

May 17, 2001

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Food and Drug Administration
Department of Health and Human Services
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CITIZEN PETITION

Mallinckrodt Inc. submits this petition pursuant to 21 C.F.R. §§ 10.20 and 10.30, under Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and 21 C.F.R. § 314.93 to request the Commissioner of Food and Drugs make a determination that an Abbreviated New Drug Application may be submitted for Hydrocodone Bitartrate and Acetaminophen Oral Solution (10 mg/500 mg per 15 mL).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration make a determination that Hydrocodone Bitartrate and Acetaminophen Oral Solution, 10 mg/500 mg per 15 mL, is suitable for submission as an Abbreviated New Drug Application. The listed drug product upon which this petition is based is Lortab[®] (Hydrocodone Bitartrate and Acetaminophen Tablets, USP) 10 mg/500 mg (manufactured by UCB). Mallinckrodt seeks a change in dosage form from that of the listed drug product to permit an oral solution.

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a new drug that differs in dosage form from a listed drug provided the FDA has approved a petition that proposed the filing of such an application. This petition involves a change in the dosage form for the proposed drug from that of the listed drug. The listed drug on which this petition is based is ANDA 40-100 Lortab[®] (Hydrocodone Bitartrate and Acetaminophen Tablets, USP) 10 mg/500 mg manufactured by UCB. A copy of the relevant pages of the 21st edition of Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) is attached for your review (Attachment 1).

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This drug is indicated for the relief of moderate to moderately severe pain. The most common side effects of hydrocodone bitartrate and acetaminophen oral solution are abdominal pain, dizziness, drowsiness, light-headedness, nausea, shortness of breath, unusual tiredness, and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients and some of these adverse reactions may be alleviated if the patient lies down.

An oral solution provides a convenient dosage form for use by children, adults and older adults who frequently experience difficulty in swallowing tablets. An oral solution provides patients with a dosage form that can be easily administered with the assurance that the patient will be able to swallow each dose. Hydrocodone Bitartrate and Acetaminophen is used in settings such as hospitals and nursing home facilities. A liquid dosage form offers these caregivers a convenient means of administering the drug product and assuring compliance as they can easily determine whether the dose has been ingested.

It should be noted the agency has already approved ANDA 81-051 Lortab[®] Elixer (Hydrocodone Bitartrate and Acetaminophen Elixer 7.5 mg/500 mg per 15 mL) manufactured by Mikart. There are many examples of narcotic analgesics that have both child and adult indications. These liquid products offer prescribers and patients alternatives based on individual need or preference. Making these alternatives available to patients increases the opportunity for compliance in certain patients because of difficulty in swallowing or other specific preferences.

It is acknowledged that Hydrocodone Bitartrate and Acetaminophen does have abuse potential. The labeling for Lortab[®] contains caution statements related to drug dependence issues. Therefore, Hydrocodone Bitartrate and Acetaminophen Oral Solution should not raise any concerns not previously evaluated by the Agency. Moreover, introduction of an additional oral solution into the market place would not be expected to promote the potential for misuse of the product or be worse than for the tableted product. In fact, an oral solution may decrease potential diversion since caregivers can actually witness ingestion of the dose. While diversion and misuse of any drug product is of concern, the benefit to the population needing the therapeutic effect provided by Hydrocodone Bitartrate and Acetaminophen is significant.

The proposed liquid dosage form should have relative bioavailability equivalent to the reference listed tableted dosage form. Therefore, inactive components in a liquid formulation should not have an impact upon bioabsorption nor have interaction with Hydrocodone Bitartrate and Acetaminophen. Inactive components should be those that are customarily used in liquid drug preparations. The petitioner believes that the proposed change in dosage form (i.e., from 10 mg/500 mg oral tablets to an oral solution 10 mg/500 mg per 15 mL) does not raise any questions or safety or effectiveness and requests that the agency approve the petition.

A copy of the reference-listed drug labeling and draft labeling for the proposed Hydrocodone Bitartrate and Acetaminophen Oral Solution 10 mg/500 mg per 15 mL are enclosed (Attachments 2 and 3 respectively). The uses, dosage and indications for the proposed product are the same as those for Lortab[®] Tablets, the listed product. In addition, the draft labeling for Hydrocodone Bitartrate and Acetaminophen Oral Solution (10 mg/500 mg per 15 mL) incorporates information which can be found in the approved package insert for Lortab[®] Elixer (Hydrocodone Bitartrate and Acetaminophen Elixer (7.5 mg/500 mg per 15 mL) as approved April 17, 2001 (Attachment 4).

C. Environmental Impact

An environmental assessment on the action requested in this petition qualifies for a categorical exclusion under 21 C.F.R. 25.31. Therefore, an environmental assessment is not required for the requested action.

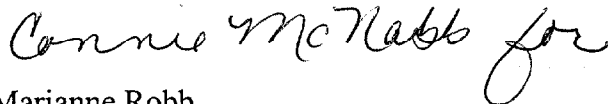
D. Economic Impact

Pursuant to 21 C.F.R. 10.30 (b), economic impact information is to be submitted only when requested by the Commissioner. Mallinckrodt Inc. will promptly provide such information if so requested.

E. Certification

Mallinckrodt Inc. certifies that, to its best knowledge and belief, this petition includes all information and views on which the petition 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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