



NDA 20604/S-048

SUPPLEMENT APPROVAL

EMD Serono
Attention: Robert Kirsch
Director Global Regulatory, Fertility and Endocrinology
One Technology Place
Rockland, MA 02370

Dear Mr. Kirsch:

Please refer to your supplemental new drug application dated May 15, 2009, received May 15, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Serostim/Zorbtive (somatropin [rDNA origin] for injection).

This "Changes Being Effected" supplemental new drug application provides for revision to the PRECAUTIONS section of the Zorbtive package insert to include information that somatropin inhibits 11 β -hydroxysteroid dehydrogenase type 1 in adipose/hepatic tissue that may impact the metabolism of cortisol and cortisone.

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed upon labeling text, which is identical to the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format submitted on May 15, 2009.

CONTENT OF LABELING

To facilitate the transmission of labeling to the National Library of Medicine for public dissemination, please resubmit the enclosed content of labeling in SPL format as soon as possible, but no later than 14 days from the date of this letter. For administrative purposes, please designate this submission, "**SPL for approved NDA20604/S-048.**"

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

REPORTING REQUIREMENTS

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

At the next printing of the package insert, we request that you replace the revised paragraph with the following:

The microsomal enzyme 11 β -hydroxysteroid dehydrogenase type 1 (11 β HSD-1) is required for conversion of cortisone to its active metabolite, cortisol, in hepatic and adipose tissue. GH and somatropin inhibit 11 β HSD-1. Consequently, individuals with untreated GH deficiency have relative increases in 11 β HSD-1 and serum cortisol. Introduction of somatropin treatment may result in inhibition of 11 β HSD-1 and reduced serum cortisol concentrations. As a consequence, previously undiagnosed central (secondary) hypoadrenalism may be unmasked and glucocorticoid replacement may be required in patients treated with somatropin. 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; this may be especially true for patients treated with cortisone acetate and prednisone since conversion of these drugs to their biologically active metabolites is dependent on the activity of 11 β HSD-1.

In addition, replace the following paragraph immediately below with the **bolded** text that follows:

The use of somatropin has been associated with cases of new onset impaired glucose intolerance, new onset type 2 diabetes mellitus and exacerbation of preexisting diabetes mellitus have been reported in patients receiving somatropin. Some patients developed diabetic ketoacidosis and diabetic coma. In some patients, these conditions improved when somatropin was discontinued, while in others the glucose intolerance persisted. Some patients necessitated initiation or adjustment of antidiabetic treatment while on somatropin. Patients with other risk factors for glucose intolerance should be monitored closely during Zorbtive[™] therapy.

The use of somatropin has been associated with cases of new onset impaired glucose intolerance and type 2 diabetes mellitus, In some patients, these conditions improved when somatropin was discontinued, while in others the glucose intolerance persisted. Some of these patients required the initiation of antidiabetic treatment. Patients with other risk factors for glucose intolerance should be monitored closely during Zorbtive[™] therapy. The use of somatropin has also been associated with exacerbation of preexisting diabetes mellitus usually requiring adjustment of antidiabetic treatment. In both instances, some patients developed diabetic ketoacidosis and diabetic coma.

These revisions can be reported to the Agency in the annual report.

If you have any questions, call Kati Johnson, Regulatory Project Manager, at (301) 796-1234.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.

Director

Division of Metabolism and Endocrinology Products

Office of Drug Evaluation II

Center for Drug Evaluation and Research

Enclosure: Package Insert

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

/s/

MARY H PARKS
08/31/2009