



NDA 20280/S-079

SUPPLEMENT APPROVAL

Pfizer Inc.
Agent for Pharmacia and Upjohn Company
Attention: Nestor Duci, MBA
Manager, Worldwide Regulatory Strategy
445 Eastern Point Road
Groton, CT 06340

Dear Mr. Duci:

Please refer to your Supplemental New Drug Application (sNDA) dated and received October 10, 2014, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Genotropin (somatropin for injection).

This Prior Approval sNDA updates the label and provides for the following revisions to the package insert (PI).

HIGHLIGHTS OF PRESCRIBING INFORMATION

- updates for consistency with revisions to the FULL PRESCRIBING INFORMATION

5 WARNINGS AND PRECAUTIONS

- moves the following statement from 4 CONTRAINDICATIONS, Acute Critical Illness subsection to 5 WARNINGS AND PRECAUTIONS, Acute Critical Illness subsection

“Two placebo-controlled clinical trials in non-growth hormone deficient adult patients (n=522) with these conditions in intensive care units revealed a significant increase in mortality (41.9% vs. 19.3%) among somatropin-treated patients (doses 5.3–8 mg/day) compared to those receiving placebo,”

- revises

5.7 Hypopituitarism

Patients with hypopituitarism (multiple pituitary hormone deficiencies) should have their other hormonal replacement treatments closely monitored during somatropin treatment.

to

5.7 Hypoadrenalism

Patients receiving somatropin therapy who have or are at risk for pituitary hormone deficiency(s) may be at risk for reduced serum cortisol levels and/or unmasking of central (secondary) hypoadrenalism. In addition, patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses following initiation of somatropin treatment [*see Section 7.1, 11- β Hydroxysteroid Dehydrogenase Type 1*].

6 ADVERSE REACTIONS

- updates the list of serious adverse reactions
- revises **6.2 Post-Marketing Experience** section, adding,

The following serious adverse reactions have been observed with use of somatropin (including events observed in patients who received brands of somatropin other than Genotropin): acute critical illness [*see Warnings and Precautions (5.1)*], sudden death [*see Warnings and Precautions (5.2)*], intracranial tumors [*see Warnings and Precautions (5.3)*], central hypothyroidism [*see Warnings and Precautions (5.8)*], cardiovascular disorders, and pancreatitis [*see Warnings and Precautions (5.14)*].

Slipped capital femoral epiphysis and Legg-Calve-Perthes disease (osteonecrosis/avascular necrosis; occasionally associated with slipped capital femoral epiphysis) have been reported in children treated with growth hormone [*see Warnings and Precautions (5.9)*]. Cases have been reported with Genotropin.

In addition, “rDNA origin” is removed from the product title in the PI and the Instructions for Use (IFU).

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 and with the minor editorial revisions listed below and reflected in the enclosed labeling.

- In HIGHLIGHTS, WARNINGS AND PRECAUTIONS subsection, the period was removed following, “Hypoadrenalism: Monitor patients for reduced serum cortisol levels and/or need for glucocorticoid dose increases in those with known hypoadrenalism
- In 6.0 ADVERSE REACTIONS italicization was removed from, Hypoadrenalism
- Revision date and Recent Major Changes dates were changed to “9/2016” to reflect the date of approval for this supplement.

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 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 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 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 supplemental application, you are exempt from this requirement.

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 Linda Galgay, Regulatory Project Manager, at (301) 796-5383.

Sincerely,

{See appended electronic signature page}

Jennifer Rodriguez Pippins, MD, MPH
Deputy Director for Safety
Division of Metabolism & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:

Content of Labeling

Package Insert

Instructions For Use for the Miniquick, Pen 12, Pen 5, and Mixer

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

/s/

JENNIFER R PIPPINS
09/06/2016