NDA 021137/S-002
NDA 021137/S-003
NDA 021137/S-004

SUPPLEMENT APPROVAL

Genus Lifesciences Inc.
Attention: William Reightler
Vice President of Regulatory Affairs
514 N. 12th Street
Allentown, PA 18102

Dear Mr. Reightler:

Please refer to your supplemental new drug applications (sNDAs) dated February 18, 2021, received February 19, 2021, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Levolet (levothyroxine sodium) tablets.

These Prior Approval sNDAs propose to demonstrate bioequivalence (BE) between Levolet (levothyroxine sodium) tablets and the following currently approved products (b) (4) (b) (4)

S-002: Unithroid (levothyroxine sodium) tablets (Jerome Stevens Pharmaceuticals, Inc.). This supplement also provides a change in the finished drug product formulation, a new manufacturing process, and a manufacturing site change and updated labeling in response to FDA's Prior Approval Supplement Request letter dated December 3, 2020.

S-003: levothyroxine sodium tablets (Mylan Pharmaceuticals, Inc.)

S-004: Levoxyl (levothyroxine sodium) tablets (King Pharmaceuticals Research and Development, LLC.)

We have determined your Levolet (levothyroxine sodium) tablets to be bioequivalent and therapeutically equivalent to Unithroid (levothyroxine sodium) tablets (Jerome Stevens Pharmaceuticals, Inc.), levothyroxine sodium tablets (Mylan Pharmaceuticals, Inc.), and Levoxyl (levothyroxine sodium) tablets (King Pharmaceuticals Research and Development, LLC.).

Our review concludes that the data establish bioequivalence between these products, and these supplements as amended are approved. [redacted]

S-002 APPROVAL & LABELING

S-002 provides for a reformulation of the finished drug product such that [redacted] has been removed and replaced with other approved excipients in order to [redacted], to meet the revised assay requirements in the United States Pharmacopeia (USP) monograph for levothyroxine tablets, and to remove precautions regarding [redacted] from product labeling that were required for the previous formulation due to the presence of [redacted].

In addition, S-002 provides for the conversion of the prescribing information (PI) according to the Physician's Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) format.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information), 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.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include 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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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).

CARTON AND CONTAINER LABELING

Submit final printed container labeling that are identical to the container labeling submitted on December 10, 2021, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Container Labeling for approved NDA 021137/S-002**." Approval of this submission by FDA is not required before the labeling is used.

OTHER

1) (b) (4)
Based on the stability data in the submission, a shelf-life of 18 months is recommended for all strengths of drug product, and you may request for an extension of shelf-life with additional supportive stability data as they become available.

2) You should initiate a revision to the official monograph for Levothyroxine Sodium Tablets under the USP Pending Monograph Process, to ensure the reformulated Levolet (levothyroxine sodium) tablets, is in alignment with the dissolution specification (method and acceptance criterion) in the USP monograph.

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, 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 FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

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

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, call Linda Galgay, Senior Regulatory Project Manager, at (301) 796-5383.

Sincerely,

{See appended electronic signature page}

Theresa E. Kehoe, M.D.
Director
Division of General Endocrinology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
- Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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