CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022074Orig1s009

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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APPLICATION NUMBER:

022074Orig1s009

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Reviews / Information Included in this NDA Review.

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APPLICATION NUMBER:

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

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 -S

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: 2014.10.22 21:45:25 -04'00'

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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APPLICATION NUMBER:

022074Orig1s009

CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **SUPPLEMENT**

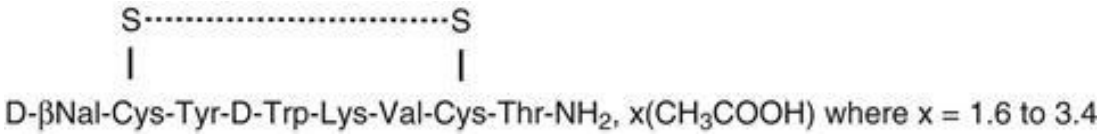
1. ORGANIZATION: ONDQA – Division of Post-Marketing Evaluation
2. NDA Number: **22074**
3. SUPPLEMENT NUMBERS/DATES: **S009 (CBE30)**
   Letter date: April 24, 2014
   Stamp date: April 25, 2014
4. AMENDMENTS/REPORTS/DATES: None
5. RECEIVED BY CHEMIST: **May 16, 2014**

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, $C_{54}H_{69}N_{11}O_{10}S_2 \bullet x(C_2H_4O_2)$ 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; Somatostostain 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	(R_X)		(OTC)
14. RECORDS & REPORTS CURRENT:	X	Yes		No
REVIEW RECORDS & REPORTS CURRENT	X	Yes		No

15. RELATED IND/NDA/DMF: NA

16. SUPPLEMENT PROVIDES FOR: An additional supplier of the laminated pouch used to package Somatuline Depot (lanreotide) Injection.

17. COMMENTS: Ispen Pharma (Ipsen) NDA 22074 for Somatuline Depot (lanreotide) Injection (Somatuline Depot) 60, 90 and 120mg was approved August 30, 2007. Ispen 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) (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) (b) (4) However, the acceptance criteria of the laminated pouches have been slightly changed in order to (b) (4) (b) (4) This is due to the addition of the acceptable margin of error for (b) (4) (b) (4)

(Chemistry Reviewer-ONDQA Premarketing) 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.

19. REVIEWER NAME	SIGNATURE	DATE COMPLETED
Lorenzo A. Rocca	Signed Electronically	

20. BRANCH CHIEF NAME	SIGNATURE	DATE COMPLETED
Ramesh Raghavachari	Signed Electronically	

cc:
ONDQA/RRaghavachari
ONDQA/LRocca
ONDQA/PKumar

F/T by: LRocca, File: C:Data\LR\Supplement\n22074pm\S009(CBE30)\22074_S-009Review1.doc

Attachment 1
IQA for 22074/S009

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

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Attachment 3

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?_____ _____

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

/s/

Lorenzo A. Rocca -S

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Date: 2014.10.21 13:04:51 -04'00'

Ramesh Raghavachari -S

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APPLICATION NUMBER:

022074Orig1s009

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22074/S-09

CBE SUPPLEMENT – ACKNOWLEDGEMENT

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