PHARMOBEDIENT

June 07, 2024

Division of Dockets Management
U.S. Food and Drug Administration
Department of Health and Human Services
Room 1061, l-IFA-305
5630 Fishers Lane
Rockville, MD 20852

ANDA Suitability Petition for Chlorzoxazone Orally Disintegrating Tablets 250 mg and 500 mg

Dear Sir/Madam,

The undersigned submits this Suitability Petition pursuant to section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("FDC Act") and in accordance with 21 C.F.R. § 10.20, 10.30 and 314.93, to request that the Commissioner of the U.S. Food and Drug Administration ("FDA") declare that the drug product, Chlorzoxazone Orally Disintegrating Tablets, 250 mg and 500 mg is suitable for submission in an Abbreviated New Drug Application ("ANDA").

A. Action Requested:

The Suitability Petition requests that the FDA determine and declare that Chlorzoxazone Orally Disintegrating Tablets (ODT), 250 and 500 mg are suitable for submission in an Abbreviated New DrugApplication (ANDA). This Suitability Petition pursuant to Section 505(j)(2)(C) of the FDC Act and 21C.F.R. §314.93, is the appropriate mechanism for securing FDA authorization to submit an ANDA for a drug product that differs in dosage form from the Reference Listed Drug (RLD).

Conventional Chlorzoxazone tablets are available in the market in 250 mg and 500 mg strengths. However, they are not suitable for acute pain of musculoskeletal condition where quick onset of action is required. Besides, the conventional tablets also show poor patient compliance particularly by the geriatric patients who experience difficulty in swallowing, and by those who are bed ridden or who are traveling and donot have an easy access of water. To provide the patients with the most conventional mode of administration, there was a need to develop rapidly disintegrating dosage form, particularly one that disintegrates and dissolves/disperses in saliva and can be administered without need of water, anytime or anywhere.

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The Reference Listed Drug (RLD) upon which this petition is based is PARAFON FORTE DSC (CHLORZOXAZONE) TABLETS from JASSEN RESEARCH AND DEVELOPMENT LLC which FDA approved on Jun 15, 1987 under NDA # 011529. PARAFON FORTE DSC is discontinued and **Federal Register determination that product was not discontinued or withdrawn for safety or effectiveness reasons**. PARAFON FORTE DSC was marketed in 500 mg strength.

Reference Standard (RS) drug listed is # A089859 of WATSON LABS and is marketed in 500 mg strength as identified in the Orange Book. The relevant copy of the pages from the current Electronic Edition of the Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) for PARAFON FORTE DSC is provided as **Attachment 1**.

Approval of this Suitability Petition would allow the sponsor to submit Chlorzoxazone Orally Disintegrating Tablets (ODT), 250 mg and 500 mg as an ANDA.

B. Statement of Grounds:

The FDC Act Section 505(j)(2)(C)(iii) and 21C.F.R. §314.93, provides for the submission of an Abbreviated New Drug Application for a drug product that has a different dosage form from the RLD product provided that the FDA has approved a suitability petition proposing such an application.

Chlorzoxazone Tablets, 500 mg, the RS for the proposed drug product, containing 500 mg of Chlorzoxazone, as immediate-release tablets, is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute, painful musculoskeletal conditions.

Pharmobedient proposes an alternative immediate-release orally disintegrating tablet dosage form, bioequivalent to Chlorzoxazone Tablets, 500 mg of Watson, in the dosage strengths of 250 mg and 500 mg.

The proposed change in dosage forms represents changes that are consistent with dosing recommendations of RS's approved labeling. The current dosing instructions in the approved labeling of the RS are as follows:

Usual Adult Dosage: One tablet three or four times daily. If adequate response is not obtained with this dose, it may be increased to one and one-half tablets (750 mg) three or four times daily. As improvement occurs dosage can usually be reduced.

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Table 1 presents the comparison between approved marketed and proposed drug product.

A copy of the most recent labeling for RS under ANDA # 089859 (Revised 7/2019) is provided as **Attachment 2**.

Table 1 - Comparison of Approved Drug Products to Proposed Drug Product

Product Name	Reference Standard (RS) and RLD Drug Products	Chlorzoxazone Orally Disintegrating Tablets by Pharmobedient Pharmaceuticals, LLC
Drug Substance	Chlorzoxazone	
Dosage Strengths	500 mg (Scored)	250 mg (Unscored) 500 mg (Unscored)
Dosage Form	Immediate release	Orally disintegrating tablets
Route of Administration	Oral	
Indication	Relief of discomfort associated with acute, painful musculoskeletal conditions.	
Method of administration (Dosing Information)	Chlorzoxazone Tablets can be taken with or without food.	Chlorzoxazone Orally Disintegrating Tablets should be taken orally and should be sucked until completely disintegrated, and then swallowed. It can be administered with or without food.

Note: - *Formulation development of ODT tablet will be done to meet all the quality and regulatory requirements.*

The proposed labeling for Pharmobedient's Chlorzoxazone Orally Disintegrating Tablets is provided as **Attachment 3;** with the changes annotated in track changes from the FDA approved labeling of the Immediate Release Tablets. The only differences between the two products' labeling are those related to the product description and strength.

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The orally disintegrating tablets formulation of Chlorzoxazone will be developed by Pharmobedient to obtain an alternative immediate-release oral dosage form bioequivalent to Reference Standard (RS) drug - Chlorzoxazone Tablets by Watson, that enhances and promotes therapeutic convenience, adherence and compliance:

- ODT does not require water or other liquids, so the developed product can be taken in situations where patients do not have access to water whatsoever contributing to treatment adherence.
- ODT serve as preferred dosage form for patients suffering from difficulty in swallowing, e.g. drug-induced esophagitis, elderly people or patients with impaired swallowing function.
- Additionally, it is worthy to note that many patients suffering from pain need a quick onset of action, where an ODT would provide that without the administration of water.
- Additional 250 mg strength allows patients to take desired dosage without needing to brake tablets. Breaking a tablet in half can be difficult for many patients and may lead to inaccurate dosing.

Considering the formulation release properties and the desired bioequivalence to the RS formulation, the bioavailability of the 500 mg dosage strength of orally disintegrating tablets shall be studied against the 500 mg dosage strength of Watson's Chlorzoxazone Tablets, 500 mg tablets against which in vitro bioequivalence must be established as provided in **Attachment 4**.

Therefore, the petitioner's request for the Commissioner to find that a change in dosage for (from tablets to ODT) in strengths of 250 mg and 500 mg should raise no questions of safety or effectiveness, and the Agency should approve the petition.

C. Pediatric Waiver Request:

In September of 2007, Congress reauthorized the Pediatric Research Equity Act of 2003 (PREA) that amended the Federal Food, Drug, and Cosmetic Act to provide the Agency authority to require drug firms to study drugs in pediatric patients, if the Agency concludes that such study would provide beneficial health data for that patient population. The Act specifically requires that a request for a new dosage form is subject to a pediatric evaluation. The act also provides for a waiver from such requirement if the drug:

(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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In the approved RS labeling, only adult dosage instruction is given. Based on this information, it is believed that it is not likely that this product would be used in a pediatric patient.

The petitioner hereby requests that a full waiver from the conduct of pediatric studies be granted for this petition to permit a subsequent ANDA filing, as the product is not recommended to use in pediatric patients for its labeled indications to the satisfaction of the Agency.

C. Environmental Impact
The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact
The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis, if requested by the Agency.

E. Certification
The undersigned certifies that to the best knowledge and belief of the undersigned, 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.

During the course of the review of this Suitability Petition, if there are any questions or comments, please do not hesitate to contact undersigned.

Sincerely,

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