



Banner Pharmacaps Inc.
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February 18, 2004

Mr. Gary Buehler, Director
FDA, OGD, HFD-600
Metro Park North II
7500 Standish Place
Rockville, MD 20855

Re: Docket No. 02P-0473/CP1 Naproxen Sodium Capsules, 220 mg

Dear Mr. Buehler:

Pursuant to your letter dated 2/3/04, and in accordance with the provisions of section 2 of the "Pediatric Research Equity Act of 2003" (PREA), we are hereby submitting an amendment to our ANDA suitability petition, referenced above, to provide the following request for waiver of pediatric studies.

As provided for in PREA Sec. 505B (a)(4)(A)(iii), we hereby request a full waiver of the pediatric study requirement for Naproxen Sodium softgel capsules. This waiver is requested on the basis that the product:

- (I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and
- (II) is not likely to be used in a substantial number of pediatric patients.



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The proposed Naproxen Sodium capsules, 220 mg, as compared with numerous marketed products which are adequately labeled for uses in the pediatric population, does not represent a significant improvement in the treatment, diagnosis, or prevention of a disease. Naproxen sodium 220 mg is an over-the-counter drug, approved for marketing by the FDA for various companies including Roche (Aleve®, NDA 20-204) and Perrigo (ANDA 74-661). The "Guidance for Industry: Labeling OTC Human Drug Products Updating Labeling in RLDs & ANDAs" (**Attachment 1**) from October 2002 establishes the following indications:

Temporarily relieves minor aches and pains due to headache, muscular aches, backache, toothache, common cold, menstrual cramps and minor pain due to arthritis. Temporarily reduces fever.

Naproxen sodium 220 mg is approved for use in children 12 years old and older for the above indications.

Also readily available in the OTC marketplace are various forms of acetaminophen, aspirin and ibuprofen.

Acetaminophen is available in concentrated drops, liquids, chewable tablets, suppositories, and oral tablets. These dosage forms are labeled for the following indications:

Temporarily reduces fever. Temporarily relieves minor aches and pains due to the common cold, flu, headache, sore throat, immunizations, and toothaches, muscle aches, sprains, and overexertion.

Acetaminophen is labeled for use in children 2 years old and older, or based on weights greater than 24 pounds. Examples of this labeling, obtained from currently marketed Acetaminophen products, are provided in **Attachment 2**.



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Aspirin is available in chewable tablets and suppositories for children. It is labeled for the following indications:

Temporarily reduces fever associated with colds, sore throat, and teething. Temporarily relieves minor aches, pains and headaches.

Aspirin is labeled for use in children 3 years old and older or based on weights greater than 32 pounds. An example of this labeling, obtained from a currently marketed Aspirin product, is provided in **Attachment 3**.

Ibuprofen is available in concentrated oral suspensions, oral suspensions and chewable tablets. These dosage forms are labeled for the following indications:

Temporarily reduces fever. Temporarily relieves minor aches and pains due to the common cold, flu, sore throat, headaches and toothaches.

Ibuprofen is labeled for use in children 6 months old and older or based on weights greater than 12 pounds when 6 months old or older. An example of this labeling, obtained from a currently marketed Ibuprofen product, is provided in **Attachment 4**.

These readily available drug therapies (acetaminophen, aspirin and ibuprofen) available to the pediatric population offer adequate therapeutic benefits for the same indications as naproxen sodium 220 mg. However, naproxen sodium 220 mg is also indicated for temporary relief of menstrual cramps and minor pain due to arthritis, which are not labeled uses of the other three therapies.



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The average onset of menses in women is 12 years old. This information is obtained from the website of the National Women's Health Information Center (www.4woman.gov), sponsored by the US Department of Health and Human Services, Office of Women's Health. Naproxen sodium 220 mg is labeled for those 12 years old and older, therefore would be available for those young women experiencing menstrual cramps at the average age of onset of menses. For those younger than 12 years old, we propose that this is not a substantial number of pediatric patients. For those less than 12 years old, seeking a physician's opinion per the labeling of naproxen sodium 220 mg for relief of menstrual cramps is appropriate care. We propose that naproxen sodium 220 mg offers no meaningful therapeutic benefit for treatment over existing therapies a physician may recommend.

Naproxen sodium 220 mg also has the indication for temporary relief of minor pain due to arthritis. We propose that treatment of arthritis symptoms with an over-the-counter therapy in those less than 12 years old is not likely to be used in a substantial number of pediatric patients. Given the severity of the disease in the juvenile population, physician care and prescription drugs are standard therapies, therefore naproxen sodium 220 mg offers no meaningful therapeutic benefit. Additionally, in the draft guidance, "Guidance for Industry: Recommendations for complying with the Pediatric Rule (21 CFR 314.55(a) and 601.27(a))" published November 2000, osteoarthritis is suggested as a disease specific waiver candidate.

In light of the enclosed information supporting a waiver of the pediatric study requirement, we respectfully request that approval of this petition be reinstated.



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If you have any questions regarding this submission, please feel free to contact me at (336) 812-8700, extension 3312.

Sincerely,

Donna Lee Finch, R.Ph.
Director, Regulatory Affairs &
Project Management

Attachments