DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203441/S-002

**SUPPLEMENT APPROVAL**

NPS Pharmaceuticals, Inc.
Attention: Diane C. Fiorenza, RAC
Senior Director, Regulatory Affairs
550 Hills Drive 3rd Floor
Bedminster, New Jersey 07921

Dear Ms. Fiorenza:

Please refer to your Supplemental New Drug Application (sNDA) dated and received August 28, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Gattex (teduglutide [rDNA origin]) for subcutaneous injection, 5 mg.

We acknowledge receipt of your amendments dated October 28, 2013, November 20, 2013, January 14, 2014, February 10, 2014, February 25, 2014, March 12, 2014, May 6, 2014, May 21, 2014, May 28, 2014, June 5, 2014, June 11, 2014, June 19, 2014, and June 25, 2014.

This Prior Approval supplemental new drug application provides for the following changes to the Package Insert:

- Section 5 WARNINGS AND PRECAUTIONS- Assorted minor editorial changes
- Section 6 ADVERSE REACTIONS- Revision to incorporate results from the complete study report
- Section 8 USE IN SPECIFIC POPULATIONS- Revision of 8.5 to reflect additional patient exposures
- Section 11 DESCRIPTION- Assorted minor editorial changes
- Section 13 NONCLINICAL TOXICOLOGY - Revision to incorporate final results of 2-year mouse carcinogenicity study
- Section 14 CLINICAL STUDIES- Revisions to incorporate results from the complete study report
- Section 17 PATIENT COUNSELING INFORMATION- Minor editorial change

This supplemental new drug application also provides for proposed modifications to the approved risk evaluation and mitigation strategy (REMS).

## 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, Medication Guide, text for the Instructions for Use), 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).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

## 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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

## RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Gattex was originally approved on December 21, 2012. The REMS consists of a

communication plan, elements to assure safe use, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of:

- revisions to the Dear Healthcare Professional and Dear Professional Society Letters to reflect the updated title of the patient and caregiver counseling guide,
- revisions to the Prescriber Education Slide Deck to reflect information from the completion of three major Gattex clinical trials, and
- revisions to the Patient and Caregiver Counseling Guide to focus on the Gattex REMS key safety messages, and to provide for improved readability, including renaming the *Patient and Caregiver Counseling Guide* to *What You Need to Know About Gattex Treatment: A Patient and Caregiver Counseling Guide*.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Your proposed modified REMS, submitted on June 19, 2014, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on December 21, 2012.

There are no changes to the REMS assessment plan described in our December 21, 2012 letter.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

> **NDA 203441 REMS CORRESPONDENCE**
> **(insert concise description of content in bold capital letters, e.g.,**
> **UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**NDA 2034412 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 2034412**
**PROPOSED REMS MODIFICATION**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)**
**FOR NDA 2034412**
**REMS ASSESSMENT**
**PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

## PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

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

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

## REPORTING REQUIREMENTS

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

We request that you submit all cases of fluid overload and increased absorption of oral concomitant drugs with a serious outcome as 15-day "Alert Reports" to the FDA.

If you have any questions, call Jennifer Sarchet, Regulatory Project Manager, at 240-402-4275.

Sincerely,

*{See appended electronic signature page}*

Joyce A. Korvick, MD., MPH
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
REMS

---

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

---

/s/

---

JOYCE A KORVICK
06/26/2014