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OFA
OUTSOURCING FACILITIES ASSOCIATION

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Bulk Drug Substance Nomination	
What is the name of the nominated ingredient?	Ipamorelin acetate
Is the ingredient an active ingredient that meets the definition of "bulk drug substance" in §207.3(a)(4)?	Yes
What is the chemical name of the substance?	(2S)-6-amino-2-[[(2R)-2-[[(2R)-2-[[(2S)-2-[(2-amino-2-methylpropanoyl)amino]-3-(1H-imidazol-5-yl)propanoyl]amino]-3-naphthalen-2-ylpropanoyl]amino]-3-phenylpropanoyl]amino]hexanamide
What is the common name of the substance?	Ipamorelin
Does the substance have a UNII Code?	Y9M3S784Z6
What is the chemical grade of the substance?	Please see the attached Certificate of Analysis.
What is the strength, quality, stability and purity of the substance?	Please see the attached Certificate of Analysis.
How is the ingredient supplied?	Powder
Is the substance recognized in foreign pharmacopeias or registered in other countries?	N/A
Has information been submitted about the substance to the USP for consideration of monograph development?	N/A
What medical condition(s) is the drug product compounded with the bulk drug substances intended to treat?	Postoperative ileus
Are there other drug products approved by the FDA to treat the same medical condition?	There are no products containing Ipamorelin approved by the FA that are actively being marketed and listed in the Orange Book.
If there are FDA approved drug products that address the same medical condition, why is there a clinical need for a compounded drug product?	Ipamorelin is not found in any FDA-approved drug products. Even if it were, as with any drug product, patients respond differently. The compounded drug product may be the only product to effectively treat the indication for which it is intended to treat.
Are there safety and efficacy data on compounded drugs using the nominated substance?	*See* Gobburu JV, Agersø H, Jusko WJ, Ynddal L. Pharmacokinetic-pharmacodynamic modeling of ipamorelin, a growth hormone releasing peptide, in human volunteers. Pharm Res. 1999 Sep;16(9):1412-6. PubMed PMID: 10496658. **Abstract** Purpose. To examine the pharmacokinetics (PK) and pharmacodynamics (PD) of ipamorelin, a growth hormone (GH) releasing peptide, in healthy volunteers.

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Methods. A trial was conducted with a dose escalation design comprising 5 different infusion rates (4.21, 14.02, 42.13, 84.27 and 140.45 nmol/kg over 15 minutes) with eight healthy male subjects at each dose level. Concentrations of ipamorelin and growth hormone were measured.

Results. The PK parameters showed dose-proportionality, with a short terminal half-life of 2 hours, a clearance of 0.078 L/h/kg and a volume of distribution at steady-state of 0.22 L/kg. The time course of GH stimulation by ipamorelin showed a single episode of GH release with a peak at 0.67 hours and an exponential decline to negligible GH concentration at all doses. The ipamorelin−GH concentration relationship was characterized using an indirect response model and population fitting. The model employed a zero-order GH release rate over a finite duration of time to describe the episodic release of GH. Ipamorelin induces the release of GH at all dose levels with the concentration (SC50) required for half-maximal GH stimulation of 214 nmol/L and a maximal GH production rate of 694 mIU/L/h. The inter-individual variability of the PD parameters was larger than that of the PK parameters.

Conclusions. The proposed PK/PD model provides a useful characterization of ipamorelin disposition and GH responses across a range of doses.

See also Beck DE, Sweeney WB, McCarter MD; Ipamorelin 201 Study Group. Prospective, randomized, controlled, proof-of-concept study of the Ghrelin mimetic ipamorelin for the management of postoperative ileus in bowel resection patients. Int J Colorectal Dis. 2014 Dec;29(12):1527-34. doi: 10.1007/s00384-014-2030-8. Epub 2014 Oct 21. PubMed PMID: 25331030.

Abstract

BACKGROUND:
Postoperative ileus is a significant clinical challenge lacking effective management strategies. Ghrelin-receptor stimulation has promotility effects in the upper and lower gastrointestinal tract.

OBJECTIVE:
This proof-of-concept, phase 2, randomized study evaluated the safety and efficacy of the ghrelin-receptor agonist ipamorelin in the treatment of postoperative ileus following abdominal surgery (ClinicalTrials.gov NCT00672074).

DESIGN:
The design was a multicenter, double-blind, placebo-controlled, clinical trial.

SETTINGS:
The settings include hospital inpatients.

PATIENTS:
The patients were adults undergoing small and large bowel resection by open or laparoscopic surgery.

INTERVENTION:
The intervention was intravenous infusions of 0.03-mg/kg ipamorelin vs

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	placebo twice daily, on postoperative day 1 to 7 or hospital discharge. MAIN OUTCOME MEASURES: Safety was assessed by monitoring adverse events and laboratory tests. The key efficacy endpoint was time from first dose of study drug to tolerance of a standardized solid meal. RESULTS: One hundred seventeen patients were enrolled, of whom 114 patients composed the safety and modified intent-to-treat populations. Demographic and disease characteristics were balanced between groups. Overall incidence of any treatment-emergent adverse events was 87.5 % in the ipamorelin group and 94.8 % in placebo group. Median time to first tolerated meal was 25.3 and 32.6 h in the ipamorelin and placebo groups, respectively ($p = 0.15$). LIMITATIONS: This proof of concept study was small and enrolled patients with a broad range of underlying conditions. CONCLUSIONS: Ipamorelin 0.03-mg/kg twice daily for up to 7 days was well tolerated. There were no significant differences between ipamorelin and placebo in the key and secondary efficacy analyses.
If there is an FDA -approved product that includes the bulk drug substance nominated, is it necessary to compound a drug product from the bulk drug substance rather than from the FDA-approved drug product?	There is no FDA-approved product that includes the bulk drug substance. Even if there was an FDA-approved product available, it may be necessary to compound a product with greater concentration than is commercially available. A patient may need a prescribed dosage form or strength not available commercially. Possible patient sensitivities to manufactured product dyes, fillers, preservatives and other excipients is another concern. Additionally, manufacturer backorders can create a situation where the patient is not able to obtain the drug product, or it is extremely difficult for the patient to obtain the drug product. Compounding pharmacies can alleviate this strain by compounding from the bulk drug substance.
What dosage form(s) will be compounded using the bulk drug substance?	Injectable
What strength(s) will be compounded from the nominated substance?	Ranging from 0.5 mg/mL – 5 mg/mL
What are the anticipated route(s) of administration of the compounded drug product(s)?	Injectable
Has the bulk drug substance been used previously to compound drug product(s)?	N/A
Is there any other relevant information?	N/A