DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-607/S-008

Pfizer Inc.
Attention: Corinne Gamper
Director/Team Leader, Worldwide Regulatory Affairs
235 East 42nd Street
New York, NY 10017

Dear Ms. Gamper:

Please refer to your supplemental new drug application dated March 21, 2003, received March 24, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Arthrotec® (diclofenac sodium/misoprostol) Tablets.

We acknowledge receipt of your submission dated January 7, 2005.

Your January 5, 2005 submission constituted a complete response to our September 24, 2003 action letter.

This supplemental new drug application provides for revising the Arthrotec labeling to be consistent with the Cytotec (misoprostol) labeling.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter. However, with the next revision of this drug label (as requested in the June 14, 2005 Supplement Request letter), please note the following:

a. Insert the following text after the third sentence of the first paragraph in the Non-teratogenic effects sub-subsection of the Pregnancy subsection of the PRECAUTIONS section:

"Misoprostol has been used to ripen the cervix, to induce labor, and to treat postpartum hemorrhage, outside of its approved indication. A major adverse effect of these uses is hyperstimulation of the uterus. Uterine rupture, amniotic fluid embolism, severe genital bleeding, shock, fetal bradycardia, and fetal and material death have been reported. Higher doses of misoprostol, including the 100 mcg tablet, may increase the risk of complications from uterine hyperstimulation. Arthrotec, which contains 200 mcg of misoprostol, is likely to have a greater risk of uterine hyperstimulation than the 100 mcg tablet of misoprostol."

b. Delete the second paragraph from the Non-teratogenic effects sub-subsection of the Pregnancy subsection of the PRECAUTIONS section and make the above revision.

c. To be more concise and be consistent with the Nursing Mothers subsection:

- Revise the only sentence in the fifth paragraph of the Patient Information section as follows:

  "~~Because ARTHROTEC may cause serious effects in nursing infants, this medication should not be used by nursing mothers.~~ ARTHROTEC is not recommended for nursing mothers."

- Revise the only sentence in the fifth paragraph of the Bottle Label Leaflet as follows:

  "~~Because ARTHROTEC may cause serious effects in nursing infants, this medication should not be used by nursing mothers.~~ ARTHROTEC is not recommended for nursing mothers."

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, HFD-410
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 Monika Houstoun, Pharm.D., Regulatory Project Manager, at (301) 827-9333.

Sincerely,

{See appended electronic signature page}

Brian E. Harvey, M.D., Ph.D.
Director
Division of Gastrointestinal & Coagulation Drug Products
Office of Drug Evaluation III
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/

Brian Harvey
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