DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203505/S-005

SUPPLEMENT APPROVAL

Shionogi Inc.
Attention: Kari Hanson
Director, Regulatory Affairs CMC
300 Campus Drive
Florham Park, NJ 07932

Dear Ms. Hanson:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 15, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for OSPHENA® (ospemifene) oral tablets, 60 mg.

We acknowledge receipt of your amendments dated January 14, and February 11, 2015.

This "Prior Approval" supplemental new drug application proposes the following agreed upon changes:

Prescribing Information (PI)

HIGHLIGHTS

- The registration symbol was added to OSPHENA, the trademark symbol was removed
- RECENT MAJOR CHANGES, Contraindications (4) was added
- "Hypersensitivity (for example, angioedema, urticaria, rash, pruritis) or any ingredients (4) was added as bullet 5 to CONTRAINDICATIONS
- "Known or suspected pregnancy" was moved to bullet 6 in CONTRAINDICATIONS

CONTENTS: Table of Contents

- Section 6 ADVERSE REACTIONS added 6.2 Postmarketing Experience
- Section 17 PATIENT COUNSELING INFORMATION was modified to include:
  17.1 Hypersensitivity Reactions
  17.2 Vaginal Bleeding
  17.3 Hot Flashes or Flushes

FULL PRESCRIBING INFORMATION

- Section 4 CONTRAINDICATIONS was updated to include as bullet 5, "Hypersensitivity (for example, angioedema, urticaria, rash, pruritis) to OPSHENA or any ingredients"
- "OSPHENA is contraindicated in women who are or may become pregnant" and the accompanying text was moved to bullet 6

- Section 6 ADVERSE REACTIONS, Subsection 6.2 Postmarketing Experience was added with the following information:
  "The following adverse reactions have been identified during post-approval use of OSPHENA. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure."
  "Immune System Disorders: allergic conditions including hypersensitivity, angioedema"
  "Skin and Subcutaneous Tissue Disorders: rash, rash erythematous, rash generalized, pruritis, urticaria"
- Section 17 PATIENT COUNSELING INFORMATION was modified and updated to include:
  17.1 Changed from **Venous Thromboembolic Events** to **Hypersensitivity Reactions** with the following information:
  Inform postmenopausal women who have had hypersensitivity reactions to OSPHENA, such as angioedema, urticaria, rash, pruritis, that they should not take OSPHENA *[see CONTRAINDICATIONS (4)]*.
  17.2 **Vaginal Bleeding** remained unchanged
  17.3 **Hypersensitivity Reactions** replaced with **Hot Flashes or Flushes** with the following information:
  OPSHENA may initiate or increase the occurrence of hot flashes in some women *[see Adverse Reactions (6.1)]*.

<u>Patient Prescribing Information (PPI)</u>

- The registration symbol was added to OSPHENA, the trademark symbol was removed
- "**What is OSPHENA?**" changed
  From:
  OSPHENA is an oral prescription medicine used to treat painful intercourse, a symptom of changes in and around your vagina, due to menopause.
  To:
  OSPHENA is an oral prescription medicine that contains ospemifene.
- "**What is OSPHENA used for**:" was added with the proposed text:
  OSPHENA is used after menopause for women with or without a uterus to:
  Treat moderate to severe pain during sexual intercourse due to changes in and around your vagina.
- "Who should not take OSPHENA?" was updated and the following information was added as bullet 5 :
  Are allergic to OSPHENA or any of its ingredients: See the list of ingredients in OSPHENA at the end of this leaflet
- "What can I do to lower my chances of a serious side effect with OSPHENA?" was updated with the following information:
  Tell your healthcare provider if you are going to have surgery or will be on bed rest.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. 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 (text for the package insert, text for the patient package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

PROMOTIONAL MATERIALS

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address below or by fax to 301-847-8444.

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

REPORTING REQUIREMENTS

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

If you have any questions, call Kim Shiley, R.N., B.S.N., Regulatory Project Manager, at (301) 796-2117.

Sincerely,

{See appended electronic signature page}

Audrey Gassman, M.D.
Deputy Director
Division of Bone, Reproductive, and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

AUDREY L GASSMAN
02/25/2015