



NDA 20-868/S-005

Pharmacia
Attn: Michael Ivey
Senior Regulatory Manager
Mail Stop: 0638-298-101
7000 Portage Road
Kalamazoo, MI 49001

Dear Mr. Ivey:

Please refer to your supplemental new drug application, dated August 25, 1999, received August 26, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Flagyl ® ER (metronidazole) extended release capsules.

This supplemental new drug application provides for revision of the **Geriatric Use** subsection in the **PRECAUTIONS** section of the package insert in accordance with the August 27, 1997 final rule and 21 CFR 201.57(f)(10). Added text is double underlined and deleted text is in ~~strikethrough~~.

1. The **Geriatric Use** subsection at the end of the **PRECAUTIONS** section of the package insert, was revised as follows:

Geriatric Use: ~~Decreased renal function does not alter the single dose pharmacokinetics of metronidazole. However, plasma clearance of metronidazole is decreased in patients with decreased liver function. Therefore, in elderly patients, monitoring of serum levels may be necessary to adjust the metronidazole dosage accordingly.~~

Geriatric Use: No overall differences have been reported in safety and effectiveness between younger and older individuals, but greater sensitivity of some older individuals cannot be ruled out. Systemic exposure to the active metabolite, 2-hydroxymethyl metronidazole, is higher in the elderly.

Metronidazole is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Although decreased renal function does not alter the single dose pharmacokinetics of metronidazole, because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Plasma clearance of metronidazole is decreased in patients with decreased liver function. Therefore, in elderly patients, monitoring of serum levels may be necessary to adjust the metronidazole dose accordingly.

2. Under the How Supplied section, the following sentence was deleted:

~~Federal law prohibits dispensing without prescription.~~

3. Rx only was added to the last page of the label.

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

The final printed labeling (FPL) must be identical to the enclosed labeling (package insert submitted August 25, 1999).

Please submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavyweight paper or similar material. For administrative purposes, these submissions should be designated “FPL for approved supplement NDA 20-868/S-005.” Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (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, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 Christine Lincoln, RN, MS, MBA, Labeling Reviewer, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and
Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
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/s/

Renata Albrecht
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