



NDA 20607/S-028

SUPPLEMENT APPROVAL

G.D. Searle LLC
Attention: Karen Baker
Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Baker:

Please refer to your Supplemental New Drug Application (sNDA) dated and received September 23, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Arthrotec (diclofenac sodium/misoprostol) Oral Tablets.

We acknowledge receipt of your amendment dated October 24, 2013.

This "Changes Being Effected" supplemental new drug application provides for the following changes to the package insert:

Contraindications

- add contraindication for patients with active gastrointestinal bleeding

Warnings

- add that the use of diclofenac/misoprostol with concomitant NSAIDs including COX-2 inhibitors should be avoided.
- expand Skin Reactions subsection

Precautions

- remove statement that nursing mothers should not take Arthrotec

Drug Interactions

- revise statement about renal function in Ace Inhibitors subsection
- add Tacrolimus subsection
- add data to Nursing Mothers subsection

Adverse Reactions

- add the following subsections:
 - Pregnancy, puerperium and perinatal conditions
 - Congenital, familial and genetic disorders
- expand upon the following subsections:
 - Body as Whole
 - Female Reproductive Disorders
 - Hemec and lymphatic system subsection
 - Metabolic and nutritional subsection

- Skin and appendages subsection
- Urinary subsection

Patient Information

- Clarify that caution should be exercised in nursing mothers
- Add that broken tablets should not be taken

APPROVAL & LABELING

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling, with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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 that includes labeling changes for this NDA, including 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 this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Heather Buck, Regulatory Project Manager, at (301) 796-1413.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURES: Content of Labeling

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

/s/

JOYCE A KORVICK
09/03/2014