DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 20-083/S-046
NDA 20-657/S-024

SUPPLEMENT APPROVAL

Ortho-McNeil-Janssen Pharmaceuticals
c/o Johnson & Johnson Pharmaceutical Research
Attention: Ms. Melissa Gannon
Director, Global Regulatory Affairs
920 Route 202 South
P O Box 300
Raritan, New Jersey 08869-0602

Dear Ms. Gannon:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sporanox® (itraconazole) Capsules (NDA 20-083) and Sporanox® (itraconazole) Oral Solution (NDA 20-657) as follows:

NDA Number	Supplement Number	Date of Submissions	Date Received
20-083	**046**	**January 26, 2010**	**January 26, 2010**
20-657	**024**		

We acknowledge receipt of your amendments dated July 7, 2010, received July 8, 2010.

For NDA 20-083, this "Changes Being Effected" sNDA provides for revisions to the **ADVERSE REACTIONS/Postmarketing Experience sub**section of the package insert and to the **WHAT ARE THE POSSIBLE SIDE EFFECTS OF SPORANOX** and the **GENERAL ADVICE ABOUT SPORANOX** subsections of the Patient Information section. For NDA 20-657 this "Changes Being Effected" sNDA provides for revisions to the **ADVERSE REACTIONS/Postmarketing Experience sub**section of the package insert.

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text submitted to each NDA January 26, 2010.

The revisions to the package inserts are as follow (additions are noted with underline and deletions with ~~strikethrough~~):

For **NDA 20-083/S-046** and **NDA 20-657/S-024:**

1. In the **ADVERSE REACTIONS/Post-marketing experience sub**section, the words "pancreatitis and pyrexia" are added to the table titled "Postmarketing Reports of Adverse Drug Reactions" as follows:

Postmarketing Reports of Adverse Drug Reactions

Blood and lymphatic system disorders:	Leukopenia, neutropenia, thrombocytopenia
Immune system disorders:	Anaphylaxis; anaphylactic, anaphylactoid and allergic reactions; serum sickness; angioneurotic edema
Metabolism and nutrition disorders:	Hypertriglyceridemia, hypokalemia
Nervous system disorders:	Peripheral neuropathy, paresthesia, hypoesthesia, headache, dizziness
Eye disorders:	Visual disturbances, including vision blurred and diplopia
Ear and labyrinth disorder:	Transient or permanent hearing loss, tinnitus
Cardiac disorders:	Congestive heart failure
Respiratory, thoracic and mediastinal disorders:	Pulmonary edema
Gastrointestinal disorders:	Pancreatitis, abdominal pain, vomiting, dyspepsia, nausea, diarrhea, constipation, dysgeusia
Hepato-biliary disorders:	Serious hepatotoxicity (including some cases of fatal acute liver failure), hepatitis, reversible increases in hepatic enzymes
Skin and subcutaneous tissue disorders:	Toxic epidermal necrolysis, Stevens-Johnson syndrome, exfoliative dermatitis, leukocytoclastic vasculitis, erythema multiforme, alopecia, photosensitivity, rash, urticaria, pruritus
Musculoskeletal and connective tissue disorders:	Myalgia, arthralgia
Renal and urinary disorders:	Urinary incontinence, pollakiuria
Reproductive system and breast disorders:	Menstrual disorders, erectile dysfunction
General disorders and administration site conditions:	Peripheral edema, pyrexia

For **NDA 20-657/S-024, the following** revisions are made to the **PATIENT PACKAGE INSERT (PPI):**

2. The **WHAT ARE THE POSSIBLE SIDE EFFECTS OF SPORANOX** section, under the subsection "**Call your doctor right away,"** is revised as follows:

   Call your doctor right away if you develop tingling or numbness in your extremities (hands or feet), if your vision gets blurry or you see double, if you hear a ringing in your ears, if you lose the ability to control your urine or urinate much more than usual.

   Additional possible side effects include upset stomach, vomiting, abdominal pain, constipation, headache, fever, inflammation of the pancreas, menstrual disorders, erectile dysfunction, dizziness, muscle weakness or pain, painful joints, unpleasant taste, or hair loss. These are not all the side effects of SPORANOX. Your doctor or pharmacist can give you a more complete list.

3. In the **GENERAL ADVICE ABOUT SPORANOX** section, the second and third paragraphs are revised as follow:

   Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use SPORANOX® for a condition for which it was not prescribed. Do not give SPORANOX® to other people, even if they have the same symptoms you have. It may harm them.

   This leaflet summarizes the most information about SPORANOX. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about SPORANOX that is written for health professionals or you can call 1-800-586-7736.

   ~~You can also call 1-800-JANSSEN or visit the SPORANOX® Internet site at **ww.sporanox.com** and the Janssen Internet site at **www.us.janssen.com**.~~

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, text for the patient package insert), and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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 for these NDAs, including pending "Changes Being Effected" (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 these supplemental applications.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about these drug products (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to these NDAs, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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 June Germain, Regulatory Health Project Manager, at (301) 796-4024.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, MD, MPH
Deputy Director for Safety
Office of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling for NDA 20-083 and NDA 20-657

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20657	SUPPL-24	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	SPORANOX
NDA-20083	SUPPL-46	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	SPORANOX

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/s/

OZLEM A BELEN
07/29/2010