CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

22074Orig1s007

Trade Name:	Somatuline
Generic or Proper Name:	lanreotide acetate
Sponsor:	Ipsen Pharma
Approval Date:	February 21, 2014
Indication:	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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APPLICATION NUMBER:

22074Orig1s007

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22074/S-007

APPROVAL LETTER

Ipsen Pharma
Attention: Steven R. Scott
VP, US Regulatory Affairs
106 Allen Road, 3rd Floor
Basking Ridge, NJ 07920

Dear Mr. Scott:

Please refer to your Supplemental New Drug Application (sNDA) dated and received October 22, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Somatuline ® (lanreotide acetate) Injection.

This "Prior Approval" supplemental new drug application provides for changes to the approved stability protocol and storage condition of the drug substance, lanreotide acetate, used in the manufacture of the finished drug product.

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,

{See appended electronic signature page}

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

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/s/

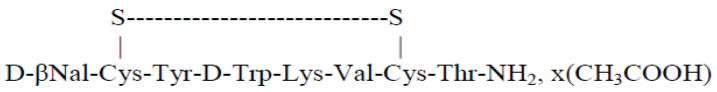
RAMESH RAGHAVACHARI
02/21/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22074Orig1s007

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW	1. ORGANIZATION:	2. NDA Number: 22-074
3. Name and Address of Applicant (City & State) Ipsen Pharma 65 Quai Georges Gorse 92100 Boulogne-Billancourt France 92100		**4. Supplement(s)** **Number(s)** **Date(s)** S-007 10/22/13
5. Drug Name Somatulin® Depot	**6. Nonproprietary Name** Lanreotide Acetate	**7. Amendments - Dates**
8. Supplement Provides For: changes to the approved stability protocol and storage condition of the drug substance, lanreotide acetate, used in the manufacture of Somatuline Depot (lanreotide) Injection 60, 90, 120mg.		
9. Pharmacological Category 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.	**10. How Dispensed** Rx	**11. Related NDAs**
12. Dosage Form(s) Injection	**13. Potency** 60, 90 and 120 mg	DMF 8974
14. Chemical Name and Structure: [cyclo S-S]-3-(2-naphthyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-L-threoninamide, acetate salt  Molecular Formula: $C_{54}H_{69}N_{11}O_{10}S_2$ Molecular Weight: 1096.33		**15. Records/Reports** **Current** **Yes X No** **Reviewed** **Yes No X**
16. Comments: Ipsen Biopharmaceuticals Inc., (Basking Ridge, NJ), the authorized US Agent of Ipsen Pharma, herewith submits a **PA Supplement** for changes to the approved stability protocol and storage condition of the drug substance, lanreotide acetate, used in the manufacture of Somatuline Depot (lanreotide) Injection 60, 90, 120mg. Because the changes are made in the DMF, this supplement is being submitted as a PA Supplement to the NDA, referencing the DMF 8974. LOA, dated 3/2/2009, to reference the DMF 8974 is provided.		
17. Conclusions and Recommendations: This supplement is "**approved**" from CMC perspective.		
18. Reviewer:		
Name: Kris Raman, Ph.D. Sr. CMC Reviewer	**Signature:**	**Date Completed: 2/20/14**

REVIEW NOTES

Currently, the drug substance, lanreotide acetate, is manufactured by Ipsen Manufacturing Ireland Limited. (b) (4)

A review of the drug substance storage condition at Ipsen Manufacturing Ireland Limited was performed concurrently with a review of the data from the stability testing program for the drug substance. Following this review, the applicant is proposing to change the lanreotide acetate drug substance storage condition at Ipsen Manufacturing Ireland Limited (b) (4) In addition a change to the approved stability protocol is proposed (b) (4)

The proposed changes in the supplement for the drug substance are incorporated by cross reference to DMF# 8974 held by Ipsen Manufacturing Ireland Limited.

The proposed changes to the storage condition and approved stability protocol have been submitted as **amendment to DMF # 8974 on October 18, 2013**. The applicant has included in this PA supplement the complete stability section VIII from Volume 1 Type II DMF#8974.

Letter of Authorization/DMF Review

LOA, dated 3/2/2009, to reference the DMF 8974 is provided. The DMF has been reviewed by Kris Raman, Ph.D., and found adequate to support this supplement.

Proposed Change to Storage Condition of API at Ipsen Manufacturing (Ireland)

(b) (4) were included in the current stability study protocol because currently API (lanreotide acetate) is stored at (b) (4)

(b) (4)

The drug substance manufacturer proposes to change (b) (4)

A total of (b) (4) and their details are provided in DMF#8974 Section VIII D, *Batches used in stability studies,* together with the rationale for the proposed (b) (4). There has been no stability concern or out-of-specification result associated with storage of lanreotide acetate (b) (4) and the stability studies have been performed according to the currently approved protocol as

demonstrated in DMF#8974 Section VIII E, *Stability Results,* which has been updated to include the latest stability data available for this drug substance as of 30 August 2013.

Lanreotide acetate stored in (b) (4) The data in DMF#8974 Section VIII E, *Stability Results,* also demonstrates that this drug substance is very stable when (b) (4)

The manufacturer has extensive experience and knowledge of this drug substance and following a review of the storage conditions (b) (4) storage is considered justified based on the current (b) (4) provided in DMF#8974 VIII E, *Stability Results.*

Changes to the Approved Stability Protocol

As the stability profile of lanreotide acetate was considered by the manufacturer to be established, a review of the stability testing program was performed (b) (4)

(b) (4)

The current and proposed stability protocols are provided in **Table 1** to **Table 4**. (b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

Conclusion

The change to the storage conditions at Ipsen Manufacturing Ireland Limited (b) (4) in the stability protocol for this established drug substance are well supported and justified by the applicant and have no effect on the product quality, efficacy or safety.

The proposed changes are reported in an amendment to DMF#8974 on October 18, 2013, including stability data to support the proposed changes.

Attachment A: Nanotechnology product evaluating questions:

1, This review contains new information added to the table below: _____Yes; __X___No Review date: _____
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?_____
4) Is the nanomaterial a reformulation of a previously approved product? Yes_____ No_____
5) What is the nanomaterial functionality? Carrier_____; Excipient_____; Packaging_____ API_____; Other_____
6) Is the nanomaterial soluble (e.g., nanocrystal) or insoluble **(**e.g., gold nanoparticle**)** in an aqueous environment? Soluble _____; Insoluble_____
7) Was particle size or size range of the nanomaterial included in the application? Yes_____(Complete 8); No_____ (go to 9).
8) What is the reported particle size? Mean particle size_____ ; Size range distribution_____; Other_____
9) Please indicate the reason(s) why the particle size or size range was not provided: _____ _____
10, What other properties of the nanoparticle were reported in the application (See Attachment E)? _____
11) List all methods used to characterize the nanomaterial?_____ _____

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/s/

KRISHNA P RAMAN
02/21/2014
This supplement is “approved” from CMC perspective.

RAMESH RAGHAVACHARI
02/21/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22074Orig1s007

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 22074/S-007

ACKNOWLEDGEMENT --
PRIOR APPROVAL SUPPLEMENT

Ipsen Pharma
Attention: Steven R. Scott
VP, US Regulatory Affairs
106 Allen Road, 3rd Floor
Basking Ridge, NJ 07920

Dear Mr. Scott:

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-007

PRODUCT NAME: Somatuline ® (lanreotide acetate) Injection

DATE OF SUBMISSION: October 22, 2013

DATE OF RECEIPT: October 22, 2013

This supplemental application proposes changes to the approved stability protocol and storage condition of the drug substance, lanreotide acetate, used in the manufacture of the finished drug product.

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 December 21, 2013 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be February 22, 2014.

SUBMISSION REQUIREMENTS

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 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, 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

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/s/

PRIYANKA KUMAR
11/25/2013