Trade Name: Somatuline Depot

Generic Name: Lanreotide Acetate

Sponsor: Ipsen Pharma

Approval Date: 10/22/2014

Indications: Somatuline Depot (lanreotide) Injection is a somatostatin analog indicated for the long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.
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### Reviews / Information Included in this NDA Review.

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<td>Administrative/Correspondence Document(s)</td>
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APPLICATION NUMBER:
022074Orig1s009

APPROVAL LETTER
NDA 22074/S-009

APPROVAL LETTER

Ipsen Pharma
Attention: Mary Jane Cheah
Senior Manager, Post-Marketing Regulatory Affairs
106 Allen Road 3rd Floor
Basking Ridge, NJ 07920

Dear Ms. Cheah:

Please refer to your Supplemental New Drug Application (sNDA) dated April 24, 2014, received April 25, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Somatuline® Depot (lanreotide acetate) Injection.

This “Changes Being Effected in 30 days” supplemental new drug application provides for changes to the pouch supplier.

We have completed our review of this supplemental new drug application. This supplement is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Priyanka Kumar, Regulatory Project Manager, at (240) 402-3722.

Sincerely,

Ramesh Raghavachari, Ph.D.
Branch Chief, Branch IX
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Digitally signed by Ramesh Raghavachari - S
Date: 2014/06/22 21:43:20 -04'00"
APPLICATION NUMBER: 022074Orig1s009

CHEMISTRY REVIEW(S)
CHEMIST REVIEW OF SUPPLEMENT
1. ORGANIZATION: ONDQA – Division of Post-Marketing Evaluation
2. NDA Number: 22074
3. SUPPLEMENT NUMBERS/DATES: S009 (CBE30)
   Letter date: April 24, 2014
   Stamp date: April 25, 2014
4. AMENDMENTS/REPORTS/DATES: None
5. RECEIVED BY CHEMIST: May 16, 2014

6. APPLICANT NAME & ADDRESS
   Ipsen Pharma
   65 Quai Georges Gorse
   92100 Boulogne-Billancourt
   France 92100
   US Authorized Agent:
   Ipsen Biopharmaceutical, Inc.
   106 Allen Road
   3rd Floor
   Basking Ridge, NJ 07920

7. NAME OF DRUG: Somatuline® Depot
8. NONPROPRIETARY NAME: lanreotide acetate
9. CHEMICAL NAME/STRUCTURE:
   [Cyclic (2→7)-disulfide]-3-(2-naphthyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-
   tryptophyl-L-lysyl-L-valyl-L-cysteinyl-L-threoninamide, acetate salt; the
   synthetic cyclical octapeptide analog of the natural hormone somatostatin
   (also known as growth hormone inhibiting hormone (GHIH) or somatotropin
   release-inhibiting factor (SRIF))
   MW: 1096.32, C$_{54}$H$_{69}$N$_{11}$O$_{10}$S$_{2}$·x(C$_{2}$H$_{4}$O$_{2}$) where x = 1.6 to 3.4

   S……………………..S
   |
   D-βNal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH$_{2}$, x(CH$_{3}$COOH) where x = 1.6 to 3.4

10. DOSAGE FORM(S): Injection, deep subcutaneous
11. POTENCY:
   60 mg, 90 mg and 120 mg (from a supersaturated solution containing
   24.6% w/w lanreotide base)
12. PHARMACOLOGICAL CATEGORY: Antineoplastic agent; Somatostatin analog indicated for the long-term
   treatment of acromegalic patients who have had an inadequate response
   to or cannot be treated with surgery and/or radiotherapy.
13. HOW DISPENSED: X (Rx) (OTC)
14. RECORDS & REPORTS CURRENT: X Yes No
   REVIEW RECORDS & REPORTS CURRENT: X Yes No
15. RELATED IND/INDA/DMF: NA
16. SUPPLEMENT PROVIDES FOR: An additional supplier of the laminated pouch used to package Somatuline
   Depot (lanreotide) Injection.
17. COMMENTS: Ipsen Pharma (Ipsen) NDA 22074 for Somatuline Depot (lanreotide) Injection (Somatuline Depot) 60, 90 and 120mg was approved August 30, 2007. Ipsen has proposed an additional supplier of the laminate pouch used to package the pre-filled syringe containing Somatuline Depot. On May 20, 2014, Dr. Priyanka Kumar, Pharm.D (Regulatory Health Project Manager-ONDQA postmarketing) issued Acknowledgment Letter stating that the proposed change would be reviewed as Changes Being Effected in 30 Days Supplement (CBE30) 22074/S009. The Initial Quality Assessment (IQA) for 22074/S009 is provided in Attachment 1.

**Background**
Somatuline Depot is packed in a pre-filled syringe, which is then packaged in a laminated pouch. The pouch is a functional secondary packaging component and provides protection of the pre-filled syringe against light and exchange with the environment. According to Ipsen, the addition of an alternate supplier for the laminated pouch helps Ipsen ensure the supply of laminated pouches for the currently approved and marketed drug product for the US.

No other change is proposed with 22074/S009, except that the applicant takes this opportunity to update section 3.2.P.7 Container Closure System of the NDA, in line with a change declared in the 2013 NDA 22074 Annual Report (AR), that the name of the needle sheath supplier is updated from __________ (b)(4) There is no change in the address of this supplier.

**Justification**
The proposed alternative supplier for the laminated pouch is __________ (b)(4) Ipsen has updated Table 7 Description of Functional Secondary Packaging Components in section 3.2.P.7.2 Secondary Packaging, to reflect this change (Attachment 2)

The addition of __________ (b)(4) as an alternate supplier for the laminated pouch does not change the pouch composition, which remains __________ (b)(4) The composition of the laminated pouch supplied by __________ (b)(4) is the same as the composition of the laminated pouch supplied by the current approved supplier, __________ (b)(4)

There is no change to the composition or thickness of the laminate layers, i.e., __________ (b)(4) However, the acceptance criteria of the laminated pouches have been slightly changed in order to __________ (b)(4) This is due to the addition of __________ (b)(4)
(Chemistry Reviewer-ONDQA Premarketin) for NDA 22074 CMC Review No. 1 with an approvable recommendation), the suitability of the container-closure system, including the laminate pouch, has been established in terms of protection, compatibility between lanreotide and packaging materials, safety, and performance. The new alternate pouch supplier (b)(4) will provide a laminated pouch of the same composition i.e., (b)(4) as the current approved pouch supplier. Thus, the proposed use of (b)(4) laminated pouch to package Somatuline Depot (lanreotide) Injection 60, 90 and 120mg will not impact the quality, efficacy or safety of the drug product.
Nanotechnology product evaluating questions are appended to this review (Attachment 3).

18 CONCLUSIONS & RECOMMENDATIONS: Recommend issuing approval letter.

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<th>REVIEWER NAME</th>
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<td>Lorenzo A. Rocca</td>
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<th>BRANCH CHIEF NAME</th>
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<td>Ramesh Raghavachari</td>
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cc:
ONDQA/RRaghavachari
ONDQA/LRocca
ONDQA/PKumar

F/T by: LRocca, File: C:\Data\LR\Supplement\n22074pm\S009(CBE30)\22074_S-009Review1.doc
IQA (Dr. Klein) for Branch IX
DATE: 5/15/14
SUPPLEMENT: N22-074, S-009, CBE-30; Paper Submission
PDUFA DUE DATE: 10/25/14
COMMENTS:
1. An additional supplier of the pouch is proposed. No change in the pouch composition. Changes to the pouch thickness are proposed. No DMF is referenced for the new supplier.

LORENZO
5/16/14
**Attachment A: Nanotechnology product evaluating questions:**

<table>
<thead>
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<th><strong>1. This review contains new information added to the table below: ____Yes; __X__No</strong></th>
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<td><strong>Review date:</strong> ____________________</td>
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|   | **2) Are any nanoscale materials included in this application? (If yes, please proceed to the next questions.) Yes______; No______; Maybe (please specify)___________________________** |

|   | **3 a) What nanomaterial is included in the product? (Examples of this are listed as search terms in Attachment B.) ________________________________** |

|   | **3 b) What is the source of the nanomaterial?** |

<table>
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<tr>
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<th><strong>4) Is the nanomaterial a reformulation of a previously approved product?</strong></th>
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<td><strong>Yes</strong></td>
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<th><strong>5) What is the nanomaterial functionality?</strong></th>
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<td><strong>Carrier__________________; Excipient__________________; Packaging__________________; Other__________________;</strong></td>
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<th><strong>6) Is the nanomaterial soluble (e.g., nanocrystal) or insoluble (e.g., gold nanoparticle) in an aqueous environment?</strong></th>
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<td></td>
<td><strong>Soluble__________________; Insoluble__________________;</strong></td>
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<th><strong>7) Was particle size or size range of the nanomaterial included in the application?</strong></th>
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<td><strong>Yes______(Complete 8); No______(go to 9).</strong></td>
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<th><strong>8) What is the reported particle size?</strong></th>
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<td><strong>Mean particle size__________________; Size range distribution__________________; Other__________________;</strong></td>
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<th><strong>9) Please indicate the reason(s) why the particle size or size range was not provided:</strong></th>
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<td><strong>_____________________________________________________________</strong></td>
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|   | **10) What other properties of the nanoparticle were reported in the application (See Attachment E)? ________________________________** |

|   | **11) List all methods used to characterize the nanomaterial?____________________________________________** |
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Digitally signed by Lorenzo A. Rocca -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=1
300136530, cn=Lorenzo A. Rocca -S
Date: 2014.10.21 13:04:51
-04'00'

Digitally signed by Ramesh Raghavachari -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=1300211793,
cn=Ramesh Raghavachari -S
Date: 2014.10.21 13:28:33 -04'00'
NDA 22074/S-09

Ipsen Pharma
Attention: Mary Jane Cheah
Senior Manager, Post-Marketing Regulatory Affairs
106 Allen Road 3rd Floor
Basking Ridge, NJ 07920

Dear Ms. Cheah:

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

**NDA NUMBER:** 22074

**SUPPLEMENT NUMBER:** S-09

**PRODUCT NAME:** Somatuline® Depot (lanreotide acetate) Injection

**DATE OF SUBMISSION:** April 24, 2014

**DATE OF RECEIPT:** April 25, 2014

This supplemental application, submitted as a “Changes Being Effected in 30 days” supplement, proposes changes to pouch supplier.

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 June 23, 2014, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 24, 2014.

Cite the application number listed above 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 Metabolic and Endocrine  
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, see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have questions, call me, at (240) 402-3722.

Sincerely,

*See appended electronic signature page*

Priyanka Kumar, Pharm. D  
Regulatory Health Project Manager  
Division of New Drug Quality Assessment III  
Office of New Drug Quality Assessment  
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/

PRIYANKA KUMAR
05/20/2014