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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Citizen Petition

The undersigned submits this petition in quadruplicate, under Section 505 (j)(2)(c) of the Federal Food, Drug and Cosmetic Act and in accordance with the procedural requirements set forth in 21 C.F.R. 10.30, on behalf of a client, to request the Commissioner of the Food and Drug Administration to make a determination that the discontinued Reference Listed Drug, Orudis KT (ketoprofen, 12.5 mg) oral tablet, the subject of NDA 020-429, held by Wyeth Consumer Healthcare, was not withdrawn for safety or effectiveness reasons.

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration determine whether Orudis KT has been voluntarily withdrawn from sale for reasons other than safety or effectiveness.

B. Statement of Grounds

The Food and Drug Administration maintains a list of approved drugs products that are eligible for submission as abbreviated new drug applications (ANDAs). The list, referred to as the Orange Book, contains all FDA-approved drug products. Orudis KT (ketoprofen, 12.5 mg) oral tablet was approved by the FDA on October 6th 1995, and is considered to be a "listed drug product". The current listing of the product in the electronic Orange Book, accessed June 26, 2006, does not list Orudis KT (ketoprofen, 12.5 mg) in the active section of the Orange Book (Attachment A). Rather, the product appears in the "Discontinued" section of the Orange Book. Orudis KT is listed in the FDA monthly new additions and new deletions to the Prescription and Over-the-Counter Drug Product List, 25th Edition: February 2006 (Attachment B). It is indicated that the drug was either discontinued from marketing or that the approval was withdrawn for other than safety or efficacy reasons. After an extensive search of the literature and other public data sources, no direct information regarding the reason for withdrawal was discovered. It is believed that the maker discontinued marketing of the drug for economic reasons.

According to section 1.11 of the Preface to the Orange Book, a drug product is listed in the Discontinued Section when a determination has already been made that withdrawal

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was not for safety and effectiveness reasons, and is accompanied by the following statement after its product strength: "Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons." There is no such annotation next to the product strength for Orudis KT (Attachment A).

The ketoprofen dose of 12.5 mg has been recognized by the FDA as safe and effective, as established in approval of NDA 20-429, Wyeth Consumer Healthcare NDA for OTC ketoprofen. The FDA re-examined safety issues at the September 2002 meeting on the Nonprescription Drug Advisory Committee and determined that ketoprofen (12.5 mg) and ibuprofen (200 mg) were considered the same for assessing risks and label changes. A supplemental New Drug Application (NDA 20-429/S-008) was submitted under section 505(b) of the Federal, Food, Drug and Cosmetic Act for Orudis KT (12.5 mg ketoprofen) tablets on May 28, 2004 by Wyeth Consumer Healthcare. (Attachment C). This supplemental new drug application provided for the addition of new organ-specific warnings to the Drug Facts label. This letter mentions the concern by the division director of the OTC Drug Products about the need for organ-specific warnings for OTC drug products containing analgesic/antipyretic active ingredients. The director stated that the proposed stomach bleeding warning was acceptable as interim language but further guidance on wording and placement of organ-specific warnings in the labeling of drug products containing NSAIDs would be provided in the future. The FDA released a Public Health Advisory for COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDS) on April 7th, 2005, in which it requests that non-prescription NSAIDS, including Orudis KT, revise their labeling to include more specific information on potential gastrointestinal (GI) and cardiovascular risks, and information for safe use of the drug (Attachment D).

Studies documented in the Journal of Clinical Pharmacology (Attachment E), the European Journal of Clinical Pharmacology (Attachment F), and Drugs Under Experimental and Clinical Research (Attachment G), indicate that ketoprofen (12.5 mg) is an effective method of pain control compared to ibuprofen 200 mg. A study in the Aliment Pharmacology Therapy (Attachment H), indicated that ketoprofen 12.5 mg three times daily resembled the effects of ibuprofen 400 mg three times daily on the stomach and duodenum, respectively. The articles do not suggest issues relating to the product's safety or effectiveness for its approved indication.

FDA's MedWatch web site captures safety-related labeling changes, drug and biologic safety alerts, Class I recalls, market withdrawals, and public health advisories from 1995 to present. The Adverse Events Reporting System (AERS) collects information about adverse events, medication errors, and product problems that occur after the administration of an approved product. Only three case reports associated with Orudis KT were found for the period reported (January 1998- December 2001 (Attachment I)). These case reports entailed episodes of GI bleeding.

It is requested that, if it is determined that Orudis KT was not withdrawn for safety or efficacy reasons, that the agency annotate the listing for Orudis KT in the Orange Book to indicate that it was not withdrawn for safety or efficacy reasons. If it is determined that Orudis KT was withdrawn from sale for safety or efficacy reasons, it is requested that the

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agency publish a notice of the determination in the Federal Register and delineate the specific safety and efficacy concerns.

C. Environmental Impact

A claim for categorical exclusion of the requirement of submission of an environmental assessment is made pursuant to 21 C.F.R. 25.31

D. Economic Impact

Pursuant to 21 CFR 10.30(b) economic impact information is to be submitted only when requested by the Commissioner. This information will promptly be submitted if requested.

E. Certification

The undersigned certifies that, to the best of their knowledge and belief, this petition includes all information and views on which the petitioner relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully Submitted,

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