DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 17-386/S-036
NDA 19-532/S-016

Celltech Pharmaceuticals, Inc.
Attention: Ms. Michele Bartlett
755 Jefferson Road
P.O. Box 31710
Rochester, NY 14603-1710

Dear Ms. Bartlett:

Please refer to your supplemental new drug applications dated July 22, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zaroxolyn (metolazone) 2 ½, 5 and 10 mg Tablets (NDA 17-386) and Mykrox (metolazone) ½ mg Tablets (NDA 19-532).

These "Special Supplement - Changes Being Effected" supplemental new drug applications provide for final printed labeling revised to strengthen WARNINGS and add ADVERSE REACTION information as follows:

NDA 17-386/S-036 (Zaroxolyn)

1. Under the WARNINGS/ Cross-Allergy subsection, the text was changed from:

   "Cross-allergy, while not reported to date, theoretically may occur when Zaroxolyn is given to patients known to be allergic to sulfonamide-derived drugs, thiazides, or quinethazone."

   To:

   "Cross-allergy may occur when Zaroxolyn is given to patients known to be allergic to sulfonamide-derived drugs, thiazides, or quinethazone."

2. Under the ADVERSE REACTIONS/ Dermatologic/Hypersensitivity subsection, "skin necrosis, petechiae and pruritus" were added to read:

   "Dermatologic/Hypersensitivity: Toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome, necrolizing angiitis (cutaneous vasculitis), skin necrosis, purpura, petechiae, dermatitis (photosensitivity), urticaria, pruritus, skin rashes."

3. Under the ADVERSE REACTIONS/ Gastrointestinal subsection, "abdominal pain" was added at the end of the list of diagnoses.

NDA 19-532/S-016 (Mykrox)

1. Under the WARNINGS/ Cross-Allergy subsection, the text was changed from:

   "Cross-allergy, while not reported to date, theoretically may occur when Mykrox Tablets are given to patients known to be allergic to sulfonamide-derived drugs, thiazides, or quinethazone."

   To:

   "Cross-allergy may occur when Mykrox Tablets are given to patients known to be allergic to sulfonamide-derived drugs, thiazides, or quinethazone."

2. Under the ADVERSE REACTIONS/ Dermatologic/Hypersensitivity subsection, "skin necrosis, petechiae, pruritus and skin rashes" were added to read:

   "Dermatologic/Hypersensitivity: Toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome, necrolizing angiitis (cutaneous vasculitis), skin necrosis, purpura, petechiae, dermatitis, photosensitivity, urticaria, pruritus, skin rashes."

3. Under the ADVERSE REACTIONS/ Gastrointestinal subsection, "nausea, diarrhea and abdominal pain" were added at the end of the list of diagnoses.

In addition, we note the following minor editorial changes:

1. The revision dates and the manufacturing codes were updated.

2. The text "All rights reserved" was added at the end of the package inserts.

We completed our review of these supplemental new drug applications, as amended, and they are approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on July 22, 2003.

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

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Mr. Daryl Allis
Regulatory Health Project Manager
(301) 594-5309

Sincerely,

{See appended electronic signature page}

Douglas C. Throckmorton, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Doug Throckmorton
8/19/03 12:50:58 PM