396).
	31-MAR-2010	31-MAR-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: Protocol MB102062, dated Mar 8, 2010, DCN 930042748. Inv.documentation for the protocol MB102062. Clinical supplies used in the conduct of the protocol MB102062, Transfer of part of the sponsor obligations to a CRO for MB102062.
	31-MAR-2010	31-MAR-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for new inv.s particpitating in the protocol MB102032 & updates to previously sibmitted inv. info. for MB102032.
	31-MAR-2010	31-MAR-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written Rpt. No. 15026636. XRef INDs 68,652 & 106,890.
	05-APR-2010	05-APR-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical rpt. for MB102037, dated Mar. 17, 2010, DCN 930040148.
	07-APR-2010	07-APR-2010	OTHER	SUBMISSION	AJ to MP: Request for FDA feedback on BMS" proposals to include the effect of dapagliflozin on weight loss & reduction of blood pressure in the USPI to be submitted with the initial NDA &/or a planned sNDA.
	09-APR-2010	09-APR-2010	OTHER	SUBMISSION	AJ to MP: Core Statistical Plan.
	12-APR-2010	12-APR-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written rpt. re: Rpt. No. 150447. X-Ref INDs 68,652 & 106,890.
	12-APR-2010	12-APR-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA confirmation that the Agency has received the "Type C" fdbk. FDA also confirmed that the Agency should be able to provide written fdbk. within the timeframe requested by BMS.
	13-APR-2010	13-APR-2010	OTHER	SUBMISSION	AJ to MP: Ltr. from the DMC, dated Mar. 24, 2010.
	16-APR-2010	16-APR-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/Tox reports for Study 930042484 dated Mar. 12, 2010; Study 930040777 dated Dec. 7, 2009, study 930038580 dated Dec 7, 2009.....
	21-APR-2010	21-APR-2010	OTHER	SUBMISSION	AJ to MP: SAP for MB102034.
	27-APR-2010	27-APR-2010	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Updates to inv. info. for the protocols MB102013, MB102034, MB102035.
	27-APR-2010	27-APR-2010	RESPONSE TO REQUEST	SUBMISSION	AJ to MP: Response to FDA request for the data as requested in the 30-Dec-09 ltr.
	29-APR-2010	29-APR-2010	CORRESPONDENCE	EMAIL	MH to PC: FDA letter w/ feedback
	05-MAY-2010	05-MAY-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Amendment 01 dated 19-Apr-2010 (DCN 930043570) & Revised protocol 01 dated 19-Apr-2010 (DCN 930042748).
	07-MAY-2010	07-MAY-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/tox rpt. for the study DN06072, dated Apr. 15, 2010, DCN 930043549.
	12-MAY-2010	12-MAY-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI - MB102030
	19-MAY-2010	19-MAY-2010	OTHER	SUBMISSION	AJ TO MP: LETTER OF CROSS REF. - PROTOCOL 4 & 6.
	20-MAY-2010	20-MAY-2010	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ TO MP: NOTIFICATION TO FDA REGARDING CHANGE OF ADDRESS FOR NEW ENGLAND IRB.
	20-MAY-2010	20-MAY-2010	CORRESPONDENCE	EMAIL	AJ to MH: BMS thank you email for FDA confirmation that comments on submissions SN0274 & SN0280 will be sent to BMS by mid-June.
	21-MAY-2010	21-MAY-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: MB102088, 930043963; NEW INVESTIGATOR, INFO. AMEND: CMC & TFR. OF OBLIGATIONS.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	26-MAY-2010	26-MAY-2010	OTHER	SUBMISSION	AJ to MP: Revised CEC charter (ver. 4.0 dated May 3,2010, DCN 930044171 which addresses the FDA's request.
	26-MAY-2010	26-MAY-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical rpt. for the study MB102006, dated Nov.4,2008, DCN 930020366.
	26-MAY-2010	26-MAY-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA request for desk copies.
	01-JUN-2010	01-JUN-2010	OTHER	SUBMISSION	AJ to MP: Request for FDA fdbk on planned NDA format & content.
	01-JUN-2010	01-JUN-2010	CORRESPONDENCE	EMAIL	AJ to MH: Email to the FDA to inform them that the NDA format and content document has been submitted for FDA feedback.
	09-JUN-2010	09-JUN-2010	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Updates to previosly submitted inv. info.
	09-JUN-2010	09-JUN-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/Tox reports for the study AZA091202-01 dated Apr. 1, 2009 (DCN 930044498); Study AZA091202-02 dated Apr. 01, 2009(DCN 930044498), Study AZA090507 dated June 30, 2009, DCN 930044475.....
	10-JUN-2010	10-JUN-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA thank you email for the notification re: the dates of conversion of Dapa INDs to eCTD.
	11-JUN-2010	11-JUN-2010	RESPONSE TO REQUEST	SUBMISSION	PC to MP: Response to FDA advice / info. request letter dated Apr. 29, 2010, concerning the revised dissolution method for Dapagliflozin tablets.
	15-JUN-2010	15-JUN-2010	OTHER	SUBMISSION	AJ to MP: Transfer of obligations for the protocols MB102062, MB102074, MB102088.
	15-JUN-2010	15-JUN-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: New Protocol MB102090, New Inv. MB102090, Info. Amendment - CMC & Transfer of onligatiosn to a CRO for MB102090.
	17-JUN-2010	17-JUN-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New inv. documentation for the protocol D1690C00019.
	17-JUN-2010	17-JUN-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/tox rpt. re: Study DN06073, dated May 11, 2010, DCN 930044081.
	17-JUN-2010	17-JUN-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA aiming to sent the letter including comments on the submissions SN0274 & SN0280 by next week.
	29-JUN-2010	29-JUN-2010	CORRESPONDENCE	EMAIL	AJ to MH: Response to FDA's email for the protocol title for D1690C0010.
	29-JUN-2010	29-JUN-2010	CORRESPONDENCE	EMAIL	AJ to MH: Thank you letter to the FDA for the electronic version of the consult from the Division of Cardio Renal for IND 68,652, Dapagliflozin.
	29-JUN-2010	29-JUN-2010	CORRESPONDENCE	LETTER	MP to AJ: Advice/Information request from the FDA.
	01-JUL-2010	01-JUL-2010	OTHER	SUBMISSION	AJ to MP: Request for proprietary name review of Ebyont.
	02-JUL-2010	02-JUL-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA confirmation that the first eCTD submission for dapa re: a request to review the proprietary name review for dapagliflozin has been received by the FDA.
	06-JUL-2010	06-JUL-2010	CORRESPONDENCE	EMAIL	AJ to MT: IND 68,652 IN review/IR.
	06-JUL-2010	06-JUL-2010	CORRESPONDENCE	EMAIL	AJ to MT: Voicemail - IND 68,652 dapagliflozin - proprietary name review.
	07-JUL-2010	07-JUN-2010	CORRESPONDENCE	EMAIL	MH to AJ: BMS response to a FDA ques. that the Initial protocol for D1690C0010 was submitted 10/02/2009; SN0227.
	07-JUL-2010	07-JUL-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Amendment and Revised protocol info. for AZ protocols D1690C00006 & D1690C00010.
	08-JUL-2010	08-JUL-2010	OTHER	SUBMISSION	AJ to MP: Amendment to request for proprietary name review/response to info. request.
	08-JUL-2010	08-JUL-2010	CORRESPONDENCE	EMAIL	AJ to MH: Request to the FDA for clarity on the Division's fdbk. re: CV safety.
	08-JUL-2010	08-JUL-2010	CORRESPONDENCE	EMAIL	MT to AJ: IND 68652 TN review/IR.
	08-JUL-2010	08-JUL-2010	CORRESPONDENCE	TELEPHONE	AJ to MH: Multiple telephone contact report (8-Jul-10, 28-Jul-10) re: FDA not being open to reserving dates for a pre-NDA mtg. prior to submitting a pre-NDA mtg. request ltr.
	12-JUL-2010	12-JUL-2010	CORRESPONDENCE	EMAIL	MH to AJ: F/U email from FDA confirming their receipt of the BMS voicemail requesting clarity on the Division's feedback on CV safety. FDA will confer with their reviewers and get back to BMS with a response.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	16-JUL-2010	16-JUL-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for new investigators participating in the AZ protocols D1690C00010, D1690C00018.
	19-JUL-2010	19-JUL-2010	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Updates to inv. info. for the protocols MB102013, MB102014, MB102029, MB102034 and MB102035.
	21-JUL-2010	21-JUL-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA waiting for a response from the review team re: CV SAP.
	22-JUL-2010	22-JUL-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: Amendment 1 dated May 6, 2010 (DCN 930043913), new inv. documentation for the protocol MB102073, clinical supplies to be used in the conduct of MB102073, Transfer of obligations to a CRO for the protocol MB102073.
	22-JUL-2010	22-JUL-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/tox report for Study DN08071 dated Jul 16, 2010 and Study DN09009 dated Jul 2, 2010.
	02-AUG-2010	02-AUG-2010	CORRESPONDENCE	EMAIL	AJ to MH: Request to the FDA for the partial feedback on the NDA format and content document, followed by the other feedback in the next couple of weeks.
	03-AUG-2010	03-AUG-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Clinical reports for study MB102032, MB102057.
	05-AUG-2010	05-AUG-2010	OTHER	SUBMISSION	AJ to MP: Pediatric plan, pediatric research equity act-request for partial waiver and deferral.
	05-AUG-2010	05-AUG-2010	OTHER	SUBMISSION	AJ to MP: DMC Charter ver 2.0 dated May 13, 2010, DCN 930039227 for the study MB102029, DMC Review ltr. dated Jul. 28, 2010.
	09-AUG-2010	09-AUG-2010	CORRESPONDENCE	EMAIL	AJ to MH: Pediatric plan and request for partial waiver and deferral from PREA (IND 68,652/ SN0312) for quick reference.
	09-AUG-2010	09-AUG-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA confirmation to email a letter with the feedback comments on the NDA format and content document, within a week.
	10-AUG-2010	10-AUG-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ to MP: New protocol for MB102066, new inv. documentation for MB102066, Transfer of obligations for MB102066.
	12-AUG-2010	12-AUG-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New inv. participating in the protocol MB102073. Updates to inv. documentation for MB102034.
	12-AUG-2010	12-AUG-2010	CORRESPONDENCE	EMAIL	AJ to MH: IND 68,652 dapagliflozin - quick ques. re: a plan to request an NDA# in the very near future.
	23-AUG-2010	23-AUG-2010	CORRESPONDENCE	LETTER	MP TO AJ: FDA ADVICE/INFORMATION REQUEST RE: AMEND. DATED 01-JUN-10, REQUESTING FEEDBACK ON FORMAT AND CONTENT FOR PLANNED NDA.
	24-AUG-2010	24-AUG-2010	CORRESPONDENCE	EMAIL	MH to AJ: IND 68,652 dapagliflozin FDA feeback that it's fine to request an NDA no. and that the no. will be valid forever.
	27-AUG-2010	27-AUG-2010	OTHER	SUBMISSION	AJ to MP: Request Pre-NDA mtg. (Type B mtg)
	27-AUG-2010	27-AUG-2010	CORRESPONDENCE	EMAIL	AJ to MH: Pre-NDA mtg. request for Dapa sent to FDA on Aug. 27, 2010 and attached to the email for ease of reference.
	27-AUG-2010	27-AUG-2010	CORRESPONDENCE	EMAIL	MH to AJ: FDA feeback on the upcoming dapagliflozin NDA format and content.
	28-AUG-2010	28-AUG-2010	CORRESPONDENCE	EMAIL	AJ to MH: Request to the FDA to have a teleconference to discuss a few questions.
	30-AUG-2010	30-AUG-2010	RESPONSE TO REQUEST	SUBMISSION	AJ to MP: Response to FDA request for info.
	31-AUG-2010	31-AUG-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Amendment 02 dated 18-Aug-2010 to MB102073 (DCN 930046122) & Revised protocol 01 dated 18-Aug-2010 to MB102073 (DCN 930043915)
	31-AUG-2010	31-AUG-2010	CORRESPONDENCE	EMAIL	AJ to MH: IND 68,652 dapagliflozin FDA fdbk.
	31-AUG-2010	31-AUG-2010	CORRESPONDENCE	EMAIL	AJ to MH: Response to FDA comments/ request for feedback to Type C request.
	31-AUG-2010	31-AUG-2010	CORRESPONDENCE	EMAIL	Mt to AJ: IND 68652 TN review/IR
	03-SEP-2010	03-SEP-2010	CORRESPONDENCE	EMAIL	AJ to MH: Change of FDA contact.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	10-SEP-2010	10-SEP-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New inv. documentation for the protocol MB102073 and updates to inv. documentation for the protocol MB102035.
	13-SEP-2010	13-SEP-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written Rpt. No. 15274897. X-Ref INDs 68,652 & 106,890.
	13-SEP-2010	13-SEP-2010	CORRESPONDENCE	EMAIL	AJ to RC: Request for an update on the status of pre-NDA mtg. request that was submitted 27-Aug-2010 to IND 68,652/SN0316.
	15-SEP-2010	15-SEP-2010	CORRESPONDENCE	EMAIL	AJ TO RC: EMAIL RE: PRE-NDA MTG. SCHEDULED FOR NOV. 9, 2010.
	15-SEP-2010	15-SEP-2010	CORRESPONDENCE	LETTER	RC TO AJ: MEETING REQUEST GRANTED FOR PRE-NDA MTG. SCHEDULED FOR 09-NOV-10.
	16-SEP-2010	16-SEP-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS QUESTIONS RELATED TO FDA FEEDBACK ON NDA FORMAT AND LOGISTICAL ASPECTS FOR PLANNED NDA.
	17-SEP-2010	17-SEP-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written rpt. Nol. 15274897. X-Ref INDs 68,652 and 106,890.
	17-SEP-2010	17-SEP-2010	CORRESPONDENCE	LETTER	MP TO AJ: FDA ADVICE/INFORMATION REQ. PERTAINING TO AMEND. DATED 25-MAR-10, CONTAINING BONE SAFETY DATA.
	23-SEP-2010	23-SEP-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: PROVIDE CLINICAL RPT. STUDY MB102020.
	23-SEP-2010	23-SEP-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PROVIDING BMS/AZ NDA FORMAT AND CONTENT DOCUMENT W/FDA RESPONSE TO BMS.
	23-SEP-2010	23-SEP-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS REQUEST TO ALIGN RPT'G INTERVALS FOR THE 2 U.S. IND AR'S TO APRIL 13.
	23-SEP-2010	23-SEP-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA REQUEST INFO. RE: 17-JUN-10, PHARM/TOX SUBMISSION.
	27-SEP-2010	27-SEP-2010	OTHER	SUBMISSION	AJ TO MP: REQUEST TO ALIGN 2 DAPAGLIFLOZIN U.S. IND ANNUAL RPTS.
	27-SEP-2010	27-SEP-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS EMAIL RE: SUBMISSION OF REQUEST TO ALIGN RPT'G INTERVAL FOR THE 2 DAPAGLIFLOZIN IND ANNUAL RPTS.
	28-SEP-2010	28-SEP-2010	OTHER	SUBMISSION	AJ TO MP: CORRECTION TO FILING DATED 27-SEPT-10, SN0323, TO CORRECT THE PROPOSED INTERVAL DATE YEAR PROVIDED IN TABLE.
	29-SEP-2010	29-SEP-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: CLINICAL RPT. MB102058, 930043784.
	05-OCT-2010	05-OCT-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI - D1690C00010, 018 & 019.
	07-OCT-2010	07-OCT-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 15274897.
	12-OCT-2010	12-OCT-2010	OTHER	SUBMISSION	AJ TO MP: PRE-NDA MTG. BRIEFING BOOK AND RESPONSE TO FDA FEEDBACK.
	12-OCT-2010	12-OCT-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI - MB102008, 029, 030 & 073.
	12-OCT-2010	12-OCT-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 15274897, URINARY TRACT INFECTION.
	13-OCT-2010	13-OCT-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: MB102077, 930043916, 930043906, 930046111; NEW INVESTIGATOR; TRANSFER OF OBLIGATIONS.
	14-OCT-2010	14-OCT-2010	OTHER	SUBMISSION	AJ TO MP: RESPONSE TO FDA FOR REQUEST FOR INFO. RE: STUDIES 930047102.
	15-OCT-2010	15-OCT-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ TO MP: PHARM TOX RPT. 930044500, DN09008; 930040066, MB102021; 930043739, MB102030; 930047027, D1690C00006; 930047029, D1690C00006.
	19-OCT-2010	19-OCT-2010	OTHER	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR INFORMATION DATED 17-SEP-10, RE: STUDY D1690C00012, 930047295.
	19-OCT-2010	19-OCT-2010	CORRESPONDENCE	EMAIL	RC TO AJ: COMMUNICATION CLARIFYING TYPE OF I.D. REQUIRED BY NON-US CITIZENS FOR MTG. PARTICIPATION.
	20-OCT-2010	20-OCT-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PROVIDING FOREIGN VISITOR FORMS AND LIST OF BMS/AZ ATTENDEES.
	20-OCT-2010	20-OCT-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA ACCEPTS PROPOSAL TO ALIGN RPT'G INTERVALS OF 2 DAPA. IND ANNUAL RPT' (IND 106890 & 68652).

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	20-OCT-2010	20-OCT-2010	CORRESPONDENCE	EMAIL	RC to AJ: IND 68,652 & 106,890 dapagliflozin IND annual reporting interval-request-slight change.
	21-OCT-2010	21-OCT-2010	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: NEW PROTCOL MB102093, NEW INVESTIGATOR & TRANSFER OF OBLIGATIONS.
	21-OCT-2010	21-OCT-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BM PROVIDING PRE-NDA MTG. PKG.
	21-OCT-2010	21-OCT-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS INDICATING RESPONSE TO FDA LTR. FILED ON 19-OCT-10 (SN0334), IN REGARDS TO BMS FILING DATED 25-MAR-10.
	21-OCT-2010	21-OCT-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PROVIDING WORD VERSIONS OF RESPONSE DOC. INLCUDED IN PRE-NDA BRIEFING PKG.
	21-OCT-2010	21-OCT-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA REQUEST TO INCLUDE WORD VERSIONS OF QUESTIONS, ATTACHMENTS & RESPONSES TO FDA FEEDBACK ON NDA FORMAT & CONTENT.
	29-OCT-2010	29-OCT-2010	OTHER	SUBMISSION	AJ to MP: DMC Charter Review Letter for MB102029 dated Jul. 28, 2010.
	03-NOV-2010	03-NOV-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Admin. ltr. 01 dated 17-Sep-2010 (DCN 930047640), Admin. ltr. 01 dated 01-Oct-2010 (DCN 930047302), Admin. ltr. 01 dated 01-Oct-2010 (DCN 930047305). New Inv. documentation for AZ protocols D1690C00010, D1690C00018 and D1690C00019, Updates to inv. info. for the AZ protocols D1690C00010, D1690C00018 and D1690C00019.
	04-NOV-2010	04-NOV-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Amend. 01 dated 05-Oct-2010 to MB102093 (DCN 930047540), Revised protocol 01 dated 05-Oct-2010 to MB102093 (DCN 930046872).
	04-NOV-2010	04-NOV-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA RESPONSE TO STATISTICAL QUESTION NOT PLANNED FOR PRE-NDA MTG.
	05-NOV-2010	05-NOV-2010	OTHER	SUBMISSION	AJ to MP: DMC Charter Minutes
	05-NOV-2010	05-NOV-2010	CORRESPONDENCE	EMAIL	KS TO PC: FDA INDICATING WHEN RESPONSES TO CMC PRENDA QUESTIONS TO BE SENT OUT.
	06-NOV-2010	06-NOV-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PROVIDING BACK-UP SLIDES FOR PRE-NDA MTG.
	08-NOV-2010	08-NOV-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Admin. ltr. 03 dated 20-Apr-2010 (DCN 930043522), Admin. ltr. 02 dated 10-Sep-2010 (DCN 930047105), Admin. ltr. 01 dated 05-Aug-2010 (DCN 930045877).
	08-NOV-2010	08-NOV-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written rpt. No. 15268410. X-Ref INDs 68,652 & 106,890.
	08-NOV-2010	08-NOV-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA TO SEND FINAL LIST OF FDA ATTENDESS.
	08-NOV-2010	08-NOV-2010	CORRESPONDENCE	LETTER	RC TO AJ: FDA PROVIDING PRELIMINARY RESPONSES TO BMS QUESTIONS FOR PRE-NDA MTG.
	09-NOV-2010	09-NOV-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PRESENTING SPECIFIC QUESTIONS RE: SITE LEVEL DATA.
	11-NOV-2010	11-NOV-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for new investigators for the protocols MB102073, MB102077. Updates to inv. documetation for the protocols MB102035.
	16-NOV-2010	16-NOV-2010	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: Administrative addenda to reports already submitted to the IND, new reports and data driven addenda.
	16-NOV-2010	16-NOV-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS INDICATING EARLIER RECIEPT OF MINUTES HELPFUL.
	17-NOV-2010	17-NOV-2010	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Revised protocol 05 dated 17-Sep-2010 (DCN 930025956), Updates to inv. info. for AZ protocols D1690C00006, D1690C00018, D1690C00019.
	18-NOV-2010	18-NOV-2010	OTHER	SUBMISSION	AJ to MP:Statistical Analysis Plans.
	19-NOV-2010	19-NOV-2010	CORRESPONDENCE	LETTER	CH TO AJ: PROPRIETARY NAME REQUEST UNACCEPTABLE PER FDA.
	21-NOV-2010	21-NOV-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PROVIDING ADD'L QUESTIONS FOR CLARIFICATION ON SITE LEVEL DATA REQUEST.
	22-NOV-2010	22-NOV-2010	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/Tox reports.
	22-NOV-2010	22-NOV-2010	CORRESPONDENCE	EMAIL	MT TO AJ: FDA PROVIDING PROPER PLANNING FOR SUBMISSION (NDA) OF PROPRIETARY NAME.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	23-NOV-2010	23-NOV-2010	OTHER	SUBMISSION	AJ to MP: Pre-NDA Mtg. Minutes dated Nov. 9, 2010.
	23-NOV-2010	23-NOV-2010	CORRESPONDENCE	EMAIL	MT TO AJ: FDA PROVIDING INFO. TO GLOBAL TRADENAME FILINGS.
	23-NOV-2010	23-NOV-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA RESPONSE TO FILLING OUT FINANCIAL DISCLOSURE FOR 3454.
	27-NOV-2010	27-NOV-2010	CORRESPONDENCE	EMAIL	AJ TO RC: COMMUNICATION RE: SCHEDULING OF AC MTG.
	01-DEC-2010	01-DEC-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS CLARIFYING 3 PHASE 2B & ELEVEN PAHSE 3 STUDIES COMPLETED THROUGH PRIMARY ENDPOINT.
	01-DEC-2010	01-DEC-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS REQUEST STATUS TO FEEDBACK RE: SITE LEVEL DATA.
	02-DEC-2010	02-DEC-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA PROVIDING RESPONSE TO BMS QUESTIONS ON SITE LEVEL DATA.
	02-DEC-2010	02-DEC-2010	CORRESPONDENCE	LETTER	RC TO AJ: FDA PROVIDING MTG. MINUTES FROM PRE-NDA MTG. HELD ON 09-NOV-10.
	03-DEC-2010	03-DEC-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA PROVIDING AMENDMENT TO OFFICIAL MTG. MINUTES.
	06-DEC-2010	06-DEC-2010	CORRESPONDENCE	EMAIL	CDER TO CP: FDA ACK. OF BMS NOTIFICATION OF PENDING NDA SUBMISSION.
	06-DEC-2010	06-DEC-2010	CORRESPONDENCE	EMAIL	RC TO AJ: FDA AGREES RE: BMS PLAN.
	21-DEC-2010	21-DEC-2010	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New Inv. participating in the protocols MB102013, MB102077. Updates to inv. info. for the protocols MB102030, MB102035, MB102073.
	21-DEC-2010	21-DEC-2010	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial writen rpt. re: Rpt. No. 15429905. XRef INDs 68,652 & 106,890.
	27-DEC-2010	21-DEC-2010	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PROVIDING STATUS ON PENDING FILING OF NDA FOR 27-DEC-10.
	07-JAN-2011	07-JAN-2011	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: IB ver. no. 07 dated Dec. 22, 2010 (DCN 930005487).
	13-JAN-2011	13-JAN-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New investigators for MB102013, MB102077. Updates to inv. info. for MB102013, MB102073.
	08-FEB-2011	08-FEB-2011	OTHER	SUBMISSION	AJ to MP: Transfer of obligations for the protocols MB102008, MB102009, MB102013, MB102014, MB102021, MB102029, MB102030, MB102032, MB102034, MB102045.
	11-FEB-2011	11-FEB-2011	CORRESPONDENCE	EMAIL	AJ TO RC: BMS NOTIFICATION RE: "QT" STUDY (D1690C00001) W/ DATASETS & CRF'S FILED 23-DEC-08.
	14-FEB-2011	14-FEB-2011	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: General Addendum 01 to Dapagliflozin IB, dated Feb. 2,2011 (930049703).
	15-FEB-2011	15-FEB-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New inv. documentation for MB102073, MB102077. Updates to inv. info. for MB102029.
	16-FEB-2011	16-FEB-2011	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Inv. info. for the protocols D1690C00010, D1690C00018, D1690C00019.
	24-FEB-2011	24-FEB-2011	OTHER	SUBMISSION	AJ TO MP: PROVIDING HEPATIC ADJUDICATION COMMITTEE CHARTER AND DATA MONITORING COMMITTEE REVIEW LETTER.
	03-MAR-2011	03-MAR-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New investigators participating in the protocol MB102073, MB102077. Updates to inv. info. for protocols MB102013, MB102029, MB102073, MB102077.
	15-MAR-2011	15-MAR-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New inv. info. for MB102029, MB102073, MB102077. Updates to inv. info. for MB102013, MB102029, MB102073, MB102077.
	24-MAR-2011	24-MAR-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New inv. documentation for MB102035, MB102073, MB102077. Updates to inv. info. for MB102035, MB102073, MB102077.
	24-MAR-2011	24-MAR-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Expedited safety report no.1 for Dapagliflozin, dated 21-Mar-11. This document is incorporated by cross-reference through inclusion of the letter only to IND 106,890.
	24-MAR-2011	24-MAR-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Expedited safety report no. 1 for Dapagliflozin dated 21-Mar-2011.
	12-APR-2011	12-APR-2011	ANNUAL REPORT	SUBMISSION	AJ to MP: IND Annual Rpt. for the period 12/01/2009 - 2/13/2011.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	21-APR-2011	21-APR-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New investigators participating in the protocols MB102073, MB102077. Updates to inv. info. for MB102073 & MB102077.
	29-APR-2011	29-APR-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for the new investigators for AZ protocol D1690C00019. Changes to inv. info. for AZ protocol D1690C00010.
	03-MAY-2011	03-MAY-2011	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ to MP: Amendment 06 dated 28-Mar-11 to MB102073 (DCN 930051130) & Revised protocol 02 dated 28-Mar-2011 (DCN 930043915).
	04-MAY-2011	04-MAY-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written report re: Rpt. No. 15692338. X-Ref INDs 68,652 & 106,890.
	09-MAY-2011	09-MAY-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#1 to a written rpt. Rpt. No. 15429905. X-Ref IND 68,652 & 106,890.
	11-MAY-2011	11-MAY-2011	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: General Addendum 02 to dapagliflozin IB dated May 6, 2011 (930051689). Admin. ltr. 03 dated 30-Oct-10 (930047983)
	20-MAY-2011	20-MAY-2011	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Inv. info. for MB102013, MB102014.
	20-MAY-2011	20-MAY-2011	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ to MP: protocols D1690C00018 & D1690C00019.
	25-MAY-2011	25-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: re: request to conduct first study in Type 1 patients under current dapaglifozin IND.
	26-MAY-2011	26-MAY-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for new investigators for MB102073, MB102077. Updates to inv. info. for MB102029 and MB102077.
	26-MAY-2011	26-MAY-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#2 to a written rpt. re: anal abscess, rpt. No. 15429905. X-Ref INDs 68,652 and 106,890.
	02-JUN-2011	02-JUN-2011	OTHER	SUBMISSION	AJ to MP: Request for Type C mtg.
	02-JUN-2011	02-JUN-2011	OTHER	SUBMISSION	AJ to MP: DMC Charter ver. 3.0 dated April 6, 2011 - Study MB102029 (DCN 930039227).
	08-JUN-2011	08-JUN-2011	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Updates to Investigator information for MB102029, MB102032.
	22-JUN-2011	22-JUN-2011	CORRESPONDENCE	LETTER	MH TO AJ: FDA RESPONSE GRANTED TO BMS REQUEST MADE 2-JUN-11 FOR A TYPE C MEETING TO BE HELD 7-SEP-11, RE: BMS PROPOSAL OF DESIGN FOR A CARDIOVASCULAR OUTCOME TRIAL.
	23-JUN-2011	23-JUN-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: Inv. documentation for MB102073, MB102077. Updates to inv. info. for MB102073.
	28-JUN-2011	28-JUN-2011	OTHER	SUBMISSION	AJ to MP: Study MB102029 DMC Charter Review letter dated June 7, 2011.
	29-JUN-2011	29-JUN-2011	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ to MP: Pharm/Tox reports for Study 930005304, Study 930052283, Study 930052026, Study 930052593, Study 1032SY, Study 1033SY.
	30-JUN-2011	30-JUN-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#1 to a written rpt, Rpt. No. 15692338. X-Ref INDs 68,652; 106,890.
	12-JUL-2011	12-JUL-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: F/U#2 to a written rpt, Rpt. No. 15692338. X-Ref INDs 68,652; 106,890.
	12-JUL-2011	12-JUL-2011	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: PROTOCOL'S D1690C00018, 00019; CLINICAL RPT. MB102002, 930052475.
	15-JUL-2011	15-JUL-2011	OTHER	SUBMISSION	AJ to MP: Updated Transfer of Obligations for AZ protocol D1690C00006, AZ protocol D1690C00010, AZ protocol D1690C00018, AZ protocol D1690C00019.
	20-JUL-2011	20-JUL-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ to MP: Initial written rpt. re: Rpt. No. 15793359. X-Ref INDs 68,652 & 106,890.
	21-JUL-2011	21-JUL-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New investigators for MB102073, MB102077. Updates to inv. info. for MB102029, MB102073, MB102077.
	26-JUL-2011	26-JUL-2011	OTHER	SUBMISSION	AJ to MP: Draft protocol MB102091 for FDA comments.
	29-JUL-2011	29-JUL-2011	OTHER	SUBMISSION	AJ to MP: Correspondence re: mtg. request for Aug 2011 and request to expand scope of scheduled 7-Sep-11 mtg. request.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	09-AUG-2011	09-AUG-2011	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ to MP: Updates to inv. info. for AZ protocol D1690C00010, AZ protocol D1690C00018 and AZ protocol D1690C00019.
	18-AUG-2011	18-AUG-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ to MP: New investigators for the protocol MB102073, MB102077. Updates for the protocols MB102073, MB102077.
	24-AUG-2011	24-AUG-2011	OTHER	SUBMISSION	AJ TO MP: TRANSFER OF OBLIGATIONS FOR STUDIES D1690C00010 & D1690C00018.
	01-SEP-2011	01-SEP-2011	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ TO MP: PROVIDING PHARM/TOX STUDY RPT. 930053120.
	13-SEP-2011	13-SEP-2011	OTHER	SUBMISSION	AJ TO MP: MTG. MATERIALS FOR SCHEDULED 04-OCT-11, MTG.
	13-SEP-2011	13-SEP-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI MB102073 & 077.
	20-SEP-2011	20-SEP-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 16038556.
	03-OCT-2011	03-OCT-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U SAFETY RPT. # 16038556.
	05-OCT-2011	05-OCT-2011	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: PROVIDING CLINICAL STUDY RPT. MB102035, 930053276.
	13-OCT-2011	13-OCT-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: NEW & COI - MB102-073 & 77.
	13-OCT-2011	13-OCT-2011	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ TO MP: PHARM/TOX RPT'S 93005304, 930052019, 920053153, 930053412 & 930054594.
	17-OCT-2011	17-OCT-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: AZ PROTOCOLS D1690C00018 & D1690C00019; OTHER: CHANGE OF INVESTIGATOR INFO- AZ PROTOCOLS D1690C00018 & D1690C00019.
	25-OCT-2011	25-OCT-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: PROTOCOLS MB102073 & MB102077; OTHER: CHANGE OF INVESTIGATOR INFO- PROTOCOLS MB102073 & MB102077
	31-OCT-2011	31-OCT-2011	OTHER	SUBMISSION	AJ TO MP: STATISTICAL ANALYSIS PLAN & DATA MONITORING COMMITTEE MTG. MINUTES - MB102029.
	03-NOV-2011	03-NOV-2011	CORRESPONDENCE	LETTER	MH TO AJ: OFFICAL FDA MINUTES FROM MEETING HELD 04-OCT-11 TO DISCUSS THE DESIGN OF PROPOSED CV OUTCOMES TRIAL AND OVERALL PHARMACOVIGILANCE PLAN.
	08-NOV-2011	08-NOV-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: D1690C00010, 00018 & 00019.
	09-NOV-2011	09-NOV-2011	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: MB102073, 930053737, 930054459 & 930043915.
	09-NOV-2011	09-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS NOTIFICATION TO FDA THAT BMS/AZ ARE CONSIDERING A POTENTIAL FUTURE FDC WITH DAPA AND SAXA, INCASE OF FDA CONTACT FOR GUIDANCE ON DEVELOPMENT.
	10-NOV-2011	10-NOV-2011	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: MB102073, 930055659 & 930043915.
	22-NOV-2011	22-NOV-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073, 077 & 029.
	23-NOV-2011	23-NOV-2011	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: CLINICAL RPT'S D1690C00006, 930055507; D1690C00018, 930055532, 930055566; AND D1690C00019, 930055526 & 930055558.
	14-DEC-2011	14-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: SAXA/DAPA PROTOCOL REVIEW REQUEST SUBMISSION TO SAXA IND.
	19-DEC-2011	19-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS STATUS OF SUBMISSIONS FOR LABEL COMMENTS AND PMR MILESTONE DATES FOR 21-DEC-11.
	20-DEC-2011	20-DEC-2011	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: CLINICAL RPT'S MB102066, 930054635; D1690C00010, 930056628.
	21-DEC-2011	21-DEC-2011	OTHER	SUBMISSION	AJ TO MP: PROT. SYNOPSIS FOR STUDY CV181169, DOCUMENTATION FILED TO BMS-477118, IND 63,634, AND XREF TO IND 68,652.
	22-DEC-2011	22-DEC-2011	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073 & 077.
	22-DEC-2011	22-DEC-2011	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 16283061.
	05-JAN-2012	05-JAN-2012	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: CLINICAL RPTS. : 104 WK. FINAL STUDY RPT. MB102029, 930053893.
	06-JAN-2012	06-JAN-2012	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: PROT. MB102-072, 930055699 & 930055697; NEW INVESTIGATOR AND TFR. OF OBLIGATIONS.
	12-JAN-2012	12-JAN-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA COMMENTS RE: PROTOCOLS MB102073 & MB102077 FOR DAPAGLIFLOZIN.
	27-JAN-2012	27-JAN-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO A WRITTEN REPORT- RPT. # 16283061.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	31-JAN-2012	31-JAN-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: PROTOCOLS MB102073 & MB102077; CHANGE OF INVESTIGATOR INFO- PROTOCOLS MB102073 & MB102077.
	15-FEB-2012	15-FEB-2012	RESPONSE TO REQUEST	SUBMISSION	AJ TO MP: PROVIDING INFO. RE: AMEND'S TO PROT'S MB102073 & 077, 10-NOV-11.
	15-FEB-2012	15-FEB-2012	CORRESPONDENCE	EMAIL	AJ TO MH: RESPONSE TO FDA COMMENTS DATED 13-JAN-12 RE: PROTOCOLS MB102073 & MB102077.
	28-FEB-2012	28-FEB-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: PROTOCOLS MB102072, MB102073, & MB102077; CHANGE OF INVESTIGATOR INFO- PROTOCOLS MB102073 & MB102077.
	29-FEB-2012	29-FEB-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U #2 TO WRITTEN RPT #16283061.
	05-MAR-2012	05-MAR-2012	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: DOCUMENTATION FOR INVESTIGATOR BROCHURE, 930005487.
	12-MAR-2012	12-MAR-2012	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ TO MP: AZ PROTOCOLS D1690C00018 & D1690C00019
	12-MAR-2012	12-MAR-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	INITIAL WRITTEN RPT #16423295.
	28-MAR-2012	28-MAR-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: THIRD F/U TO WRITTEN RPT. #16283061. INITIAL RPT. DATED 22-DEC-11.
	29-MAR-2012	29-MAR-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: PROTOCOLS MB102072, MB102073, & MB102077; OTHER: CHANGE OF INVESTIGATOR INFO.- PROTOCOLS MB102072, MB102073, & MB102077.
	29-MAR-2012	29-MAR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: TARGETING TO SUBMIT THE DRAFT CVOT ON 02-APR-12 FOR FDA REVIEW.
	02-APR-2012	02-APR-2012	OTHER	SUBMISSION	AJ TO MP: CVOT PROTOCOL D1693C0001, 930052214 AND CLINICAL EVENTS COMMITTEE CHARTER FOR REVIEW, 930058686. RESPONSE REQUEST BY 30-MAY-12.
	06-APR-2012	06-APR-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: AZ PROTOCOL D1690C00010; OTHER: CHANGE OF INVESTIGATOR INFO- AZ PROTOCOL D1690C00010.
	06-APR-2012	06-APR-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO WRITTEN RPT. #16283061.
	09-APR-2012	09-APR-2012	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ TO MP: AZ PROTOCOL D1690C00010.
	11-APR-2012	11-APR-2012	ANNUAL REPORT	SUBMISSION	AJ TO MP: IND ANNUAL RPT. FOR PERIOD 14-FEB-11 TO 13-FEB-12.
	11-APR-2012	11-APR-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL WRITTEN RPT. #16492563.
	18-APR-2012	18-APR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: REQUEST FOR ADD'L COMMENTS IN AGREEMENT OR NOT WITH REGARDS TO INFO WITHIN THE DRAFT CVOT PROTOCOL SUBMITTED ON 02-APR-12 (SN0422).
	25-APR-2012	25-APR-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO A WRITTEN RPT. #16423295. ALSO SUBMITTED THRU CROSS-REF. TO IND #106,890.
	27-APR-2012	27-APR-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: PROTOCOL MB102072, MB102073, & MB102077; OTHER: CHANGE OF INVESTIGATOR INFO.- MB102072, MB102073, & MB102077.
	30-APR-2012	30-APR-2012	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: PROTOCOL MB102091; PROT. AMEND.: NEW INVESTIGATOR- MB102091; TRANSFER OF OBLIGATIONS TO A CRO.
	01-MAY-2012	01-MAY-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO WRITTEN RPT. #16492563. X-REF LTR. TO IND 106,890.
	04-MAY-2012	04-MAY-2012	CORRESPONDENCE	EMAIL	AJ TO MH: INQUIRY IF PROPOSED PRIMARY & SENSITIVITY ANALYSIS FOR BP STUDIES PROVIDED IN RESPONSE DATED 15-FEB-12 ARE ACCEPTABLE.
	04-MAY-2012	04-MAY-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RESPONSE TO QUESTION DATED 15-FEB-12 RE: INQUIRY OF FDA COMMENTS/RECOMMENDATIONS PROVIDED IN THE 12-JAN-12 EMAIL FOR PROTOCOLS MB102073 & MB102077.
	09-MAY-2012	09-MAY-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA ACCEPTANCE OF PROPOSED PRIMARY & SENSITIVITY ANALYSIS FOR BP STUDIES IN RESPONSE DATED 15-FEB-12.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	10-MAY-2012	10-MAY-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO WRITTEN RPT. #16492563. CROSS-REF. TO IND 106,890.
	18-MAY-2012	18-MAY-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: AZ PROTOCOL D1690C00018; OTHER: CHANGE OF INVESTIGATOR INFO.- AZ PROTOCOLS D1690C00018 & D1690C00019.
	30-MAY-2012	30-MAY-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: PROTOCOLS MB102073 & MB102077; OTHER: CHANGE OF INVESTIGATOR INFO.- PROTOCOLS MB102072, MB102073, & MB102077.
	30-MAY-2012	30-MAY-2012	CORRESPONDENCE	EMAIL	MP TO AJ: FDA ADVICE/INFORMATION RE: AMENDMENT SUBMITTED 02-APR-12.
	01-JUN-2012	01-JUN-2012	OTHER	SUBMISSION	AJ TO MP: AMENDMENT TO PEDIATRIC PLAN SUBMITTED 05-AUG-10 (SEQ. NO. 0312) RE: ALIGNMENT WITH THE FDA ON THE DESIGN OF THE PEDIATRIC CLINICAL EFFICACY & SAFETY STUDY TO SATISFY THE PREA REQ. SHOULD NDA 202293 BE APPROVED. REQUEST FOR FDA REVIEWAL & COMMENTS BY 31-JUL-12. CROSS-REF. TO NDA 202-293.
	13-JUN-2012	13-JUN-2012	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: 48 WEEK FINAL STUDY RPT. FOR D1690C00010, 930059209 & ERRATUM FOR AZ STUDY D1690C00010, 930060301.
	14-JUN-2012	14-JUN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: PLANNING TO PROVIDE FDA WITH AN UPDATED CVOT PROTOCOL & RESPONSE TO ADVICE/INFORMATION PROVIDED 30-MAY-12, BY THE FIRST WEEK IN JULY 2012.
	22-JUN-2012	22-JUN-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RESPONSE TO REQUEST FOR ADD'L COMMENTS MADE 18-APR-12 WITH REGARDS TO INFO WITHIN THE DRAFT CVOT PROTOCOL SUBMITTED ON 02-APR-12 (SN0422).
	28-JUN-2012	28-JUN-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: PROTOCOLS MB102073 & MB102077; OTHER: CHANGE OF INVESTIGATOR INFO- MB102072, MB102073, & MB102077.
	29-JUN-2012	29-JUN-2012	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ TO MP: STUDY DT11112, 930060438.
	29-JUN-2012	29-JUN-2012	CORRESPONDENCE	EMAIL	AJ TO MH/JW: TARGETING TO SUBMIT UPDATED DRAFT CVOT PROTOCOL INCLUDING THE HEPATIC CHARTER THE WEEK OF 02-JUL-12. THIS SUBMISSION WILL ALSO REQUEST A WAIVER FROM SAE REPORTING FOR EVENTS RELATED TO THE PRIMARY ENDPOINT.
	03-JUL-2012	03-JUL-2012	INFO AMENDMENT - CMC	SUBMISSION	AJ TO MP: NEW FACILITY, ALMAC GROUP, FOR PACKAGING & LBL'G; OTHER: CROSS REF. LTR TO IND 63,634 - SN 0467 FOR RESPONSE TO FDA ADVICE/INFO REQUEST LTR DATED 03-JUL-12 CONTAINING PROTOCOL CV181169 AND SN 0468 DATED 03-JUL-12 FOR PROTOCOL CV181168.
	16-JUL-2012	16-JUL-2012	CORRESPONDENCE	EMAIL	AJ TO MH: BMS UPDATE RE: IND 68,652 W/X-REF TO NDA (CVOT) PROTOCOL AND IND 106,890, DELAY OF FILING FOR PROPOSED TRADENAME.
	23-JUL-2012	23-JUL-2012	CORRESPONDENCE	EMAIL	AJ TO MH: BMS REQUEST FOR STATUS RE: AGENCY'S REVIEW/COMMENTS ON DRAFT PED. CLINICAL EFFICACY AND SAFETY STUDY FILED 01-JUN-12 (SN0434).
	24-JUL-2012	24-JUL-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073 & MB102077; OTHER: CHANGE OF INVESTIGATOR INFO- MB102073 & MB102077.
	26-JUL-2012	26-JUL-2012	CORRESPONDENCE	EMAIL	MG TO AJ: FDA POSSIBLY AUGUST OR BEFORE TO PROVIDE COMMENTS ON DRAFT PED. CLINICAL EFFICACY AND SAFETY STUDY FILED 01-JUN-12 (SN0434).
	06-AUG-2012	06-AUG-2012	OTHER	SUBMISSION	AJ TO MP: DRAFT PROT. FOR REVIEW (CVOT), RESPONSE TO AGENCY'S COMMENTS.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	06-AUG-2012	06-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO MH: PROVIDING INFO THAT THE DRAFT PROT. FOR REVIEW (CVOT) WILL BE SUBMITTED 06-AUG-12. REMINDER THAT THE SPONSER IS LOOKING FOR A QUICK REVIEWWITH REQUEST TO COMPLETE REVIEW/COMMENTS BY 14-SEP-12.
	07-AUG-2012	07-AUG-2012	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: MB102091, 930053351, 930061523.
	07-AUG-2012	07-AUG-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL SAFETY RPT. # 16813370.
	13-AUG-2012	13-AUG-2012	OTHER	SUBMISSION	AJ TO MP: CROSS REF. PROTOCOL CV181191, 930062779, SUBMITTED TO BMS-477118, IND 63,634.
	13-AUG-2012	13-AUG-2012	CORRESPONDENCE	LETTER	MP TO AJ: FDA ADVICE/INFO. REQUEST RE: THE PROTOCOL SYNOPSIS FOR A PEDIATRIC CLINICAL EFFICACY & SAFETY STUDY DATED 01-JUN-12.
	13-AUG-2012	13-AUG-2012	CORRESPONDENCE	SUBMISSION	MH TO AJ: UPDATE ON CHANGE OF FDA PROJECT MANAGER TO ABOLADE (BOLA) ADEOLU FOR IND 68,652, IND 106,890, & NDA 202-293. ALSO- FEEDBACK RE: THE CVOT PROT. SUBMITTED 06-AUG-12 WILL NOT RECEIVE EXPEDIENT REVIEW- FEEDBACK WILL BE AVAILABLE 08-OCT-12.
	23-AUG-2012	23-AUG-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073, MB102077, & MB102091; OTHER: CHANGE OF INVES. INFO- MB102073, MB102077, & MB102091.
	27-AUG-2012	27-AUG-2012	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: PROTOCOL MB102091, 930053351 & 930063632.
	27-AUG-2012	27-AUG-2012	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: PROTOCOL MB102129, 930062052 & 930062037; PROT. AMEND.: NEW INVEST.- MB102129; OTHER: TRANSFER OF OBLIGATIONS TO A CRO.
	30-AUG-2012	30-AUG-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO WRITTEN RPT. #16492563.
	05-SEP-2012	05-SEP-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO WRITTEN RPT. #16813370. CROSS-REF. TO IND 106,890.
	05-SEP-2012	05-SEP-2012	CORRESPONDENCE	EMAIL	AA TO AJ: FDA REQUEST TO SUBMIT A SUMMARY OF CHANGES TO THE UPDATED CVOT DRAFT.
	07-SEP-2012	07-SEP-2012	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: PROTOCOL MB102073, 930063562 & 930043915; PROTOCOL MB102077, 930063577 & 930043916.
	10-SEP-2012	10-SEP-2012	CORRESPONDENCE	EMAIL	AJ TO AA: RESPONSE TO FDA REQUEST TO SUBMIT A SUMMARY OF CHANGES TO THE UPDATED CVOT DRAFT DATED 05-SEP-12.
	11-SEP-2012	11-SEP-2012	OTHER	SUBMISSION	AJ TO MP: UPDATED DRAFT CVOT PROTOCOL, AS REQUESTED FROM THE AGENCY ON 05-SEP-12, RE: A TRACK OF CHANGES & SUMMARY OF CHANGES MADE.
	13-SEP-2012	13-SEP-2012	CORRESPONDENCE	EMAIL	AJ TO AA: F/U ON THE PEDIATRIC PK/PD PROTOCOL MB102-091 INCLUDING REQUEST FOR FEEDBACK.
	19-SEP-2012	19-SEP-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073 & MB102077; OTHER: CHANGE OF INVESTIGATOR INFO.- MB102072, MB102073, & MB102077.
	19-SEP-2012	19-SEP-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO WRITTEN RPT. # 14668792. CROSS-REF. TO IND 106,890.
	20-SEP-2012	20-SEP-2012	CORRESPONDENCE	EMAIL	AJ TO AA: PLANS TO SUBMIT AN ESR FOR DAPA ON 21-SEP-12. INQUIRY OF WHEN TO EXPECT THE COMMENTS ON THE DAPA PK PROTOCOL & THE LOCATION FOR THE MEETING TO BE HELD 04-OCT-12.
	22-SEP-2012	22-SEP-2012	CORRESPONDENCE	EMAIL	AA TO AJ: FDA RESPONSE TO FDA INQUIRY DATED 20-SEP-12- REVIEW OF THE PK/PD PEDIATRIC PROTOCOL HAS BEEN COMPLETED, THERE ARE NO COMMENTS TO CONVEY.
	26-SEP-2012	26-SEP-2012	CORRESPONDENCE	EMAIL	AA TO AJ: FDA REQUEST FOR RESPONSE RE: SUBMITTING A DMC CHARTER AND ADD'L QUESTIONS WHICH ARE STILL PENDING.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	26-SEP-2012	26-SEP-2012	CORRESPONDENCE	EMAIL	AJ TO AA: RESPONSE TO FDA REQUEST FOR RESPONSE RE: SUBMITTING A DMC CHARTER AND ADD'L QUESTIONS WHICH ARE STILL PENDING.
	01-OCT-2012	01-OCT-2012	CORRESPONDENCE	EMAIL	AA TO AJ: CLARIFICATION ON INFO. SO THAT THE DAPA TEAM CAN PLAN ACCORDINGLY RE: CVOT COMMENTS, PHARM/TOX ISSUE, & PROPOSED AMENDMENTS.
	02-OCT-2012	02-OCT-2012	CORRESPONDENCE	EMAIL	AA TO AJ: RESPONSE TO CLARIFICATION DATED 01-OCT-12- CVOT COMMENTS TO BE PROVIDED BY COB 05-OCT-12, TO PROVIDE COMMENTS TO THE PHAR/TOX ISSUE AFTER RECEIPT OF RESPONSES, & WILL RESPOND TO PROPOSED AMENDMENTS IN THE FOLLOWING WEEK.
	04-OCT-2012	04-OCT-2012	CORRESPONDENCE	EMAIL	MP TO AJ: FDA ADVICE/INFORMATION REQUEST RE: AMENDMENT SUBMITTED 07-AUG-12 CONTAINING AN UPDATED DRAFT PROTOCOL FOR CV OUTCOME CLINICAL TRIAL, PROTOCOL D1693C00001.
	10-OCT-2012	10-OCT-2012	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U TO WRITTEN RPT. #14557383.
	10-OCT-2012	10-OCT-2012	CORRESPONDENCE	EMAIL	AA TO AJ: FDA PROVIDING RESPONSES TO QUESTIONS SENT VIA EMAIL ON 13-SEP-12 & 01-OCT-12.
	17-OCT-2012	17-OCT-2012	CORRESPONDENCE	EMAIL	BMS providing update on NDA resubmission and CVOT protocol.
	18-OCT-2012	18-OCT-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073, MB102-077, MB102091, & MB102129; OTHER: CHANGE OF INVESTIGATOR INFO.- MB102073 & MB102077.
	06-NOV-2012	06-NOV-2012	OTHER	SUBMISSION	AJ TO MP: PROVIDING CROSS-REFERENCE TO INVESTIGATOR INFO. SUBMITTED TO IND 63,634 (SN0472, SN0477, SN0478, AND SN0481) FOR PROTOCOLS CV181168, CV181169, & CV181191.
	13-NOV-2012	13-NOV-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073 & MB102129; OTHER: CHANGE OF INVESTIGATOR INFO.- MB102072, MB102073, & MB102077.
	19-NOV-2012	19-NOV-2012	PROT. AMEND.: NEW PROTOCOL	SUBMISSION	AJ TO MP: D1693C0001, 930052214; OTHER: TRANSFER OF OBLIGATIONS, DRAFT DOCS. FOR FDA REVIEW RELATED TO THE NEW PROTOCOL (DMC CHARTER, STATISTICAL ANAL. PLAN, & ENDPT. REPORTING MANUAL), AND RESPONSE TO FDA REQUEST FOR INFO DATED 31-MAY-12. CROSS-REF TO NDA 202-293.
	19-NOV-2012	19-NOV-2012	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: MB102073, 930064635, 930043915 & MB102077, 930065045.
	20-NOV-2012	20-NOV-2012	CORRESPONDENCE	EMAIL	FDA providing responses to BMS questions pertaining to SAS progam errors.
	27-NOV-2012	27-NOV-2012	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: PROVIDING THE AGENCY WITH THE ERRATA PREPARED AS A RESULT OF THE MACRO ERROR.
	28-NOV-2012	28-NOV-2012	OTHER	SUBMISSION	AJ TO MP: RESUBMISSSION OF AGENCY FORM FDA 3674 AND PROVIDING THE NATIONAL CLINICAL TRIAL NUMBER (NCT) FOR SN0456 PROT. AMEND.: NEW PROT.
	04-DEC-2012	04-DEC-2012	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE LTR. TO INCORPORATE INVESTIGATOR INFO. FOR CV181168 & CV181169 SUBMITTED UNDER IND 63,634 SN0483 AND REVISED PROTOCOL INFO UNDER SN0485.
	14-DEC-2012	14-DEC-2012	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102091 & MB102129; OTHER: CHANGE OF INVESTIGATOR INFO.- MB102073 & MB102077.
	18-DEC-2012	18-DEC-2012	CORRESPONDENCE	EMAIL	BMS providing CVOT with track changes.
	19-DEC-2012	19-DEC-2012	RESPONSE TO REQUEST	SUBMISSION	AJ TO MP: PROVIDING THE UPDATED DRAFT CVOT PROTOCOL IN TRACK CHANGES, INCLUDING A SUMMARY OF THE CHANGES AS REQUESTED BY THE FDA ON 10-DEC-12.
	09-JAN-2013	09-JAN-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102091 & MB102129; OTHER-CHANGE OF INVESTIGATOR INFO.: MB102073, MB102077, MB102091, & MB102129.

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	23-JAN-2013	23-JAN-2013	CORRESPONDENCE	EMAIL	AJ TO AA: BMS UPDATE ON SUBMISSION OF TRADE NAME & FUTURE CVOT CEC SUBMISSION, AS WELL AS, INQUIRY RE: US (CONVENTIONAL) UNITS USED IN SUBMISSIONS.
	24-JAN-2013	24-JAN-2013	CORRESPONDENCE	EMAIL	AA TO AJ: RESPONSE TO 23-JAN-13 INQUIRY RE: US (CONVENTIONAL) UNITS- FDA POLICY THAT ALL DATA SHOULD BE REPRESENTED IN US (CONVENTIONAL) UNITS.
	29-JAN-2013	29-JAN-2013	OTHER	SUBMISSION	AJ TO MP: PROVIDING DRAFT CLINICAL EVENTS COMMITTEE (CEC) CHARTER FOR REVIEW FOR THE PLANNED DECLARE CVOT-TARGETING FIRST PT. FIRST VISIT FOR APRIL 2013. REQUEST TO PROVIDE COMMENTS BY 25-MAR-13. CROSSREF. TO NDA 202-293.
	29-JAN-2013	29-JAN-2013	CORRESPONDENCE	EMAIL	AJ TO AA: INQUIRY OF FDA REVIEW STATUS RE: DAPA/MET FDC NDA QUESTIONS & CVOT PROTOCOL SUBMITTED 19-NOV-12 (SN 0456).
	31-JAN-2013	31-JAN-2013	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: MB102091, 930053351 & 930063827.
	05-FEB-2013	05-FEB-2013	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: PROVIDING CLINICAL RPTS.- 52 WEEK FINAL STUDY RPT. FOR D1690C00018, 930060800 & 52 WEEK FINAL STUDY RPT. FOR D1690C00019, 930060314.
	07-FEB-2013	07-FEB-2013	CORRESPONDENCE	LETTER	MP TO AJ: FDA ADVICE/INFO. REQUEST RE: CVOT PROTOCOL SUBMISSION SUBMITTED 19-NOV-12 (SN 0456).
	08-FEB-2013	08-FEB-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102091 & MB102129; OTHER: CHANGE OF INVESTIGATOR INFO.- MB102072
	14-FEB-2013	14-FEB-2013	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE LTR. TO INCORPORATE INVESTIGATOR INFO. FOR CV181168 & CV181169 SUBMITTED UNDER IND 63,634 SN0493 & SN0497.
	19-FEB-2013	19-FEB-2013	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: INVESTIGATOR BROCHURE, VER. NO. 09, 930005487.
	25-FEB-2013	25-FEB-2013	OTHER	SUBMISSION	AJ TO MP: UPDATED TRANSFER OF OBLIGATIONS FOR PROTOCOLS MB102073 & MB102077.
	27-FEB-2013	27-FEB-2013	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: D1693C00005- RPT. #17383738. CROSSREF. TO IND 106,890 & NDA 202-293.
	27-FEB-2013	27-FEB-2013	CORRESPONDENCE	EMAIL	AJ TO AA: SUBMITTING FORM FOR STUDY D1693C00005 AS REQUESTED BY THE AGENCY.
	04-MAR-2013	04-MAR-2013	CORRESPONDENCE	EMAIL	AJ TO AA: SPONSER ADD'L QUESTIONS RE: AGENCY ADVICE/INFO, REQUEST DATED 07-FEB-13 RE: CVOT PROTOCOL SUBMITTED 19-NOV-12 (SN 0456).
	11-MAR-2013	11-MAR-2013	CORRESPONDENCE	EMAIL	AA TO AJ: FDA RESPONSES TO BMS ADD'L QUESTIONS DATED 04-MAR-13 RE: FDA ADVICE/INFO DATED FOR CVOT PROTOCOL SUBMITTED 19-NOV-12 (SN 0456)
	11-MAR-2013	11-MAR-2013	CORRESPONDENCE	EMAIL	AJ TO AA: ADDRESSING TIME CONCERNS RE: FDA REQUEST TO CONDUCT A TYPE C MEETING TO FURTHER DISCUSS CVOT TRIAL SUBMITTED 19-NOV-12 (SN 0456).
	11-MAR-2013	11-MAR-2013	INFO AMENDMENT - CMC	SUBMISSION	PC TO MP: PROVIDING CMC INFO. FOR THE ADDITION OF TWO FACILITIES- BMS REED LANE, MORETON, UK AS A PACKAGING AND TESTING SITE & AZ MOLNDAL, SWEDEN AS A LBL'G AND RELEASE SITE ASSOCIATED WITH PROTOCOL D1693C0001.
	12-MAR-2013	12-MAR-2013	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ TO MP: MB102073, MB102077, MB102091, & MB102129.
	14-MAR-2013	14-MAR-2013	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE LTR. TO INCORPORATE INVESTIGATOR INFO. FOR CV181168 & CV181169 SUBMITTED UNDER IND 63,634 SN0501.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	27-MAR-2013	27-MAR-2013	CORRESPONDENCE	EMAIL	AJ TO AA: SPONSER AGREEMENT TO FDA STAT COMMENTS ON THE CVOT LTR. RECEIVED 07-FEB-13, PLANS TO SUBMIT A REVISED SAP TO INCORPORATE COMMENTS; NO FURTHER NEED TO REQUEST A MEETING WITH THE AGENCY TO DISCUSS CVOT TRIAL SUBMITTED 19-NOV-12 (SN 0456).
	27-MAR-2013	27-MAR-2013	CORRESPONDENCE	EMAIL	AJ TO MH: F/U RE: PLANS TO AGREE TO FDA STAT COMMENTS ON THE CVOT LTR. RECEIVED 07-FEB-13 AND TO SUBMIT A REVISED SAP TO INCORPORATE COMMENTS; NO FURTHER NEED TO REQUEST A MEETING WITH THE AGENCY TO DISCUSS CVOT TRIAL SUBMITTED 19-NOV-12 (SN 0456).
	28-MAR-2013	28-MAR-2013	CORRESPONDENCE	EMAIL	MH TO AJ: PLANS TO SUBMIT REVISED SAP FOR CVOT DISCUSSED ON 27-MAR-13 DEEMED TO BE ACCEPTABLE BY FDA.
	29-MAR-2013	29-MAR-2013	CORRESPONDENCE	EMAIL	AA TO AJ: FDA RESPONSE TO QUESTION POSED BY SPONSER IN SUBMISSION DATED 31-JAN-13 (SN 0466); AMENDMENTS FOUND TO BE ACCEPTABLE FOR PROTOCOL MB102091, WILL MEET PREA REQUIREMENTS.
	10-APR-2013	10-APR-2013	ANNUAL REPORT	SUBMISSION	AJ TO MP: IND ANNUAL RPT. FOR PERIOD 14-FEB-12 TO 13-FEB-13 IN DSUR FORMAT.
	18-APR-2013	18-APR-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102129; PROT. AMEND.: CHANGE OF INVESTIGATOR INFO.- MB102073, MB102077, AND MB102129.
	19-APR-2013	19-APR-2013	CORRESPONDENCE	EMAIL	AJ TO MH: UPDATE RE: PEDIATRIC CLINICAL TRIALS (T2D).
	23-APR-2013	23-APR-2013	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE LTR. TO INCORPORATE INVESTIGATOR INFO. FOR CV181168 & CV181169 SUBMITTED UNDER IND 63,634 SN0504.
	26-APR-2013	26-APR-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL WRITTEN RPT. #18786673. CROSS-REF. TO IND 106,890.
	09-MAY-2013	09-MAY-2013	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	AJ TO MP: PROVIDING REVISED PROTOCOL 01 (930052214), PROTOCOL AMENDMENT 01 (930069296), AND THE DMC CHARTER FOR THE DECLARE CVOT STUDY (930069941). CROSS-REF. TO NDA 202-293.
	17-MAY-2013	17-MAY-2013	INFO AMENDMENT - PHARM/TOX	SUBMISSION	AJ TO MP: PROVIDING STUDY 930058573, STUDY 930066037, STUDY 930067105, STUDY BMSR-4157 (930068633), ETC.
	31-MAY-2013	31-MAY-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL WRITTEN RPT. #18742841. CROSS-REF. TO IND 106,890.
	31-MAY-2013	31-MAY-2013	CORRESPONDENCE	SUBMISSION	AJ TO AA: NOTIFICATION OF THE SUBMISSION OF AN IND SAFETY RPT.
	03-JUN-2013	03-JUN-2013	OTHER	SUBMISSION	AJ TO MP: PROVIDING STATISTICAL ANALYSIS PLANS FOR MB102072 (930064431). MB102073 (930068256), MB102077 (930068258).
	05-JUN-2013	05-JUN-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102073, MB102077, MB102129; PROT. AMEND.: CHANGE OF INVEST. INFO.- MB102072, MB102073, MB102077, & MB102129.
	07-JUN-2013	07-JUN-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL WRITTEN RPT. #18948927. CROSS-REF. TO 106,890.
	07-JUN-2013	07-JUN-2013	CORRESPONDENCE	SUBMISSION	AJ TO AA: NOTIFICATION OF UPCOMING SUBMISSION OF A 7-DAY IND SAFETY RPT.
	11-JUN-2013	11-JUN-2013	OTHER	SUBMISSION	AJ TO MP: TRANSFER OF OBLIGATIONS TO CRO FOR PROTOCOLS MB102073 & MB102077.
	11-JUN-2013	11-JUL-2013	CORRESPONDENCE	EMAIL	Submission of the revised SAP for IND 068652(dapagliflozin)
	13-JUN-2013	13-JUN-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U #1 TO WRITTEN RPT. #18742841. CROSS-REF. TO IND 106,890.
	13-JUN-2013	13-JUN-2013	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE LTR. TO INCORPORATE INVESTIGATOR INFO. FOR CV181168 & CV181169 SUBMITTED UNDER IND 63,634 SN0509 & SN0510.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	13-JUN-2013	13-JUN-2013	CORRESPONDENCE	EMAIL	Dapa - f/u on safety report from 31-May-2013
	14-JUN-2013	14-JUN-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U #1 TO WRITTEN RPT. #18948927. CROSS-REF. TO IND 106,890.
	14-JUN-2013	14-JUN-2013	CORRESPONDENCE	EMAIL	F/U No. 1 to Safety Report No. 18948927.
	21-JUN-2013	21-JUN-2013	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: PROVIDING CLINICAL RPTS.- 104 WEEK FINAL STUDY RPT. FOR D1690C00018, 930070248 & 104 WEEK FINAL STUDY RPT. FOR D1690C00019, 930070353.
	02-JUL-2013	02-JUL-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL WRITTEN RPT. #18913749. CROSS-REF. TO IND 106, 890.
	02-JUL-2013	02-JUL-2013	INFO AMENDMENT - CLINICAL	SUBMISSION	AJ TO MP: PROVIDING FINAL STUDY RPTS. FOR MB102073 (930068227) & MB102077 (930068216).
	03-JUL-2013	03-JUL-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: INITIAL WRITTEN RPT. #19007848. CROSS-REF. TO IND 106, 890.
	11-JUL-2013	11-JUL-2013	OTHER: CHANGE OF INVESTIGATOR INFO	SUBMISSION	AJ TO MP: MB102073 & MB102077.
	31-JUL-2013	31-JUL-2013	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR FDA REVIEW/FEEDBACK FOR DRAFT PROTOCOL AMENDMENT FOR STUDY MB102091.
	31-JUL-2013	31-JUL-2013	CORRESPONDENCE	EMAIL	Submission of the Dapa-Pediatric PK/PD study amendment
	02-AUG-2013	02-AUG-2013	CORRESPONDENCE	EMAIL	Correspondence regarding fdc and dapa NDA and IND.
	05-AUG-2013	05-AUG-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO MP: F/U #1 TO WRITTEN RPT. #18913749. CROSS-REF. TO IND 106,890.
	06-AUG-2013	06-AUG-2013	CORRESPONDENCE	EMAIL	Correspondence regarding no acknowledgement received for SN0496.
	14-AUG-2013	14-AUG-2013	CORRESPONDENCE	EMAIL	Dapa-Pediatric PK/PD study amendment for study MB102-091.
	27-AUG-2013	27-AUG-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO MP: MB102091 & MB102129; PROT. AMEND.: CHANGE OF INVEST. INFO.- MB102129.
	29-AUG-2013	29-AUG-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO JG: INITIAL WRITTEN RPT. #19134964. CROSS-REF. TO IND 106,890 & NDA 202-293.
	29-AUG-2013	29-AUG-2013	CORRESPONDENCE	EMAIL	Correspondence regarding BMS-512148 (dapagliflozin).
	29-AUG-2013	29-AUG-2013	CORRESPONDENCE	EMAIL	Correspondence regarding acting director of the Division of Metabolism and Endocrinology Products.
	03-SEP-2013	03-SEP-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Dapa Target Plan.
	04-SEP-2013	04-SEP-2013	OTHER	SUBMISSION	AJ TO JG: PROVIDING REVISED STATISTICAL ANALYSIS PLAN (SAP) (930065684), RESPONSE TO AGENCY'S COMMENTS DATED 07-FEB-13 (930071606), AND REVISED DMC CHARTER (930069941 & 930072663). CROSS-REF. OF SUBMISSION TO NDA 202-293.
	05-SEP-2013	05-SEP-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	AJ TO JG: F/U #1 TO WRITTEN RPT. #19134964. CROSS-REF. TO IND 106,890 AND NDA 202-293.
	12-SEP-2013	12-SEP-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	AJ TO JG: NEW AND UPDATED INVESTIGATOR INFO. FOR D1693C0001.
	16-SEP-2013	16-SEP-2013	CORRESPONDENCE	EMAIL	Correspondence regarding policy change for opening a new IND for T1DM.
	19-SEP-2013	19-SEP-2013	OTHER	SUBMISSION	Cross Reference Letter - Protocol CV181168 and CV181169 for investigator information.
	02-OCT-2013	02-OCT-2013	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	Protocol MB102-129, 930070881, 930062052.
	11-OCT-2013	11-OCT-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Initial Safety Report # 19438522, X-ref 106,890.
	11-OCT-2013	11-OCT-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	New Investigator for studies MB102-091 and MB102-129 and Changes to previously submitted Principal Investigator for study MN102-129
	15-OCT-2013	15-OCT-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	Provide Investigator documentation for new PIs participating in study D1693C00001.
	17-OCT-2013	17-OCT-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	F/U No. 1 to Safety Report No. 19438522 Pyelonephritis and Acute Renal Failure. X-ref 106,890 Seq No. 0087
	28-OCT-2013	28-OCT-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Safety Report No. 19670728. X-ref with 106,890.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	28-OCT-2013	28-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Dapa 7 day IND safety report.
	30-OCT-2013	30-OCT-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Safety Report No. 19630334.
	01-NOV-2013	01-NOV-2013	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	Submission of amendment 05 and updated protocol for Study MB102091 (dapagliflozin pediatric PK/PD study). Revised Protocol 05 dated 22-October-2013 to MB102091. Amendment 05 dated 22-October-2013 to MB102091.
	01-NOV-2013	01-NOV-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Initial Safety Report No. 19651728. X-ref with 106,890.
	05-NOV-2013	05-NOV-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Follow up No. 1 to Safety Report No. 19670728. X-ref 106-890.
	12-NOV-2013	12-NOV-2013	INFO AMENDMENT - CLINICAL	SUBMISSION	This submission provides the Final Study Report for MB102-072
	15-NOV-2013	15-NOV-2013	LETTER OF CROSS-REFERENCE	SUBMISSION	This submission authorizes reference of IND 68,652 by the FDA and Ralph A. DeFronzo, MD.
	18-NOV-2013	18-NOV-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Initial Safety Report Number 19775774. X-ref 106,890.
	18-NOV-2013	18-NOV-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Initial Safety Report Number 19792159. X-ref 106,890.
	20-NOV-2013	20-NOV-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	This submission provides Investigator documentation for new investigators and changes to previously submitted investigator information for study D1693C00001.
	20-NOV-2013	20-NOV-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Follow up No. 2 to Safety Report Number. X-ref INDs 68,652, 106,890 and NDA 202-293.
	21-NOV-2013	21-NOV-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Initial Safety Report No. X-ref 106,890.
	21-NOV-2013	21-NOV-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	Protocol Amendment: New Investigator and Change of Investigator Information - provide Investigator documentation for new investigators participating in study MB102-091 and MB102-129 as well as changes to previously submitted investigator information for study MB102-091 and study MB102-129.
	02-DEC-2013	02-DEC-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Follow up Number 1 to Safety Report No. 19775774. X-ref IND 106,890.
	05-DEC-2013	05-DEC-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Safety Report No. X-ref INDs 68,652 and 106,890.
	16-DEC-2013	16-DEC-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Follow up No. 1 to IND Safety Report No. X-ref INDS 68,652 and 106,890.
	17-DEC-2013	17-DEC-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Initial Safety Report No. 19890805. X-ref INDs 68,652, 106,890, and 202-293.
	18-DEC-2013	18-DEC-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Follow up No. 2 to Safety Report No. 19845767. X-ref INDs 68,652 and 106,890.
	20-DEC-2013	20-DEC-2013	OTHER	SUBMISSION	OTHER: REQUEST FOR TYPE B END-OF-PHASE 2 MEETING (T1DM)
	26-DEC-2013	26-DEC-2013	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	Providing revised protocol 02 and protocol amendment 02 for DECLARE CVOT study (930052214 & 930076108) . Cross-Ref. to NDA 202-293.
	27-DEC-2013	26-DEC-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	Initial Safety Rpt. # 19899939. Cross-ref to IND 106,890.
	31-DEC-2013	31-DEC-2013	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	MB102091; Prot. Amend.: Change in Investigator Info.- MB102091 & MB102129.
	31-DEC-2013	31-DEC-2013	SAFETY REPORT: INITIAL/FOLLOW-UP	SUBMISSION	F/U #1 to Written Rpt. #19890805. Cross-Ref. from to IND 106,890 & NDA 202-293.
	03-JAN-2014	03-JAN-2014	PROT. AMEND.: NEW INVESTIGATOR	SUBMISSION	D1693C00001; Prot. Amend.: Change in Investigator Info.- D1693C00001.
	07-JAN-2014	07-JAN-2014	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	Providing Changes to Investigator Info. Re: Western IRB Address Change effecting sites under MB102-091 & MB102-129.
	08-JAN-2014	08-JAN-2014	PROT. AMEND.: CHANGE IN PROTOCOL	SUBMISSION	Changes to Investigator Information re: Quorum Review IRB address change for Protocol D1693C00001.

Country/Agency UNITED STATES OF AMERICA
Initial Application Number 202-293
Initial Application Type MARKETING
Common Drug Name DAPAGLIFLOZIN
Initial Application Title (DAPAGLIFLOZIN) 5 MG PER 1 FILM COATED TABLET, --10 MG PER 1 FILM COATED TABLET

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	25-AUG-2010	25-AUG-2010	CORRESPONDENCE	EMAIL	CDER TO DB: FDA PROVIDING PRE-ASSIGNED NDA NUMBER 202-293.
	06-DEC-2010	06-DEC-2011	CORRESPONDENCE	LETTER	AJ TO FDA: OFFICIAL MINUTES FROM TELECON. ON 6-DEC-11 INCLUDING LIST OF ATTENDEES, RE: PMRS.
	10-DEC-2010	10-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS RESPONSE QUESTIONS TO FDA LABELING COMMENTS.
01-JUL-2008	27-DEC-2010	27-DEC-2010	INITIAL APPLICATION	SUBMISSION	(DAPAGLIFLOZIN) 5 MG PER 1 FILM COATED TABLET, --10 MG PER 1 FILM COATED TABLET
	28-DEC-2010	28-DEC-2010	CORRESPONDENCE	LETTER	FDA TO AJ: FDA STAMP RECEIPT OF NDA COVER LTR. DATED 27-DEC-10.
	05-JAN-2011	05-JAN-2011	OTHER	SUBMISSION	AJ TO MP: PROVIDING ADD'L PATENT INFORMATION.
	07-JAN-2011	07-JAN-2011	CORRESPONDENCE	EMAIL	AJ TO RC: EMAIL CONTACT RE: REQUEST TO CONDUCT A APPLICANT ORIENTATION PRESENTATION WITH FDA.
	12-JAN-2011	12-JAN-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING CRF MISSING FROM INITIAL NDA FOR STUDY D1690C00005-2001-3.
	12-JAN-2011	12-JAN-2011	CORRESPONDENCE	EMAIL	AJ TO RC: BMS REQUEST FOR "EMDAC" DATES FOR 2011 TO BE PUBLISHED.
	12-JAN-2011	12-JAN-2011	CORRESPONDENCE	EMAIL	AJ TO RC: BMS RESPONSE TO FDA REQUEST TO "SAS" CODE TO CREATE ANALYSIS DATA SETS AND KEY TABLES IN CLINICAL STUDY RPTS.
	12-JAN-2011	12-JAN-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA RESPONSE THAT OF NO NEED FOR APPLICANT ORIENTATION MTG. REQUESTS WILL BE MADE AS NEEDED.
	13-JAN-2011	13-JAN-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA CONFIRMING TELECON. AVAILABILITY TO DISCUSS/CLARIFY REQUEST FOR INFO. BY FDA STATISTICIAN.
	14-JAN-2011	14-JAN-2011	CORRESPONDENCE	EMAIL	CP TO "CDER ESUB" - BMS PROVIDING REFERENCE TO "APIXABAN IND 66106 DSI PRE-NDA COMMENTS IN REGARDS TO "SITE LEVEL DATA."
	14-JAN-2011	14-JAN-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA NEED TO RESCHEDULE TELECON..
	14-JAN-2011	14-JAN-2011	CORRESPONDENCE	TELEPHONE	AJ TO FDA: BMS MET WITH FDA TO DISCUSS/CLARIFY REQUEST FOR ADDITIONAL STATISTICAL INFORMATION.
	21-JAN-2011	21-JAN-2011	CORRESPONDENCE	EMAIL	AJ TO SL: BMS CONFIRMING "SUMMARY LEVEL CLINICAL SITE DATA" ON TRACK FOR FILING 28-JAN-11.
	21-JAN-2011	21-JAN-2011	CORRESPONDENCE	EMAIL	CR TO CP: FDA SUGGEST TO USING "DATA-LISTINGDATASET" VS. "LEGACY-CLINICAL-STUDY-REPORT" WHERE THERE ARE NO SPECIFIC FILE TAGS.
	21-JAN-2011	21-JAN-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA ACK. LTR. OF NDA FILING DATED 27-DEC-10.
	25-JAN-2011	25-JAN-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA CONFIRMING FDA ACK. LTR. SENT 21-JAN-11, RE: NDA FILING DATED 27-DEC-10.
	27-JAN-2011	27-JAN-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST DATED 11-JAN-11, FOR EFFICACY PROGRAMS.
	27-JAN-2011	27-JAN-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA ADVISES BMS TO HOLD OFF FILING "SAS PROGRAM REQUEST" UNTIL STATISTICAL REVIEWER CAN RESPOND.
	27-JAN-2011	27-JAN-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA WILL CLARIFY FORMAT RE: "MHI" RAW DATASETS.
	28-JAN-2011	28-JAN-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA FOR SITE-LEVEL-DATA.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	28-JAN-2011	28-JAN-2011	CORRESPONDENCE	EMAIL	AJ TO RC: BMS NOTIFICATION RE: 2 AMEND'S TO PENDING NDA, SN# 0003 & 0004.
	28-JAN-2011	28-JAN-2011	CORRESPONDENCE	EMAIL	AJ TO RC: BMS WILL PROVIDE "MHI" RAW DATASET AS NONSTD. PIDS, AND WILL ALSO PROVIDE UPDATED DATASETS WITH STD. PIDS.
	31-JAN-2011	31-JAN-2011	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR PROPRIETARY NAME REVIEW
	31-JAN-2011	01-FEB-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR UPDATED MONTREAL HEART INSTITUE (MHI) DATA SET USING STANDARD PID'S.
	02-FEB-2011	02-FEB-2011	CORRESPONDENCE	EMAIL	MT TO AJ: FDA CONFIRMING PROPER REFERENCE RE: LOCATION OF PROPOSED LABELING TO SUPPORT TRADENAME REVIEW.
	09-FEB-2011	09-FEB-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA REQUEST RESPONSE TO STATISTICAL REVIEWER RE: PRIMARY EFFICACY ANALYSIS, BE PROVIDED BY APPROX. 18-FEB-11.
	15-FEB-2011	15-FEB-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA CONFIRMING FILING MTG. TAKEN PLACE AND MEHREEN HAI (FDA) WILL NOW SUPPORT NDA.
	16-FEB-2011	16-FEB-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO REQUEST FOR CLARIFICATION ON EFFICACY ANALYSES.
	24-FEB-2011	24-FEB-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS REQUESTING CLARIFICATION ON RECEIPT OF PENDING NDA ACK. LTR.
	04-MAR-2011	04-MAR-2011	CORRESPONDENCE	LETTER	MP to AJ: FDA ltr. confirming completion of filing review of submissions dated Jan. 5, 12, 27, 28 and 31, and Feb. 1 & 16, 2011; and has determined that the application is sufficiently complete to permit a substantive review. During review, FDA identified some potential review issues and requested BMS to submit additional info.
	07-MAR-2011	07-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA recommendation to contact Paul Tran prior to BMS' discussion w/FDA re: timing for the Division's review of briefing book and presentation slides.
	09-MAR-2011	09-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA response to BMS' questions (3, 6 & 9).
	23-MAR-2011	23-MAR-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to FDA request for information as per 04-Mar-11 Filing Communication Letter from the Agency.
	24-MAR-2011	24-MAR-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA PROVIDING LOGISTIC INFO. FOR REVIEW FOR AC MTG.
	24-MAR-2011	24-MAR-2011	CORRESPONDENCE	EMAIL	PT to AJ: Email communications w/FDA re: Dapagliflozin Advisory Committee meeting tentatively scheduled for Jul. 19, 2011.
	25-MAR-2011	25-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA advice to submit the documents concerning CEC, after Dr.Leibenhaut sends a formal request.
	25-MAR-2011	25-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA confirmation that re: Question 1, BMS' proposal is acceptable.
	25-MAR-2011	25-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA esponse to questions 2 & 3. FDA confirmed that response to Q1 and other BMS emails will be provided shortly.
	29-MAR-2011	29-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA confirmation that they require information only for 6 of the Phase 3 studies (MB102013, MB102014, MB102030, MB102034, D160C00004 and D160C00006).
	29-MAR-2011	29-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA responses to BMS' questions regarding the AC meeting.
	30-MAR-2011	30-MAR-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for information - SCE Analysis Questions.
	30-MAR-2011	30-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA request for biopharmaceutics information request (complete disintegration method report (Method 0121) and supporting validation data) for NDA 202293 (dapagliflozin).

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	30-MAR-2011	30-MAR-2011	CORRESPONDENCE	EMAIL	PT to AJ: FDA request to BMS for a copy of the main slides and back-up slides in PDF format, so that it is ready to be posted on the web after the Dapagliflozin Advisory Committee meeting (scheduled tentatively for July 19, 2011), without needing to convert from PowerPoint to PDF.
	31-MAR-2011	31-MAR-2011	CORRESPONDENCE	EMAIL	AJ to MH: BMS confirmation to provide Disintegration method, as requested by the FDA within 2 weeks.
	31-MAR-2011	31-MAR-2011	CORRESPONDENCE	EMAIL	AJ to MH: Email confirming that BMS submitted the information requested by FDA on March 30, 2011 (SN0009).
	31-MAR-2011	31-MAR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA email clarifying their request for Validation method. FDA confirmed that the term Validation was used to refer to all data supporting the suitability of the method for the product, as well as BMS' rationale for the use of disks. FDA accepted the proposed timeline of 2 weeks.
	07-APR-2011	07-APR-2011	CORRESPONDENCE	EMAIL	AJ to MH: Preliminary information in response to FDA's voice message re' NDA 202-293.
	07-APR-2011	07-APR-2011	CORRESPONDENCE	EMAIL	Dapa-voice mail from FDA-Division of Science investigation - f/u discussion.
	08-APR-2011	08-APR-2011	CORRESPONDENCE	EMAIL	AJ to MH: Clarification re: Annex 2, 3 and 5 referenced in the Risk Management Plan submitted for the Dapagliflozin NDA.
	08-APR-2011	08-APR-2011	CORRESPONDENCE	EMAIL	AJ to SL: Email to the FDA confirming that the appropriate contact for Dr.Montoro's site is Dr.Baudilio Cusco, since Dr.Montoro & Dr.Issac Kirsner have passed away.
	11-APR-2011	11-APR-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for CEC Charter information.
	12-APR-2011	12-APR-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for Disintegration Method.
	12-APR-2011	12-APR-2011	CORRESPONDENCE	EMAIL	AJ to MH: Correction re: 4 month safety update which will be SN0012.
	12-APR-2011	12-APR-2011	CORRESPONDENCE	EMAIL	AJ to MH: FDA responses to BMS' question re: comment#2.
	12-APR-2011	12-APR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA info. request re: PopPK.
	13-APR-2011	13-APR-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for RMP Annexes.
	13-APR-2011	13-APR-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA confirmation that the status of the trade name review can be obtained from Margarita Tosa, OSE RPM.
	13-APR-2011	13-APR-2011	CORRESPONDENCE	EMAIL	MT to AJ: FDA confirmation that the TN review is in progress and TN PDUFA date is 04/29/2011. BMS will receive a TN letter on or before this date.
	14-APR-2011	14-APR-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for population pharmacokinetics dataset.
	15-APR-2011	15-APR-2011	CORRESPONDENCE	EMAIL	AJ to SL: BMS confirmation re: the inspection of ICON by FDA.
	15-APR-2011	15-APR-2011	CORRESPONDENCE	EMAIL	AJ to SL: Email to notify the FDA that BMS is following up w/ ICON, w.r.t an email notifcation informing ICON about an upcoming FDA inspection of their Poland Office.
	19-APR-2011	19-APR-2011	CORRESPONDENCE	EMAIL	AJ to MH: BMS email confirmation that FDA's info. request for NDA 202293 re:Comment#2 is targeted for submission Fri this week or Mon of next week.
	22-APR-2011	22-APR-2011	AMENDMENT	SUBMISSION	AJ to MP: Agency requested program files and response documents in Module 5.3.5.1, under the STF for each phase 3 study, & Module 5.3.5.3 for the response to Q3.
	25-APR-2011	25-APR-2011	CORRESPONDENCE	EMAIL	AJ to PT: BMS email to the FDA which includes the financial disclosure tables submitted w/ the initial IND. Also includes 4-month safety update financial disclosure tables which includes only new investigators not submitted in the initial NDA or updated financial disclosure information for inv. submitted w/initial NDA.
	25-APR-2011	25-APR-2011	CORRESPONDENCE	EMAIL	PT to AJ: Dapagliflozin Advisory committee mtg. FDA email indicating that they are still in the process of selecting meeting location for Jul 19th.
	26-APR-2011	26-APR-2011	CORRESPONDENCE	EMAIL	MT to AJ: TN letter for NDA 202293 from the FDA.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	26-APR-2011	26-APR-2011	CORRESPONDENCE	LETTER	CH to AJ: FDA letter re: proprietary name request.
	28-APR-2011	28-APR-2011	AMENDMENT	SUBMISSION	AJ to MP: 4-month clinical safety update.
	28-APR-2011	28-APR-2011	CORRESPONDENCE	EMAIL	AJ to MH: Email confirming that BMS will provide a response within 2 wks, re: FDA's info. request/comment for the dapagliflozin NDA.
	02-MAY-2011	02-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MW: BMS confirmation by email to provide the requested information to the FDA re: upcoming clinical inspections in Argentina for NDA 202-293 during the time frames 5/30/2011 - 6/03/2011 and 6/06/2011-6/10/2011. FDA requested BMS to complete the inspection in Cordoba during the 1st wk. followed by the inspection in Beunos Aires.
	02-MAY-2011	02-MAY-2011	CORRESPONDENCE	LETTER	MW to AJ: Ltr. announcing & requesting confirmation of the routine BIMO inspections to be conducted by the US FDA to determine if the facility & operations of the clinical inv.s &/or sites are in accordance w/ Clinical GCP reg.s.
	03-MAY-2011	03-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MH: FDA Tcon request to have a brief discussion abt. Dapagliflozin re: a cardiovascular trial that BMS needs to conduct as a postmarketing requirement.
	03-MAY-2011	03-MAY-2011	CORRESPONDENCE	EMAIL	AJ to SL: Email to the FDA to give a heads up on an inspection from Health Canada of site 127 for the MB102029 study.
	03-MAY-2011	03-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA info. request for dapagliflozin re: bioanalytical methods, chiral chromatography data & Pharmacology.Toxicology data.
	03-MAY-2011	03-MAY-2011	CORRESPONDENCE	EMAIL	MW to AJ: Studies reviewed for the clinical inspections in Argentina for NDA 202-293.
	04-MAY-2011	04-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MH: BMS ques' on FDA's info. request dated 04-May-2011.
	04-MAY-2011	04-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MH: Email to the FDA re Tcon w/FDA on Thursday, May 5, 2011.
	04-MAY-2011	04-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MW: Argentina sites had some challenges w/FDA's proposed inspection dates. BMS email to the FDA w/newly proposed dates
	04-MAY-2011	04-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: Another information request from the FDA for dapagliflozin (NDA 202293). FDA has requested a response within 1 week for some requests and within 2 weeks for the remainder.
	05-MAY-2011	05-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA responses to BMS' f/u questions on the dapa info. request dated May 4, 2011.
	06-MAY-2011	06-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MH: BMS response for the clinical pharmacology ques. that will be formally submitted next week. Responses to the Pharm/Tox questions to be provided next week.
	06-MAY-2011	06-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA info. request for dapa (NDA 20293).
	09-MAY-2011	09-MAY-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for Clin Pharm and Pharm Tox information. Response doc.s for the clinical pharmacology requests were emailed to Mehreen Hai on 6-May-2011.
	09-MAY-2011	09-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: Quick Info. request from the FDA for dapa.
	09-MAY-2011	09-MAY-2011	CORRESPONDENCE	SUBMISSION	MH TO AJ: OFFICIAL FDA MINUTES OF MEETING HELD 05-MAY-11 TO DISCUSS REQUIREMENT TO CONDUCT A CV CLINICAL TRIAL AS A PMR.
	10-MAY-2011	10-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: Thank you email from FDA for the PID list as per FDA's request email dated 09-May-2011.
	10-MAY-2011	10-MAY-2011	CORRESPONDENCE	LETTER	LM to MW: Ltr. from the PI Dr.Laura Maffei, to confirm availability for the routine BIMO GCP clinical inspection to be conducted by US FDA on 13 to 17 June 2011 at Buenos Aires, Argentina. The inspection initiation mtg. w/FDA inv., Mr.Thomas Gordon will begin at 08h00am on the first day of inspection.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	11-MAY-2011	11-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MH: Dapa May 4 Info. request re: Ques. 1(hepatic) response doc, Ques. 2(bone marker data) response doc. & requested tables, Ques. 3(serum phosphorus) response doc & Ques. 4 (Active comparator study) response doc.
	11-MAY-2011	11-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MW: Signed confirmation letters from both sites (Cordoba & Buenos Aires in Argentina), containing the requirements laid forth in FDA Clinical Inspection Announcement letter dated 2-May-11. FDA Investigator's itinerary to be sent out soon w/ the ground transportation & other details.
	11-MAY-2011	11-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: Status update on the Dapa. Info request per FDA email dated 06-May-2011.
	11-MAY-2011	11-MAY-2011	CORRESPONDENCE	LETTER	AA to AJ: FDA's request for a prompt written request re: CMC sections of NDA.
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	EMAIL	AJ to DH: BMS to contact FDA shortly re: the planned timeline for response re: FDA's CMC info. request letter dated 12-May-2011.
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MH: Clarification request to the FDA re: Acetamide. This BMS request is a f/u to FDA request email dated 12-May-2011.
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MH: Dapa - May 4 Info. request - correction on one table.
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	EMAIL	AJ to MW: Email to confirm whether FDA will be contacting ANMAT re: the upcoming Clinical Site inspections in Argentina.
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: Dapa - Info. request - status update.
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: FDA confirmation that they need narratives for all SAE and non-SAE cases re: FDA request 3 dated 06-May-2011.
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	EMAIL	MH to AJ: Non-clinical info. request from the FDA for dapagliflozin (ND 202293).
	12-MAY-2011	12-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MH: CORRECTION TO RESPONSE TO MAY 4TH, FDA REQUEST RE: LAB PARAMETERS.
	13-MAY-2011	13-MAY-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for clinical safety and D1690C0004 control.
	13-MAY-2011	13-MAY-2011	CORRESPONDENCE	EMAIL	DH to AJ: Final response doc.s to be sent to FDA on May 26th without publishing & formally submit them the 1st wk. of June (after publishing & submitting in eCTD). This is re: CMC info. request letter from the FDA dated 12-May-2011.
	16-MAY-2011	16-MAY-2011	AMENDMENT	SUBMISSION	AJ to MP: Additional supporting data for the proposed waiver of microbial testing. This is in reference to the 28-Apr-2011 CMC request/comment from the Agency (via email from Dr.Mehreen Hai) re: the inclusion of microbial limits release criterion in the drug product specification.
	17-MAY-2011	17-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MW: BMS PROVIDING ITINERARY FOR FDA INVESTIGTOR.
	17-MAY-2011	17-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MW: BMS STATUS UPDATE OF FDA CMC REQUESTS DATED 28-APR-11.
	17-MAY-2011	17-MAY-2011	CORRESPONDENCE	SUBMISSION	MW TO AJ: FDA CONFIRMING 'ANMAT" NOTIFIED OF PENDING SITE INSPECTION.
	17-MAY-2011	17-MAY-2011	CORRESPONDENCE	SUBMISSION	MW TO AJ: FDA REQUEST FOR INFO. RE: HY'S LAW AND 4 MONTH SAFETY UPDATE (4MSU).
	18-MAY-2011	18-MAY-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to Agency's request for Clinical safety & Efficacy information for questions 4-12 which were not provided in SN0018.
	18-MAY-2011	18-MAY-2011	CORRESPONDENCE	SUBMISSION	MH TO AJ: FDA CONFIRMING NO NEED FOR RESPONSE TO ACETAMIDE.
	19-MAY-2011	19-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MH: BMS RESPONSE TO FDA REQUEST 17-MAY-11, FDA REQUEST FOR INFO. RE: HY'S LAW AND 4 MONTH SAFETY UPDATE (4MSU).
	19-MAY-2011	19-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MW: BMS PROVIDING GROUND TRANSPORTATION AND CONTACT INFO. FOR FDA INSPECTOR.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	20-MAY-2011	20-MAY-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to the 06-May-2011 request from the Agency for additional clinical safety info.
	20-MAY-2011	20-MAY-2011	OTHER	SUBMISSION	AJ to MP: Cross-reference submission in regards to the Agency's request dated 06-May-11.
	20-MAY-2011	20-MAY-2011	CORRESPONDENCE	SUBMISSION	MH TO AJ: FDA REQUEST FOR INFO.
	23-MAY-2011	23-MAY-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR INFORMATION RE: CMC STABILITY UPDATE DATA.
	23-MAY-2011	23-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MH: BMS PROVIDING DRAFT 'EMDAC' BRIEFING DOCUMENT.
	24-MAY-2011	24-MAY-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR CLINICAL SAFETY INFORMATION.
	24-MAY-2011	24-MAY-2011	CORRESPONDENCE	LETTER	MW TO AJ: FDA LTR. NOTIFICATION OF A SPONSOR INSPECTION FOR NDA 202-293; AZ, WEDEL, GERMANY.
	24-MAY-2011	24-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MH: RESPONSE TO FDA QUESTIONS OF MAY 20.
	24-MAY-2011	24-MAY-2011	CORRESPONDENCE	SUBMISSION	MW TO AJ: FDA NOTIFICATION OF A SPONSOR INSPECTION FOR NDA 202-293.
	25-MAY-2011	25-MAY-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA CONFIRMING START OF STUDY CAN BEGIN IN TYPE 1 PTS. UNDER CURRENT DAPA. IND.
	25-MAY-2011	25-MAY-2011	CORRESPONDENCE	SUBMISSION	MH TO AJ: FDA REQUEST FOR INFO. RE: BMS RESPONSE DATED 09-MAY-11.
	26-MAY-2011	26-MAY-2011	CORRESPONDENCE	EMAIL	AJ TO DH: BMS PROVIDNG CMC RESPONSE DOCUMENT TO FDA REQUEST DATED 11-MAY-11.
	26-MAY-2011	26-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MH: BMS REQUESTING CLARIFICATION RE: FDA REQUEST DUE MAY 27 AND JUNE 1, 2011.
	26-MAY-2011	26-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MW: BMS ADVISING FDA RE: DR. GOLDBERGS SITE UNDERGOING MINOR CONSTRUCTION PRIOR TO THE ARRIVAL OF INSPECTOR.
	26-MAY-2011	26-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MW: BMS CHECKING WHETHER FDA WILL NOTIFY HEALTH CANADA OF PLANNED INSPECTION.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS FILING ZIP FILES TO FDA REQUEST DATED 26-MAY-11.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING CV OUTCOME TRIAL SYNOPSIS AND MTG. REQUEST LTR.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING DATASETS FOR MAY 26 FDA REQUEST.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING FINAL RESPONSES TO FDA Q1-5 OF MAY 26.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	AJ TO MW: BMS CONFIRMING DATES OF INSPECTION AT AZ SITE IN GERMANY.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA ADVISE TO X-REF NEW NONCLINICAL RPTS TO THE NDA.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA CONFIRMING PROPSED LISTING TO FDA REQUEST 26-MAY-11, IS ACCEPTABLE.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST FOR INFO.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	EMAIL	MW TO AJ: FDA CONFIRMING THEY WILL NOTIFY CANADA AND GERMANY HA. OF INSPECTIONS.
	27-MAY-2011	27-MAY-2011	CORRESPONDENCE	SUBMISSION	AJ TO MH: BMS PROVIDING RECOMMENDED HOTELS DURING INSPECTION.
	31-MAY-2011	31-MAY-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDNG TRAVEL INFO. FOR CLINICAL INSPECTION IN ARGENTINA.
	31-MAY-2011	31-MAY-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA CLARIFYING REQUEST FOR INFO. ALSO INLCUDES 'eDISH" INFORMATION.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	31-MAY-2011	31-MAY-2011	CORRESPONDENCE	EMAIL	RC TO AJ: FDA REQUEST FOR INFO. FROM BMS FINAL RESPONSE PROVIDED 27-MAY-11.
	01-JUN-2011	01-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING RESPONSES TO REMAINING 3 QUESTIONS FROM MAY 26, 2011.
	01-JUN-2011	01-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO RC: BMS PROVIDING TELECON. INFORMATION TO DISCUSS NARRATIVE DATASET.
	01-JUN-2011	01-JUN-2011	CORRESPONDENCE	EMAIL	MW TO AJ: FDA PROVIDING ITINERARY OF FDA AUDITS IN CANADA & GERMANY.
	01-JUN-2011	01-JUN-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA WILL NOTIFY BMS RE: STATUS OF 'FR' NOTICE FOR AC MTG.
	02-JUN-2011	02-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to Agency's request dated 20-May-11.
	02-JUN-2011	02-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to Agency's request dated 12-May-11 for additional CMC information.
	02-JUN-2011	02-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MW: BMS PROVIDING F/U HOTEL INFO. FOR FDA INSPECTOR IN GERMANY.
	02-JUN-2011	02-JUN-2011	CORRESPONDENCE	TELEPHONE	AJ TO MH: TELECON. FOR CLARIFICATION WITH RESPECT TO 'EDISH' NARRATIVE DATASET REQUEST.
	03-JUN-2011	03-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to the 26-May-2011 request from the Agency for additional clinical information.
	03-JUN-2011	03-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Cross-reference submission.
	03-JUN-2011	03-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING DATASET.
	03-JUN-2011	03-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING DATASETS IN TRANSPORT FILE FORMAT.
	03-JUN-2011	03-JUN-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA INDICATES NO ACTION YET REQUIRED RE: SAFETY ASSESSMENT.
	03-JUN-2011	03-JUN-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA INDICATES START OF PED. PK/PD STUDY CAN START UPON RECEIPT OF COMMENTS ON PROTOCOL TO ENSURE STUDY MEETS 'PREA' REQUIREMENTS.
	03-JUN-2011	03-JUN-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST BMS PROVIDE STATUS INFO. (ER &PR) FOR PTS. IN ADDITION TO DETAILED SUMMARY OF 24-MAY-11 RESULTS.
	03-JUN-2011	03-JUN-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST LIST OF PERSONS ON TELECON. 02-JUN-11.
	03-JUN-2011	03-JUN-2011	CORRESPONDENCE	EMAIL	MW TO JA:FDA PROVIDING TRAVEL UPDATE FOR FDA INSPECTOR FOR AGENTINA INSPECTION.
	06-JUN-2011	06-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: MULTI. COMMUNICATIONS RE: LOGISTICS FOR FDA AUDITS IN CANADA.
	06-JUN-2011	06-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: MUTLI. COMMUNICATIONS RE: EDISH DEMODATA AND LIVERDATA DATASETS.
	06-JUN-2011	06-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO SI: MULTI. COMMUNICATIONS RE: ARGENTIAN INSPECTION & DATA CONTAINING 'HBA1c' VALUES AT CURRENT AND PLANNED INSPECTION SITES.
	07-JUN-2011	07-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING UPDATED DATASETS RE: EDISH DEMODATA AND LIVERDATA DATASETS.
	07-JUN-2011	07-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: MULTI. COMMUNICATIONS RE: BEST DELIVERY OF 'HBA1C' DATA FROM QUINTILES REFERENCED UNDER INSPECTION IN ARGENTINA.
	07-JUN-2011	07-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: MULTI. CONTACTS (MAY 24-JUNE 7) RE: NON CLINICAL INFO. AND PEDIATRICS
	07-JUN-2011	07-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MW: BMS PROVIDING LOGISTIC INFO. RE: FDA AUDITS IN CANADA AND GERMANY.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	07-JUN-2011	07-JUN-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST FOR INFO. RE: INSULIN REGIMENS; EVENTS OF UTI, ANALYSIS OF PTS. IN PHASE 2B/3, AND REQUEST TO SUMMARIZE TABLE SENT ON JUNE 2.
	07-JUN-2011	07-JUN-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA PROVIDING STATUS OF PENDING AC MTG. AND PUBLISHING IN FEDERAL REGISTER.
	08-JUN-2011	08-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING CASES PER 03-JUN-11, REQUEST.
	08-JUN-2011	08-JUN-2011	CORRESPONDENCE	EMAIL	SW TO AJ: FDA SUGGESTS TO SEND 'HBA1C' DATA FROM QUINTILES TO AZ GERMANY.
	08-JUN-2011	08-JUN-2011	CORRESPONDENCE	TELEPHONE	JL TO MP: CONTACT RE: MID CYCLE REVIEW, DISCUSSION AND BRIEFING BOOK.
	09-JUN-2011	09-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING EDISH REQUESTED PDF. NARRATIVES.
	09-JUN-2011	09-JUN-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA INDICATES TEMP. VOTING MEMBERS CAN BE IDENTIFIED 2 BUS. DAYS PRIOR TO MTG.
	10-JUN-2011	10-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to the 27-May-11 reuest from the Agency for 3 SAS datasets and optional narrative PDF files for all phase 2b/3 trials to support eDish analysis.
	10-JUN-2011	10-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: CONTACT RE: ISSUE WITH PREPARATION OF NARRATIVE DATASET.
	10-JUN-2011	10-JUN-2011	CORRESPONDENCE	EMAIL	DB TO MH: BMS PROVIDING SAS DISH NARRATIVE DATASETS.
	13-JUN-2011	13-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to the 25-May-2011 request from the Agency for additional clinical pharmacology information.
	13-JUN-2011	13-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING STATUS UPDATE RE: PLANNED SUBMISSIONS AND RESPONSES FOR DAPA.
	13-JUN-2011	13-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO PT: DMDAC QUESTIONS FOR SPONSOR SECTION.
	13-JUN-2011	13-JUN-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA STATUS REQUEST.
	14-JUN-2011	14-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to the 3-Jun-2011 request from the Agency.
	14-JUN-2011	14-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING RESPONSES TO JUNE 7 REQUEST.
	14-JUN-2011	14-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MW: BMS PROVIDING TRANSPORTATION ITINERARY FOR FDA INSPECTOR WHILE IN GERMANY.
	15-JUN-2011	15-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING FINAL BRIEFING DOC FOR 19-JUL-11 EMDAC.
	15-JUN-2011	15-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO PT: BMS PROVIDING COPY OF EMDAC BRIEFING DOC.
	15-JUN-2011	15-JUN-2011	CORRESPONDENCE	EMAIL	DH TO AJ: FDA STATUS INDICATING CMC SECTIONS ARE STILL BEING REVIEWED.
	16-JUN-2011	16-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to request for clinical information related to study D1690C00012.
	16-JUN-2011	16-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PROVIDING ST & LT STUDY PERIODS.
	16-JUN-2011	16-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS RESPONSE PERTAINING TO CMC RESPONSE 02-JUN-11. NO INTENTION TO USE DIFFERENT GRADES OF EXCIPIENTS IN CURRENT DP MFG. PROCESS.
	16-JUN-2011	16-JUN-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA PROVIDING DETAILS FOR EMDAC MTG.
	17-JUN-2011	17-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to FDA request via email dated 7-Jun-11 for additional clinical information.
	20-JUN-2011	20-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS NOTIFICATION OF PLAN TO ISSUE PRESS RELEASES AT ADA.
	20-JUN-2011	20-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO PT: BMS ASKING WHETHER FDA'S BRIEFING DO. WILL BE PROVIDED BY 28-JUN-11.
	20-JUN-2011	20-JUN-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA BRIEFING DOC. WILL BE SENT OVERNIGHT.
	20-JUN-2011	20-JUN-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA REPSONSE TO AC SEATING.
	21-JUN-2011	21-JUN-2011	CORRESPONDENCE	EMAIL	AJ TO PT: BMS PROVIDING LIST OF EXTERNAL CONSULTANTS TO BE PRESENT AT AC.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	22-JUN-2011	22-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Summary of the additional safety asessment.
	22-JUN-2011	22-JUN-2011	CORRESPONDENCE	EMAIL	PT TO AJ: FDA REQUEST INFO. RE: DR. BRIAN STROM, AS A CONSULTANT IN UPCOMING AC.
	22-JUN-2011	22-JUN-2011	CORRESPONDENCE	TELEPHONE	LA TO CH: FDA INVESTIGATOR INQUIRED WHETHER SITE IS 'PAI' READY FOR INSPECTION OF FILING 202293.
	24-JUN-2011	24-JUN-2011	AMENDMENT	SUBMISSION	AJ to MP: Response to FDA's email request of 15-Jun-11 for additional CMC information.
	30-JUN-2011	30-JUN-2011	OTHER	SUBMISSION	AJ to MP: Cross-reference submission of pharmacology/toxicology reports, which were submitted to IND 68,652.
	13-JUL-2011	13-JUL-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING RESPONSE TO FDA REQUEST 08-JUL-11, FOR CLINICAL INFO.
	13-JUL-2011	13-JUL-2011	CORRESPONDENCE	LETTER	MH TO AJ: FDA MEETING MINUTES FROM TELECON. HELD 7-JUL-11, RE: REQUIRMENT TO CONDUCT A CARDIOVASCULAR CLINICAL TRIAL AS A PMR FOR DAPA. WILL FURTHER DISCUSS AT NEXT TELECON. SCHEDULED FOR 7-SEP-11.
	22-JUL-2011	22-JUL-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING UPDATED SITE LEVEL DATA INFO. INLCUDING TATA CONSULTANCY.
	01-AUG-2011	01-AUG-2011	AMENDMENT	SUBMISSION	AJ TO MP: F/U RE: REQUEST TO MEET IN AUGUST AFTER EMDAC MTG. IN PREP. FOR 07-SEP-11, MTG.
	12-AUG-2011	12-AUG-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR CLINICAL INFO. DATED 05-AUG-11.
	17-AUG-2011	17-AUG-2011	AMENDMENT	SUBMISSION	PC TO MP: RESPONSE TO FDA REQUEST FOR MICROBIAL LIMITS, 29-JUL-11.
	19-AUG-2011	19-AUG-2011	AMENDMENT	SUBMISSION	AJ TO MP: REPSONSE TO FDA REQUEST FOR ADD'L CLINICAL INFO. 15-AUG-11.
	22-AUG-2011	22-AUG-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST 15-AUG-11, FOR PEDICATRIC PLAN INFO.
	25-AUG-2011	25-AUG-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING DATASETS (SEQ. 0032)
	26-AUG-2011	26-AUG-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING UPDATED RISK MGMT. PLAN AND EPIDEMIOLOGY PROTOCOLS FOR 04-OCT-11, MTG.
	30-AUG-2011	30-AUG-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING TOPLINE 6-MO DATA FROM STUDIES D1690C00018 & D1690C00019.
	01-SEP-2011	01-SEP-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING NEW USPI AND MEDICATION GUIDE.
	01-SEP-2011	01-SEP-2011	CORRESPONDENCE	LETTER	JM TO AJ: FDA DISCOVERED DEFICIENCIES PRECLUDE DISCUSSION OF LABELING AND POSTMARKETING REQUIREMENTS/COMMITMENTS.
	02-SEP-2011	02-SEP-2011	OTHER	SUBMISSION	AJ TO MP: PROVIDING MTG. MATERIALS FOR 04-OCT-11, MTG.
	07-SEP-2011	07-SEP-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING MARKED UP VERSION OF RISK MGMT. PLAN.
	09-SEP-2011	09-SEP-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO REQUEST FOR MICROAL BUMINURIA INFO. 05-AUG-11 & 15-AUG-11.
	14-SEP-2011	14-SEP-2011	OTHER	SUBMISSION	AJ TO MP: RESPONSE TO REQUEST FOR INFO. RE: CETERO.
	19-SEP-2011	19-SEP-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO QUESTIONS AND ISSUES RAISED AT DAPA. EMDAC MTG.
	20-SEP-2011	20-SEP-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING PRELIMINARY CV META ANALYSIS.
	23-SEP-2011	23-SEP-2011	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR PROPRIETARY NAME REVIEW - 'FORXIGA.'
	29-SEP-2011	29-SEP-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS INQUIRY OF REPORTS TO BE FILED TO EITHER THE IND OR BOTH THE IND AND THE NDA.
	29-SEP-2011	29-SEP-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA PRELIMINARY COMMENTS TO TELECON SCHEDULED FOR 4-OCT-11.
	03-OCT-2011	03-OCT-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS/AZ LIST OF ATTENDEES AND DISCUSSION SLIDES FOR TELECON SCHEDULED 3-OCT-11.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	04-OCT-2011	04-OCT-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RESPONSE TO BMS INQUIRY ON 29-SEP-11, RE: REPORTS TO FILE TO EITHER THE IND OR BOTH THE IND AND NDA.
	05-OCT-2011	05-OCT-2011	CORRESPONDENCE	EMAIL	AJ TO MH: LIST OF BMS/AZ ATTENDEES TO THE MEETING HELD 4-OCT-11.
	12-OCT-2011	12-OCT-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA ADVISORY TO SUBMIT THE MEETING MINUTES FROM 4-OCT-11 TO BOTH THE IND AND THE NDA.
	13-OCT-2011	13-OCT-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS UPDATE ON PLANNED FUTURE SUBMISSIONS. IND SUBMISSION- 17-OCT-11. NDA SUBMISSIONS- 21-OCT-11, 27-OCT-11, 3-NOV-11, 15-NOV-11, 30-NOV-11.
	18-OCT-2011	18-OCT-2011	OTHER	SUBMISSION	AJ TO MP: BMS/AZ MINUTES FROM 04-OCT-11, WITH FDA
	18-OCT-2011	18-OCT-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REVIEW OF BMS PLANNED SUBMISSIONS. FDA UNLIKELY TO BE ABLE TO REVIEW THE 30-NOV-11 SUBMISSION AS PART OF THE NDA REVIEW; WOULD LIKE BMS TO MOVE THE 15-NOV-11 SUBMISSION UP TO 7-NOV-11.
	20-OCT-2011	20-OCT-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 15-AUG-11, INFO. REQUEST - 6-MONTH DATASETS FOR ONGOING CLINICAL TRIALS D1690C00018 AND D1690C00019.
	20-OCT-2011	20-OCT-2011	CORRESPONDENCE	EMAIL	AJ TO MH: NOTICE TO THE FDA THAT THE 6-MONTH DATASETS ARE AVAIL. ON THE SERVER & UPDATE THAT BMS WILL TRY TO MEET THE REQUESTED SUBMISSION TIMELINE DISCUSSED ON 18-OCT-11.
	20-OCT-2011	20-OCT-2011	CORRESPONDENCE	EMAIL	AJ TO MH: UPDATE TO FDA THAT SUBMISSION PLANNED FOR 30-NOV-11 WILL BE AVAIL. FOR 15-NOV-11.
	26-OCT-2011	26-OCT-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS TO ISSUE A PRESS RELEASE ON 26-OCT-11, RE: THE PDUFA EXTENSION.
	26-OCT-2011	26-OCT-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA APPROVED EXTENSION LETTER FOR DAPA.
	26-OCT-2011	26-OCT-2011	CORRESPONDENCE	LETTER	MP TO AJ: REVIEW EXTENSION - MAJOR AMENDMENT DATED 20-OCT-11; EXTENDED USER FEE GOAL DATE NOW 28-JAN-11.
	27-OCT-2011	27-OCT-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 15-AUG-11 INFO. REQUEST, 930054621, 930054306, 930055263, 930055312 & 930055311.
	28-OCT-2011	28-OCT-2011	CORRESPONDENCE	EMAIL	AJ TO MH: EMAILED REPORTS D1690C00018 & D1690C00019; OFFICIAL REPORTS TO BE DELIEVERED TO FDA BY 2-NOV-11.
	31-OCT-2011	31-OCT-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST FOR ADDITIONAL INFO. RE: SAS CODE USED TO CREATE ANALYSIS DATA SETS AND KEY TABLES FOR CLINICAL STUDY REPORTS D1690C00018 & D1690C00019.
	31-OCT-2011	31-OCT-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RFAI, RE: SUBMITTING THE SAS CODES IN STUDIES D1690C00018 & D1690C00019.
	02-NOV-2011	02-NOV-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 15-AUG-11 INFO. REQUEST, 930055532 & 930055526.
	02-NOV-2011	02-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS NOTIFICATION OF DOCUMENTS SUBMITTED ON 27-OCT-11 & 02-NOV-11.
	03-NOV-2011	03-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RFAI, RE: STUDY D1690C00019, PATIENT D1690C00019-7803-1 & PATIENT D1690C00019-7833-2.
	03-NOV-2011	03-NOV-2011	CORRESPONDENCE	SUBMISSION	MH TO AJ: OFFICIAL FDA MEETING MINUTES FROM MEETING HELD 04-OCT-11 TO DISCUSS THE DESIGN OF PROPOSED CV OUTCOMES TRIAL & OVERALL PHARMACOVIGILANCE PLAN.
	04-NOV-2011	04-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS/FDA ACKNOWLEDGEMENT THAT SUBMISSIONS WITH STANDARD TABULATIONS AND LISTINGS THAT ARE GENERATED USING CLINPLUS CANNOT BE INCLUDED.
	04-NOV-2011	04-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RFAI, RE: CLARIFICATION OF STUDY LOCATION/INCLUSION IN SUBMISSION.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	07-NOV-2011	07-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS RESPONSE TO FDA RFAI.
	07-NOV-2011	07-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: D1690C00018 PROGRAM AND DATA SET FILES.
	07-NOV-2011	07-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: D1690C00019 PROGRAM AND DATASET FILES.
	07-NOV-2011	07-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RFAI.
	08-NOV-2011	08-NOV-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 15-AUG-11 INFO. REQUEST, 930055622, 930055566, 930055558 , 930055622 & 930055311.
	08-NOV-2011	08-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS CLARIFICATION ON FDA RFAI.
	08-NOV-2011	08-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS RESPONSE TO FDA RFAI ON 03-NOV-11, RE: STUDY D1690C00019, PATIENTS D1690C00019-7803-1 &D1690C00019-7833-2.
	08-NOV-2011	08-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS SUBMISSION & UPDATED LIST OF PLANNED SUBMISSION DATES.
	08-NOV-2011	08-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RESPONSE TO BMS CLARIFICATION.
	09-NOV-2011	09-NOV-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 31-OCT-11 & 03-NOV-11, REQUEST FOR INFO. 930055726.
	09-NOV-2011	09-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS FINAL RESPONSE TO FDA RFAI RE: FOR ALL PHASE 2B AND 3 STUDIES- PROVIDE SUBJECT NUMBERS, AND TOTAL PERSON-TIME OF FOLLOW-UP AFTER RANDOMIZATION FOR EACH OF THE AGE BRACKETS IN TABLE 1.
	09-NOV-2011	09-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA CONFIRMATION OF BMS SUBMISSION RE: CODES FOR SENSITIVITY ANALYSES OF THE PRIMARY HBA1C ENDPOINT.
	09-NOV-2011	09-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RFAI, RE: PATIENT ID# D1690C00018-201-8.
	10-NOV-2011	10-NOV-2011	OTHER	SUBMISSION	AJ TO MP: PROVIDING DRAFT PROTOCOL FOR MB102-118, 930053430.
	10-NOV-2011	10-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS FINAL RESPONSE FOR FDA RFAI ON 7-NOV-11,
	10-NOV-2011	10-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS SUBMITTAL OF CODES FOR SENSITIVITY ANALYSES OF THE PRIMARY HBA1C ENDPOINT & DATES OF REMAINING PLANNED SUBMISSIONS.
	10-NOV-2011	10-NOV-2011	CORRESPONDENCE	LETTER	MH TO AJ: FDA MEETING MINUTES FROM 4-OCT-11, RE: THE DESIGN OF BMS PROPOSED CARDIOVASCULAR OUTCOMES TRIAL AND OVERALL PHARMACOVIGILANCE PLAN.
	11-NOV-2011	11-NOV-2011	OTHER	SUBMISSION	AJ TO MP: PROVIDING PATENT INFORMATION.
	15-NOV-2011	15-NOV-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING STUDY DATASETS FOR THE 15-JUL-11 DATACUT.
	16-NOV-2011	16-NOV-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 07-NOV-11, 08-NOV-11 & 09-NOV-11, INFO. REQUEST 930055851, 930055775 & 930055804.
	17-NOV-2011	17-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ/DM: FDA RFAI FROM BMS DOCUMENT SUBMITTED 27-OCT-11, RE: USE OF THE COCHRAN-MANTEL-HAENSZEL EXPOSURE WEIGHTS.
	18-NOV-2011	18-NOV-2011	CORRESPONDENCE	EMAIL	DM TO MH: BMS RESPONSE TO FDA RFAI FROM DOCUMENT SUBMITTED 27-10-11, RE: USE OF THE COCHRAN-MANTELHAENSZEL EXPOSURE WEIGHTS.
	22-NOV-2011	22-NOV-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 17-NOV-11 INFO. REQUEST 930055970.
	22-NOV-2011	22-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: UPDATE ON STATUS OF OFFICIAL SUBMISSIONS.
	29-NOV-2011	29-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MH: INFORMAL RESPONSE TO FDA RFAI ON 28-NOV-11, RE: UPDATE ON ONGOING PORTION OF STUDIES 18 AND 19.
	29-NOV-2011	29-NOV-2011	CORRESPONDENCE	EMAIL	AJ TO MT: F/U ON PROPOSED TRADENAME SUBMITTED 26-SEP-11.
	29-NOV-2011	29-NOV-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RFAI, RE: UPDATE ON ONGOING PORTION OF STUDIES 18 AND 19.
	29-NOV-2011	29-NOV-2011	CORRESPONDENCE	EMAIL	MT TO AJ: RESPONSE TO BMS F/U ON PROPOSED TRADENAME-TRADENAME IS STILL UNDER REVIEW BY DMEPA.
	02-DEC-2011	02-DEC-2011	AMENDMENT	SUBMISSION	AJ TO MP: UPDATED FINANCIAL DISCLOSURE TABLES, 930056190.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	02-DEC-2011	02-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: TELECON. SCHEDULED FOR 6-DEC-11, RE: DISCUSSION OF PMRS.
	02-DEC-2011	02-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST FOR ADDITIONAL INFO.
	05-DEC-2011	05-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: LIST OF ATTENDEES FOR TELECON. SCHEDULED 6-DEC-11.
	06-DEC-2011	06-DEC-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 28-NOV-11 & 29-NOV-11 INFO. REQUEST.
	06-DEC-2011	06-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: FOLLOW-UP FROM RFAI 2-DEC-11
	06-DEC-2011	06-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: INQUIRY OF FDA PMRS TO DISCUSS IN TELECON. ON 6-DEC-11; INCLUDING F/U ON BMS CLARIFICATION OF FDA REVIEWAL TIME PERIOD.
	07-DEC-2011	07-DEC-2011	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO 02-DEC-11 QUESTION.
	07-DEC-2011	07-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA COMMENTS ON EPI PROTOCOLS.
	08-DEC-2011	08-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: RESPONSE TO FDA RFAI RE: SIX MONTHS AND ONE YEAR EXPOSURES TO DAPA VS. CONTROL.
	08-DEC-2011	08-DEC-2011	CORRESPONDENCE	LETTER	CH TO AJ: FDA CONDITIONALLY ACCEPTABLE" LTR." RE: PROPOSED PROPRIETARY NAME- FORXIGA.
	09-DEC-2011	09-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS INQUIRY OF FDA EXPECTED FINISH OF LABELING COMMENTS.
	10-DEC-2011	10-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS/AZ VERSION OF MINUTES FROM TELECON HELD 6-DEC-11; BMS INQUIRY OF TIMELINES FOR NESTED CASE-CONTROLS STUDIES.
	10-DEC-2011	10-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA PRELIMINARY LABELING COMMENTS & EDITS TO THE PACKAGE INSERT
	12-DEC-2011	12-DEC-2011	AMENDMENT	SUBMISSION	AJ TO MP: EXPOSURES AT 15-JUL-11 DATA CUT.
	12-DEC-2011	12-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RESPONSE TO BMS QUESTION FROM 6-DEC-11 RE: TIMELINES FOR NEWSTED CASE CONTROL STUDIES.
	12-DEC-2011	12-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RESPONSES TO BMS QUESTIONS ON LABELING COMMENTS.
	13-DEC-2011	13-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS TIMELINE OF EXPECTED RESPONSE FOR LABELING COMMENTS.
	13-DEC-2011	13-DEC-2011	CORRESPONDENCE	EMAIL	MT TO AJ: FDA INQUIRY OF BMS RECEIPT OF TN LETTER.
	14-DEC-2011	14-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS QUESTION RE: FDA CARTON AND CONTAINER LABELING COMMENTS & UPDATING THE USPI.
	14-DEC-2011	14-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA CARTON AND CONTAINER LABELING COMMENTS.
	15-DEC-2011	15-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS REVISION TO FDA REQUEST OF CHANGES TO CONTAINER LABELS, RE: 5MG AND 10MG COLORING TO DIFFERENTIATE STRENGTHS.
	16-DEC-2011	16-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA RESPONSE TO BMS QUESTION OF CHANGES TO KEEP THE USPI CONSISTENT WITH LABELING COMMENTS.
	19-DEC-2011	19-DEC-2011	OTHER	SUBMISSION	AJ TO MP: MINUTES FROM 06-DEC-11 TELECON.
	19-DEC-2011	19-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: BMS TARGET TO HAVE LABEL COMMENTS REVIEWED AND SUBMITTED BY 21-DEC-11; PLAN TO CHANGE IND ANNUAL REPORT INTO DSUR FORMAT.
	19-DEC-2011	19-DEC-2011	CORRESPONDENCE	EMAIL	MH TO AJ: FDA ACCEPTANCE OF BMS MODIFICATIONS TO REQUESTED FDA LABEL CHANGES, RE: COLOR OF 5MG AND 10MG.
	20-DEC-2011	20-DEC-2011	CORRESPONDENCE	EMAIL	AJ TO MH: UPDATED PROPOSED USPI; PMR MILESTONES AS REQUESTED AT THE 6-DEC-11 TELECON.
	29-DEC-2011	29-DEC-2011	AMENDMENT	SUBMISSION	AJ TO MP: PROVIDING UPDATED CARTON AND CONTAINER LABELS.
	04-JAN-2012	04-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: STATUS OF FDA REVIEW OF LABEL & MEDICATION GUIDE COMMENTS; FDA REQUEST FOR ADDITIONAL INFO.
	05-JAN-2012	05-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: RESPONSE TO FDA REQUEST FOR ADD'L. INFO.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	06-JAN-2012	06-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: BMS INQUIRY FOR RESPONSE REFERENCE TABLES IN LT CSRS FOR AZ06 AND AZ04 SUBMITTAL.
	09-JAN-2012	09-JAN-2012	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO REQUEST FOR INFO.
	09-JAN-2012	09-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: SCHEDULED MEETING FOR 10-JAN-12, RE: UPDATE ON FDA LABELING COMMENTS.
	09-JAN-2012	09-JAN-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST FOR MEETING TO DISCUSS LABELING COMMENTS.
	10-JAN-2012	10-JAN-2012	OTHER	SUBMISSION	AJ TO MP: PROVIDING 6 MONTH ERRATUM FOR AZ STUDY D1690C00018 & 00019.
	10-JAN-2012	10-JAN-2012	CORRESPONDENCE	TELEPHONE	MH TO AJ: TELECON TO DISCUSS STATUS OF FDA LBL'G REVIEW; BMS EXPECTED TO RECEIVE ACTION LETTER PRIOR TO 28-JAN-10.
	13-JAN-2012	13-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: FDA/BMS/AZ TELECONF. ON 13-JAN-11, RE: CLARIFICATION ON FDA CONCERNS; BMS/AZ MINUTES.
	17-JAN-2012	17-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: INQUIRY ON TIMING OF NDA ACTION LETTER.
	17-JAN-2012	17-JAN-2012	CORRESPONDENCE	LETTER	CR TO AJ: FDA COMPLETE RESPONSE LETTER
	19-JAN-2012	19-JAN-2012	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR TYPE B END-OF-REVIEW MEETING RE: DEFICIENCIES AS DESCRIBED IN CRL & STEPS FOR THE FUTURE.
	19-JAN-2012	19-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: TYPE B MEETING REQUEST LETTER TO FDA.
	24-JAN-2012	24-JAN-2012	OTHER	SUBMISSION	AJ TO MP: PROVIDING BMS/AZ'S MINUTES OF THE 13-JAN-12 MEETING.
	24-JAN-2012	24-JAN-2012	CORRESPONDENCE	EMAIL	AJ TO MH: SCHEDULING OF TYPE B MEETING REQUEST FOR END OF APRIL RE: END OF REVIEW CONFERENCE TO DISCUSS DEFICIENCIES & EXPECTED RESPONSES FOR THE CRL.
	26-JAN-2012	26-JAN-2012	CORRESPONDENCE	LETTER	MH TO AJ: TYPE B MEETING REQUEST GRANTED FOR 30-APR-12 RE: END-OF-REVIEW TO DISCUSS DEFICIENCIES DESCRIBED IN CRL DATED 17-JAN-12.
	02-FEB-2012	02-FEB-2012	CORRESPONDENCE	EMAIL	AJ TO MH: CLARIFICATION ON FINANCIAL DISCLOSURE TEXT IN CRL- SPECIFIC DETAILS TO BE PROVIDED FOR "REPORTABLE" FINANCIAL INTERESTS.
	03-FEB-2012	03-FEB-2012	CORRESPONDENCE	EMAIL	MH TO JJ: CLARIFICATION THAT THE REQUEST FOR MEETING IS TO HOLD A HIGH LEVEL DISCUSSION ON BENEFIT/RISK REQ. FOR DIABETES DRUGS & SEEK AGENCY VIEWS ON THE NEED FOR NEW CLASSES OF DRUGS
	06-FEB-2012	06-FEB-2012	CORRESPONDENCE	EMAIL	JJ TO MH: FDA AGREEMENT TO WORK WITH DMEP TO SCHEDULE THE REQUEST FOR A MEETING TO DISCUSS BENEFIT/RISK REQ. FOR DIABETES DRUGS & AGENCY VIEWS ON THE NEED FOR NEW CLASSES OF DRUGS.
	07-FEB-2012	07-FEB-2012	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR A TYPE C MEETING RE: BENEFIT/RISK REQUIRED FOR DIABETES DRUGS & INQUIRY OF VIEWS ABOUT THE NEED FOR NEW CLASSES OF DRUGS VS. THE KNOWN BENEFIT/RISKS OF EXISTING CLASSES.
	09-FEB-2012	06-FEB-2012	CORRESPONDENCE	EMAIL	AJ TO MH: SCHEDULING FOR A TYPE C MEETING TO TAKE PLACE PRIOR TO SCHEDULED EOR MEETING ON 30-APR-12 RE: HIGH LEVEL DISCUSSION ON BENEFIT/RISK REQ. FOR DIABETES DRUGS, INCLUDING FDA VIEWS ON THE NEED FOR NEW CLASSES OF DRUGS VS. THE KNOWN BENEFITS/RISKS OF EXISTING CLASSES.
	09-FEB-2012	09-FEB-2012	CORRESPONDENCE	LETTER	MH TO AJ: TYPE C MEETING REQUEST GRANTED FOR 30-APR-12 RE: HIGH LEVEL DISCUSSION ON THE BENEFIT/RISK REQ. FOR DIABETES DRUGS, INCLUDING VIEWS ABOUT THE NEED FOR NEW CLASSES OF DRUGS VS. KNOWN BENEFITS/RISKS OF EXISTING DRUG CLASSES.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	21-FEB-2012	21-FEB-2012	CORRESPONDENCE	TELEPHONE	PH TO JJ: OVERALL INQUIRY OF STATUS OF DAPA FILE.
	23-FEB-2012	23-FEB-2012	CORRESPONDENCE	EMAIL	JJ TO PH: FURTHER FDA F/U RE: STATUS OF DAPA FILE & RESPONSE TO CRL. VARIOUS ISSUES TO BE DISCUSSED AS PART OF THE EORC.
	02-MAR-2012	02-MAR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: UPDATE TO FDA RE: BREIFING DOCUMENTS ON TARGET FOR BOTH 30-APR-12 MEETINGS. DOCUMENTS WILL BE EMAILED BY 30-MAR-12 & HARD COPIES THE WEEK AFTER.
	06-MAR-2012	06-MAR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: INQUIRY TO SUBMIT EACH BREIFING DOCUMENT SEPARATELY FOR EACH 30-APR-12 MEETING; ALSO INQUIRY IF UPCOMING SUBMISSIONS CAN BE SUBMITTED TO THE IND WITH CROSS-REF. LETTER TO NDA. FDA APPROVAL OF BOTH CIRCUMSTANCES.
	22-MAR-2012	22-MAR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: RESPONSE TO FDA INFO REQUEST RE: TOTAL PATIENT-YEARS EXPOSURE IN THE 19 PHASE 2/3 TRIALS INCLUDED IN THE UPDATED META-ANALYSIS.
	22-MAR-2012	22-MAR-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA INFO REQUEST RE: TOTAL PATIENT-YEARS EXPOSURE IN THE 19 PHASE 2/3 TRIALS INCLUDED IN THE UPDATED META-ANALYSIS.
	29-MAR-2012	29-MAR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: EMAILED BRIEFING DOCUMENTS & BMS/AZ TENTATIVE ATTENDEES FOR BOTH MEETINGS TO BE HELD ON 30-APR-12.
	29-MAR-2012	29-MAR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: TARGETING TO SUBMIT DRAFT CVOT ON 02-APR-12. REQUESTING COMMENTS NO LATER THAN 30-MAY-12, IN ORDER TO MEET POTENTIAL PMR REQUIREMENTS & EU HEALTH AUTHORITY TIMELINES.
	30-MAR-2012	30-MAR-2012	OTHER	SUBMISSION	AJ TO MP: MEETING MATERIALS FOR HIGH LEVEL DIABETES DISCUSSION SCHEDULED FOR 30-APR-12. EIGHT PAPER DESK COPIES TO BE PROVIDED TO AGENCY BY 03-APR-12.
	30-MAR-2012	30-MAR-2012	OTHER	SUBMISSION	AJ TO MP: MEETING MATERIALS FOR TYPE B END-OFREVIEW MEETING SCHEDULED FOR 30-APR-12. TWENTYFIVE DESK COPIES TO BE PROVIDED TO FDA BT 03-APR-12.
	02-APR-2012	02-APR-2012	OTHER	SUBMISSION	AJ TO MP: CROSS-REF. SUBMISSION OF DRAFT CVOT PROTOCOL (D1693C0001, 930052214) & CLINICAL EVENTS COMMITTEE CHARTER (930058686) THAT WAS SUBMITTED TO IND 68,652.
	02-APR-2012	02-APR-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA CONFIRMATION OF DELIVERY OF PAPER COPIES FOR 30-APR-12 BRIEFING DOCUMENTS.
	17-APR-2012	17-APR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: UPDATED LIST OF BMS/AZ ATTENDEES FOR 30-APR-12 MEETINGS.
	18-APR-2012	18-APR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: REQUEST FOR SPECIFIC FDA COMMENTS ON DRAFT CVOT SUBMITTED 02-APR-12, RE: RECORDING OF ADVERSE EVENTS & ADJUDICATION OF SUSPECTED CV ENDPOINTS.
	20-APR-2012	20-APR-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA REQUEST FOR ADD'L INFO FROM PREVIOUSLY SUBMITTED BRIEFING DOC. FOR SCHEDULED 30-APR-12 EOR MEETING.
	25-APR-2012	25-APR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: RESPONSE TO FDA REQUEST FOR ADD'L INFO DATED 20-APR-12.
	27-APR-2012	27-APR-2012	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR ADD'L INFO DATED 20-APR-12 RE: QUESTIONS ABOUT THE BRIEFING DOC. FOR THE UPCOMING EOR MEETING SCHEDULED FOR 30-APR-12.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	27-APR-2012	27-APR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: INQUIRY IF ALL ATTENDEES FOR THE SCHEDULED 30-APR-12 HIGH LEVEL MEETING HAD ATTENDED THE FDA INTERNAL PREMEETING REPRESENTED IN THE PRELIMINARY FEEDBACK DATED 27-APR-12.
	27-APR-2012	27-APR-2012	CORRESPONDENCE	EMAIL	MH TO AJ: EMAILED FDA PRELIMINARY COMMENTS FOR THE HIGH-LEVEL MEETING & FOR THE EOR MEETING, BOTH TO BE HELD 30-APR-12.
	27-APR-2012	27-APR-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA DENIAL FOR DISCLOSURE OF ATTENDEES PRESENT AT PREVIOUSLY HELD INTERNAL MEETING. FURTHER DISCUSSION RE: SCHEDULE, LOCATION, & TECHNOLOGY OF BOTH MEETINGS TO BE HELD 30-APR-12.
	27-APR-2012	27-APR-2012	CORRESPONDENCE	LETTER	MH TO AJ: FDA PRELIMINARY COMMENTS ON TYPE C MEETING SCHEDULED FOR 30-APR-12, RE: HIGH-LEVEL DISCUSSION ON THE BENEFIT/RISK REQ. FOR DIABETES DRUGS, AS WELL AS, HOW THE FDA VIEWS THE NEED FOR NEW CLASSES OF DRUGS VERSUS THE KNOWN BENEFITS/RISKS OF EXISTING DRUG CLASSES.
	30-APR-2012	30-APR-2012	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE SUBMISSION OF PROTOCOL MB102091 FROM IND 68,652.
	30-APR-2012	30-APR-2012	CORRESPONDENCE	EMAIL	AJ TO MH: BMS PRESENTATION SLIDES FOR BOTH MEETINGS HELD 30-APR-12.
	07-MAY-2012	07-MAY-2012	CORRESPONDENCE	EMAIL	AJ TO MH: EMAILED MEETING MINUTES & PRESENTATION SLIDES FROM BOTH DISCUSSIONS HELD ON 30-APR-12.
	09-MAY-2012	09-MAY-2012	OTHER	SUBMISSION	AJ TO MP: MEETING MINUTES FROM HIGH LEVEL DIABETES POLICY DISCUSSION & DAPA END-OF-REVIEW MEETING, BOTH HELD ON 30-APR-12.
	10-MAY-2012	10-MAY-2012	CORRESPONDENCE	EMAIL	AJ TO MH: PER REQUEST FROM EOR MEETING HELD 30-APR-12, EMAILED COPY OF THE EU SWP NONCLINICAL RPT.
	16-MAY-2012	16-MAY-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA ACTION REQUEST TO SUBMIT EU SWP NONCLINICAL RPT.
	29-MAY-2012	29-MAY-2012	CORRESPONDENCE	EMAIL	AJ TO MH: PLANNING TO SUBMIT A DRAFT SYNOPSIS FOR THE PEDIATRIC CLINICAL SAFETY & EFFICACY STUDY FOR REVIEW/COMMENT; INQUIRY OF STATUS OF MINUTES FROM BOTH 30-APR-12 MEETINGS; INQUIRY ON STATUS OF ADVICE/INFORMATION REQUEST ON THE CVOT PROTOCOL SUBMITTED 02-APR-12.
	30-MAY-2012	30-MAY-2012	OTHER	SUBMISSION	AJ TO MP: EU SWP SUBMITTED PER FDA REQUEST DATED 16-MAY-12.
	30-MAY-2012	30-MAY-2012	CORRESPONDENCE	EMAIL	MH TO AJ: FDA MINUTES FROM BOTH MEETINGS HELD 30-APR-12.
	01-JUN-2012	01-JUN-2012	OTHER	SUBMISSION	AJ TO MP: CROSS-REF. SUBMISSION OF PEDIATRIC AMEDMENTS SUBMITTED TO IND 68,652 ON 01-JUN-12 (SEQ. NO. 0434) RE: ALIGNMENT WITH FDA ON THE DESIGN OF THE PEDIATRIC CLINICAL EFFICACY AND SAFETY STUDY TO SATISFY THE PREA REQ. SHOULD THIS NDA BE APPROVED. REQUEST FOR FDA REVIEWAL & COMMENTS TO BE COMPLETED BY 31-JUL-12.
	27-JUN-2012	27-JUN-2012	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR AN EXTENSION TO RESUBMIT APPLICATION PAST THE ONE YEAR REQUIREMENT IN RESPONSE TO THE CRL DATED 17-JAN-12. LENGTH OF EXTENSION FOR RESUBMISSION PERIOD TBD.
	29-JUN-2012	29-JUN-2012	CORRESPONDENCE	EMAIL	AJ TO MH/JW: NOTIFICATION THAT PLANS FOR A RESUBMISSION IN RESPONSE TO THE CRL & REQUEST FOR EXTENSION PERIOD PAST THE 1 YEAR DEADLINE WERE SUBMITTED ON 27-JUN-12.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	29-JUN-2012	29-JUN-2012	CORRESPONDENCE	SUBMISSION	MH TO AJ: FDA NOTIFICATION OF RECEIPT OF SUBMISSION REQUESTING AN EXTENSION TO RESUBMIT APPLICATION IN RESPONSE TO CRL, DATED 27-JUN-12 (SN 0084).
	16-JUL-2012	16-JUL-2012	CORRESPONDENCE	EMAIL	AB TO AJ: FDA ACK. OF BMS EMAIL RE: PLAN TO SUBMIT DISPUTE RESOLUTION REQUEST FOR NDA 202-293.
	16-JUL-2012	16-JUL-2012	CORRESPONDENCE	TELEPHONE	AJ TO MH: CONTACT RE: PLAN TO SUBMIT DISPUTE RESOLUTION REQUEST FOR NDA 202-293.
	17-JUL-2012	17-JUL-2012	CORRESPONDENCE	EMAIL	AJ TO AB: BMS NOTIFICATION RE: SUBMISSION OF DISPUTE DOCUMENT.
	18-JUL-2012	18-JUL-2012	OTHER	SUBMISSION	AJ TO MP: FORMAL DISPUTE RESOLUTION REQUEST AND REQUEST FOR A TYPE A MEETING TO FURTHER DISCUSS THE DISPUTE RESOLUTION REQUEST.
	20-JUL-2012	20-JUL-2012	CORRESPONDENCE	EMAIL	AJ TO AB: BMS PROVIDING POSSIBLE DATES (AUG. 14 OR 15) RE: DISPUTE RESOLUTION REQUEST.
	23-JUL-2012	23-JUL-2012	CORRESPONDENCE	EMAIL	AJ TO MH: BMS F/U REQUESTING STATUS OF COMMENTS RE: SUBMISSION OF PEDIATRIC AMENDMENTS SUBMITTED TO IND 68,652 ON 01-JUN-12 (SEQ. NO. 0434)
	25-JUL-2012	25-JUL-2012	CORRESPONDENCE	EMAIL	AB TO AJ: FDA REQUEST AUG. 17, TO MEET RE: DISPUTE RESOLUTION REQUEST.
	27-JUL-2012	27-JUL-2012	CORRESPONDENCE	EMAIL	AJ TO AB: BMS PROVIDING TENTATIVE LIST OF BMS/AZ ATTENDEES RE: DISPUTE RESOLUTION REQUEST.
	31-JUL-2012	31-JUL-2012	CORRESPONDENCE	EMAIL	AB TO AJ: FDA ACKNOWLEDGMENT OF DISPUTE APPEAL & MEETING REQUEST GRANTED, TO BE HELD 17-AUG-12.
	02-AUG-2012	02-AUG-2012	CORRESPONDENCE	EMAIL	AB TO AJ: REQUEST TO CHANGE THE TYPE A MEETING FOR THE DISPUTE APPEAL FROM AUG. 17TH TO AUG. 15TH OR 16TH, BASED UPON UNAVAILABLE FDA ATTENDEES.
	02-AUG-2012	02-AUG-2012	CORRESPONDENCE	SUBMISSION	AJ TO AB: F/U RE: CHANGING THE DATE OF THE DISPUTE APPEAL TYPE A MEETING. AGREEMENT TO CHANGE DATE TO AUG. 15TH.
	03-AUG-2012	03-AUG-2012	CORRESPONDENCE	EMAIL	AB TO AJ: CONFIRMATION OF RESCHEDULED AUG. 15TH MEETING TO DISCUSS DISPUTE APPEAL; INCLUDING A BRIEF SUMMARY OF THE EXPECTED AGENDA FOR THE MEETING.
	03-AUG-2012	03-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO AB: UPDATED BMS/AZ ATTENDEE LIST FOR AUG. 15TH TYPE A MEETING.
	06-AUG-2012	06-AUG-2012	OTHER	SUBMISSION	AJ TO MP:DRAFT PROT. (CVOT), RESPONSE TO REQUEST FOR INFO. 31-MAY012, WAIVER FROM RPT'G STUDY ENDPOINTS AS SERIOUS AE'S.
	13-AUG-2012	13-AUG-2012	CORRESPONDENCE	EMAIL	MH TO AJ: UPDATE ON CHANGE OF FDA PROJECT MANAGER TO ABOLADE (BOLA) ADEOLU FOR IND 68,652, IND 106,890, & NDA 202-293.
	16-AUG-2012	16-AUG-2012	CORRESPONDENCE	EMAIL	BA TO AA: FDA REQUEST TO SUBMIT ADD'L INFO ON A PT. IN CASE D1690C00004-4402.
	27-AUG-2012	27-AUG-2012	CORRESPONDENCE	EMAIL	AA TO AJ: RECOMMENDATIONS TO CONSIDER A STUDY
	27-AUG-2012	27-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO AA: REQUEST TO REVIEW THE RECOMMENDATION FOR A STUDY.
	27-AUG-2012	27-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO AA: SCHEDULED TELECON FOR 30-AUG-12 TO DISCUSS THE RECOMMENDATION FOR A STUDY.
	28-AUG-2012	28-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO AA: RESPONSE TO FDA REQUEST TO SUBMIT ADD'L INFO ON A PT. IN CASE D1690C00004-4402.
	29-AUG-2012	29-AUG-2012	AMENDMENT	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR ADD'L INFO DATED 16-AUG-12 RE: AN UPDATED NARRATIVE FOR SUBJECT D1690C00004-4402-6.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	29-AUG-2012	29-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO AA/AB: UPDATED RESPONSE TO RESPONSE TO FDA REQUEST TO SUBMIT ADD'L INFO ON A PT. IN CASE D1690C00004-4402. (PREVIOUS SUBMITTED INFO CONTAINED ERRORS)
	29-AUG-2012	29-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO AA: PROVIDING BMS SLIDES TO FACILITATE THE DISCUSSION FOR SCHEDULED TELECON ON 30-AUG-12 TO DISCUSS THE RECOMMENDATION FOR A STUDY.
	30-AUG-2012	30-AUG-2012	CORRESPONDENCE	EMAIL	AJ TO AA: TELECON ORIGINALLY SCHEDULED FOR 30-AUG-12 RESCHEDULED FOR 06-SEP-12 TO DISCUSS THE RECOMMENDATION FOR A STUDY.
	30-AUG-2012	30-AUG-2012	CORRESPONDENCE	SUBMISSION	AJ TO AA: ATTEMPTS TO RESCHEDULE THE TELECON FOR 30-AUG-12 TO DISCUSS THE RECOMMENDATION FOR A STUDY.
	05-SEP-2012	05-SEP-2012	CORRESPONDENCE	EMAIL	AA TO AJ: REQUEST FOR CLARIFICATION .
	05-SEP-2012	05-SEP-2012	CORRESPONDENCE	EMAIL	AJ TO AA: RESPONSE TO REQUEST THAT SN 0056 SUBMITTED 27-OCT-11.
	06-SEP-2012	06-SEP-2012	CORRESPONDENCE	EMAIL	AJ TO AA: F/U TO TELECON HELD 06-SEP-12, PROVIDING THE PRASUGREL ARTICLE AS REQUESTED.
	13-SEP-2012	13-SEP-2012	CORRESPONDENCE	EMAIL	AJ TO AA: F/U ON THE PEDIATRIC PK/PD PROTOCOL MB102-091 INCLUDING REQUEST FOR FEEDBACK.
	20-SEP-2012	20-SEP-2012	CORRESPONDENCE	SUBMISSION	AJ TO AA: PLANS TO SUBMIT AN ESR FOR DAPA (EVENT: HEPATITIS) ON 21-SEP-12. INQUIRY OF WHEN TO EXPECT THE COMMENTS ON THE DAPA PK PROTOCOL & THE LOCATION FOR THE MEETING TO BE HELD 04-OCT-12.
	22-SEP-2012	22-SEP-2012	CORRESPONDENCE	EMAIL	AA TO AJ: FDA RESPONSE TO FDA INQUIRY DATED 20-SEP-12-REVIEW OF THE PK/PD PEDIATRIC PROTOCOL HAS BEEN COMPLETED, THERE ARE NO COMMENTS TO CONVEY.
	01-OCT-2012	01-OCT-2012	CORRESPONDENCE	EMAIL	AA TO AJ: CLARIFICATION ON INFO. SO THAT THE DAPA TEAM CAN PLAN ACCORDINGLY RE: CVOT COMMENTS, PHARM/TOX ISSUE, & PROPOSED AMENDMENTS.
	02-OCT-2012	02-OCT-2012	CORRESPONDENCE	EMAIL	AA TO AJ: RESPONSE TO CLARIFICATION DATED 01-OCT-12- CVOT COMMENTS TO BE PROVIDED BY COB 05-OCT-12, TO PROVIDE COMMENTS TO THE PHAR/TOX ISSUE AFTER RECEIPT OF RESPONSES, & WILL RESPOND TO PROPOSED AMENDMENTS IN THE FOLLOWING WEEK.
	26-OCT-2012	26-OCT-2012	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR FDA FEEDBACK ON NDA RESUBMISSION PLAN IN RESPONSE TO THE CRL ISSUED 17-JAN-12 & THE DISPUTE RESOLUTION FDA DECISION LTR. DATED 14-SEP-12. ALSO- F/U ON THE NDA RESUBMISSION EXTENSION REQUEST SUBMITTED 27-SEP-12 (SN0084) THAT IF THE PROPOSED RESUBMISSION PLAN IS ACCEPTED BY THE AGENCY, TARGET RESUBMISSION FOR THE NDA TO BE END-JUNE/EARLY-JULY 2013.
	19-NOV-2012	19-NOV-2012	CORRESPONDENCE	SUBMISSION	MP TO AJ: FDA GENERAL ADVICE LTR. IN RESPONSE TO THE SPONSER'S REQUEST FOR ADVICE ON THE PROPOSED NDA RESUBMISSION PLAN SUBMITTED 26-OCT-12 (SN 0088).
	21-NOV-2012	21-NOV-2012	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE SUBMISSION OF PROTOCOL D1693C00001 THAT WAS SUBMITTED TO IND 68,652.
	28-NOV-2012	28-NOV-2012	CORRESPONDENCE	LETTER	FDA agrees to extensions to resubmit application in July 2013.
	03-DEC-2012	03-DEC-2012	CORRESPONDENCE	EMAIL	BMS questions and FDA responses pertaining to programming errors in SAS program affecting dapagliflozin clinical study reports.
	11-DEC-2012	11-DEC-2012	OTHER	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST TO PROVIDE A TABLE OF THE STUDIES THE SPONSER PLANS TO SUBMIT IN SUPPORT OF THE NDA RESUBMISSION.

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	13-DEC-2012	13-DEC-2012	CORRESPONDENCE	SUBMISSION	AA TO AJ: FDA RESPONSES TO SPONSER QUESTIONS POSED VIA EMAIL ON 03-DEC-13.
	23-JAN-2013	23-JAN-2013	CORRESPONDENCE	SUBMISSION	AJ TO AA: BMS UPDATE ON SUBMISSION OF TRADE NAME & FUTURE CVOT CEC SUBMISSION, AS WELL AS, INQUIRY RE: US (CONVENTIONAL) UNITS USED IN SUBMISSIONS.
	24-JAN-2013	24-JAN-2013	CORRESPONDENCE	SUBMISSION	AA TO AJ: RESPONSE TO 23-JAN-13 INQUIRY RE: US (CONVENTIONAL) UNITS- FDA POLICY THAT ALL DATA SHOULD BE REPRESENTED IN US (CONVENTIONAL) UNITS.
	29-JAN-2013	29-JAN-2013	CORRESPONDENCE	SUBMISSION	AJ TO AA: INQUIRY OF FDA REVIEW STATUS RE: DAPA/MET FDC NDA QUESTIONS & CVOT PROTOCOL SUBMITTED 19-NOV-12 TO IND 68,652 (SN 0456) & 202-293 (SN 0089).
	30-JAN-2013	30-JAN-2013	OTHER	SUBMISSION	AJ TO MP: AJ TO MP: CROSS-REF. FROM IND 68,652 OF DRAFT CLINICAL EVENTS COMMITTEE (CEC) CHARTER PROVIDED FOR REVIEW FOR THE PLANNED DECLARE CVOTTARGETING FIRST PT. FIRST VISIT FOR APRIL 2013. REQUEST TO PROVIDE COMMENTS BY 25-MAR-13.
	04-FEB-2013	04-FEB-2013	OTHER	SUBMISSION	AJ TO MP: CROSS-REFERENCE SUBMISSION OF REVISED PROTOCOL MB102091 FROM IND 68,652 (PREVIOUSLY CROSS-REFERENCED ON 30-APR-12/SN0080).
	28-FEB-2013	28-FEB-2013	OTHER	SUBMISSION	AJ TO MP: CROSS-REF. LTR. SUBMITTED TO IND 68,652 (SN 0472) ON 27-FEB-12 FOR PROTOCOL D1693C00005, RPT. #17383738.
	18-APR-2013	18-APR-2013	CORRESPONDENCE	TELEPHONE	FDA TO MH: DISCUSSION REGARDING RESUBMISSION AND STEPS FORWARD.
	08-MAY-2013	08-MAY-2013	CORRESPONDENCE	SUBMISSION	AJ TO AA: F/U WITH FDA RE: NDA ORIENTATION MEETING FOR NEW FDA REVIEW TEAM MEMBERS.
	13-MAY-2013	13-MAY-2013	OTHER	SUBMISSION	AJ TO MP: CROSS-REF. SUBMISSION OF REVISED PROTOCOL (D1693C00001) AND THE DMC CHARTER FOR THE DECLARE CVOT STUDY FROM IND 68,652.
	11-JUL-2013	11-JUL-2013	OTHER	SUBMISSION	AJ TO MP: RESUBMISSION OF NDA IN RESPONSE TO CRL DATED 17-JAN-12.
	12-JUL-2013	12-JUL-2013	CORRESPONDENCE	EMAIL	AJ TO MH: FDA CONFIRMATION OF RECEIPT OF RESUBMISSION OF NDA 202-293 SENT 11-JUL-13.
	15-JUL-2013	15-JUL-2013	CORRESPONDENCE	EMAIL	MT TO AJ: FDA REQUEST FOR RE-SUBMISSION OF PROPRIETARY NAME REVIEW NOT INCLUDED IN THE COMPLETE RESPONSE.
	16-JUL-2013	16-JUL-2013	OTHER	SUBMISSION	AJ TO MP: REQUEST FOR PROPRIETARY NAME RE-REVIEW OF "FORXIGA" BY ALL RELEVANT OFFICES/DIVISIONS OF FDA.
	25-JUL-2013	25-JUL-2013	CORRESPONDENCE	ACKNOWLEDGEMENT	JM TO AJ: FDA ACKNOWLEDGEMENT LTR. FOR RESUBMISSION OF DAPA NDA DATED 11-JUL-13. CONSIDERED A CLASS 2 RESPONSE WITH A USER FEE GOAL DATE OF 11-JAN-14.
	02-AUG-2013	02-AUG-2013	CORRESPONDENCE	EMAIL	F/U to the FDA email of 10-Jul-2013 regarding Dapa dataset questions; fdc and dapa NDA and IND
	07-AUG-2013	07-AUG-2013	OTHER	SUBMISSION	AJ TO MP: RESPONSE TO FDA REQUEST FOR INFO DATED 01-AUG-13 RE: MOST UP-TO-DATE AND COMPREHENSIVE DATASETS FOR THE CORE 21 CLINICAL TRIALS.
	29-AUG-2013	29-AUG-2013	CORRESPONDENCE	EMAIL	Change to FDA Met Leader from Dr. Park to Dr. Guettier
	03-SEP-2013	03-SEP-2013	OTHER	SUBMISSION	AJ TO JG: CROSS-REF. SUBMISSION OF INITIAL WRITTEN RPT. #1913496. CROSS-REF. FROM IND 68,652.
	05-SEP-2013	05-SEP-2013	OTHER	SUBMISSION	AJ TO JG: CROSS-REF. SUBMISSION FROM IND 68,652 PROVIDING REVISED STATISTICAL ANALYSIS PLAN (SAP) (930065684), RESPONSE TO AGENCY'S COMMENTS DATED 07-FEB-13 (930071606), AND REVISED DMC CHARTER (930069941 & 930072663).

Planned Submission Filing Date	Sent Date	Submission Filing Date	Submission Type	Correspondence Type	Submission Title
	06-SEP-2013	06-SEP-2013	OTHER	SUBMISSION	AJ TO JG: RESPONSE TO FDA REQUEST DATED 21-AUG-13 RE: SIDE BY SIDE COMPARISON LBL'G DOCUMENT.
	09-SEP-2013	09-SEP-2013	OTHER	SUBMISSION	AJ TO JG: CROSS-REF. SUBMISSION OF F/U #1 TO WRITTEN RPT. #19134964.
	09-SEP-2013	09-SEP-2013	OTHER	SUBMISSION	AJ TO JG: AMENDMENT TO PROPRIETARY NAME REVIEW REQUEST DATED 16-JUL-13 FOR FDA TO NOW REVIEW THE PROPRIETARY NAME 'FARXIGA'.
	16-SEP-2013	16-SEP-2013	CORRESPONDENCE	EMAIL	Response to FDA Request for Information dated 11-Sep-2013.
	17-SEP-2013	17-SEP-2013	OTHER	SUBMISSION	Response to FDA request.
	17-SEP-2013	17-SEP-2013	CORRESPONDENCE	EMAIL	Updated response.
	19-SEP-2013	19-SEP-2013	CORRESPONDENCE	MEMO	EMDAC Sponsor Letter regarding upcoming meeting tentatively scheduled for December 12th and 13th, 2013 to discuss the efficacy and safety of new drug application NDA 202293
	20-SEP-2013	20-SEP-2013	CORRESPONDENCE	EMAIL	EMDAC sponsor letter - proposed finalization for meeting tentatively scheduled for December 12th and 13th.
	23-SEP-2013	23-SEP-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Dapa tradename labeling.
	26-SEP-2013	26-SEP-2013	CORRESPONDENCE	EMAIL	EMDAC sponsor letter - List of Investigators
	03-OCT-2013	03-OCT-2013	CORRESPONDENCE	EMAIL	Response to FDA Request for Information regarding Datasets.
	04-OCT-2013	04-OCT-2013	OTHER	SUBMISSION	Response to FDA Questions dated 02-Oct-2013 30 Month Safety Update located in Module 5.3.5.3 for the submission.
	04-OCT-2013	04-OCT-2013	CORRESPONDENCE	EMAIL	Rquest for Information regarding TD2M dosage.
	04-OCT-2013	04-OCT-2013	CORRESPONDENCE	EMAIL	Updated Investigator list for DAPA.
	07-OCT-2013	07-OCT-2013	CORRESPONDENCE	LETTER	Proprietary Name Request Conditionally Acceptable letter for Forxiga
	08-OCT-2013	08-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding TN Farxiga granted.
	08-OCT-2013	08-OCT-2013	CORRESPONDENCE	EMAIL	EMDAC Sponsor Letter - development of agenda for the upcoming meeting to be held on December 12, 2013
	08-OCT-2013	08-OCT-2013	CORRESPONDENCE	EMAIL	Response to FDA Request for Information regarding TD2M dosage.
	08-OCT-2013	08-OCT-2013	CORRESPONDENCE	EMAIL	Tentative meeting date of December 12, 2013 for the Advisory Committee to discuss dapagliflozin.
	09-OCT-2013	09-OCT-2013	CORRESPONDENCE	EMAIL	Response to Information Request regarding TD2M data request.
	10-OCT-2013	10-OCT-2013	OTHER	SUBMISSION	30 Month Safety Update - Response to FDA Question (dosing) dated 04-Oct-2013 (930073910, v1.0)
	10-OCT-2013	10-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Dapagliflozin labeling questions.
	10-OCT-2013	10-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding the pharmacoepidemiology protocol.
	11-OCT-2013	11-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Dapa Labeling
	11-OCT-2013	11-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding table request from the SCS and 4 Month Safety Update.
	11-OCT-2013	11-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding the effect of SGLT2 inhibitors on assays.
	11-OCT-2013	11-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding updated dosing information and EMDAC meeting information.
	16-OCT-2013	16-OCT-2013	OTHER	SUBMISSION	Propose Trade and Sample Carton/Container Labels for NDA 202-293
	16-OCT-2013	16-OCT-2013	OTHER	SUBMISSION	Additional Patent Information
	16-OCT-2013	16-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding the updated carton/ containers for dapagliflozin with confirmation of receipt by FDA.
	17-OCT-2013	17-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding EMDAC questions; due date of briefing materials.
	18-OCT-2013	18-OCT-2013	OTHER	SUBMISSION	Response to FDA Request for Information; SGLT2 inhibitors.
	18-OCT-2013	18-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding PV-EPI response.
	21-OCT-2013	21-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Dapa-Exec summary for meeting with FDA re EMDAC scheduled for 12-December-2013.

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	22-OCT-2013	22-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding PV-EPI response.
	24-OCT-2013	24-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence regarding response to FDA's request for SCS and 4 Month Safety Update tables.
	25-OCT-2013	25-OCT-2013	OTHER	SUBMISSION	Response to FDA Request for Information dated October 9, 2013.
	28-OCT-2013	28-OCT-2013	CORRESPONDENCE	EMAIL	Correspondence containing the preliminary list of presenters and responders for the Dapa-EMDAC meeting.
	01-NOV-2013	01-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Container Closure System.
	04-NOV-2013	04-NOV-2013	OTHER	SUBMISSION	Provide FDA with updated sample carton/container labels for 10mg hudblstr.
	04-NOV-2013	04-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding 30 month erratum.
	05-NOV-2013	05-NOV-2013	OTHER	SUBMISSION	Correspondence to provide the Agency with a 30 month update errata.
	05-NOV-2013	05-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding the posting of the EMDAC date.
	06-NOV-2013	06-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding Display and Publication Dates for EMDAC.
	06-NOV-2013	06-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding EMDAC briefing book.
	07-NOV-2013	07-NOV-2013	CORRESPONDENCE	EMAIL	Confirmation of receipt of EMDAC briefing document by FDA.
	13-NOV-2013	13-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding labeling question; next labeling meeting is scheduled for Monday, November 18, 2013.
	15-NOV-2013	15-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding EMDAC questions - maximum number of seats for the meeting and submission of complete list of presenters and responders due by November 20, 2013.
	19-NOV-2013	19-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence providing the list of people sitting in the sponsor section and /or presenting on behalf of BMS/AZ at the dapa EMDAC.
	19-NOV-2013	19-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding labeling and briefing book.
	20-NOV-2013	20-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence regarding the Agency's inability to share sections of labeling.
	21-NOV-2013	21-NOV-2013	OTHER	SUBMISSION	OTHER - Cross-Reference Submission - This submission provides the FDA with a second follow-up report to the MedWatch forms submitted on 29-Aug-2013 and 5-Sept-2013.
	22-NOV-2013	22-NOV-2013	CORRESPONDENCE	EMAIL	Correspondence requesting information for Renal Impairment/Failure, Volume Depletion and Hyperkalemia.
	06-DEC-2013	06-DEC-2013	OTHER	SUBMISSION	Response to FDA Request for Information - This submission provides information for the Agency's request of 22-November-2013 regarding renal impairment/failure and volume depletion.
	18-DEC-2013	18-DEC-2013	OTHER	SUBMISSION	OTHER: Cross-Reference Submission - This submission provides the Agency with a MedWatch form.
	24-DEC-2013	24-DEC-2013	OTHER	SUBMISSION	OTHER: PROPOSED CARTON/CONTAINER LABELS FOR NDA 202-293 - This submission provides the Agency with updated proposed carton/container labels for the dapagliflozin NDA 202-293.
	26-DEC-2013	26-DEC-2013	OTHER	SUBMISSION	Providing Revised Protocol 02 & Amendment 02 for Study D1693C00001. Cross-Ref. submission from IND 68,652.
	31-DEC-2013	31-DEC-2013	OTHER	SUBMISSION	IND Safety Rpt.: F/U #1 to Written Rpt. #19890805. Cross-Ref. from IND 68,652.
		22-OCT-2013	OTHER	SUBMISSION	Response to FDA Request for Information dated 10-Oct-2013

EXHIBIT K

PTO/SB/96 (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: AstraZeneca AB

Application No./Patent No.: 6515117 Filed/Issue Date: May 20, 2002

Titled: C-Aryl Glucoside SGLT2 Inhibitors and Method

AstraZeneca AB , a corporation
(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.

states that it is:

1. ☒ the assignee of the entire right, title, and interest in;

2. ☐ an assignee of less than the entire right, title, and interest in (The extent (by percentage) of its ownership interest is _____ %); or

3. ☐ the assignee of an undivided interest in the entirety of (a complete assignment from one of the joint inventors was made)

the patent application/patent identified above, by virtue of either:

A. ☐ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy therefore is attached.

OR

B. ☒ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: the inventors To: Bristol-Myers Squibb Company

The document was recorded in the United States Patent and Trademark Office at
Reel 012918 , Frame 0698 , or for which a copy thereof is attached.

2. From: Bristol Myers-Squibb Company To: AstraZeneca AB

The document was recorded in the United States Patent and Trademark Office at
Reel 032347 , Frame 0115 , or for which a copy thereof is attached.

3. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____ , Frame _____ , or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☒ As required by 37 CFR 3.73(b)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (*i.e.*, a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/David M. Gryte, Reg. No. 41809/ March 3, 2014
Signature Date

David M. Gryte Senior Patent Attorney
Printed or Typed Name Title

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.