PHARMOBEDIENT

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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

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ANDA Suitability Petition for Diclofenac Potassium Orally Disintegrating Tablets 25 mg and 50mg

Dear Sir/Madam,

The undersigned, on behalf of a client Amici Pharmaceuticals LLC, 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 Diclofenac Potassium Orally Disintegrating Tablets, 25 mg and 50 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 Diclofenac Potassium Orally Disintegrating Tablets (ODT), 25 mg and 50 mg is 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 anANDA for a drug product that differs in dosage form from the Reference Listed Drug (RLD).

Conventional diclofenac potassium tablets are available in market in both 25mg and 50 mg strengths. However, they are not suitable for acute pain or inflammatory conditions where quick onset of action is required. Besides, the conventional tablets also show poor patient compliance particularly by the geriatric and pediatric 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 CATAFLAM film-coated tablets from NOVARTIS PHARMACEUTICAL CORP, which FDA approved on Nov 24, 1983 under NDA # N020142. CATAFLAM is discontinued and **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**.

Reference Standard (RS) drug listed is # A075463 of RK PHARMA INC and is marketed in a 50 mg strength tablet 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 CATAFLAM is provided as Attachment 1.

Approval of this Suitability Petition would allow Amici Pharmaceuticals LLC to submit Diclofenac Potassium Orally Disintegrating Tablets (ODT), 25 mg and 50 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.

Diclofenac Potassium Tablets, USP 50 mg, the RS for the proposed drug product, containing 50 mg of Diclofenac Potassium, as film-coated immediate-release tablets, is a Nonsteroidal Anti-Inflammatory Drug (NSAID) indicated for the following:

- For treatment of primary dysmenorrhea
- For relief of mild to moderate pain
- For relief of the signs and symptoms of osteoarthritis
- For relief of the signs and symptoms of rheumatoid arthritis

A copy of the most recent labeling for RS under ANDA # 075463 (Revised September 15, 2021) is provided as Attachment 2.

Amici proposes an alternative immediate-release oral tablet dosage form, bioequivalent to Diclofenac Potassium Tablets, USP 50 mg of RK PHARMA INC, in the exact same dosage strengths (25mg and 50 mg).

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

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

Product Name	Reference Standard (RS) drug - Diclofenac Potassium Tablets by RK PHARMA INC.	Diclofenac Potassium Orally Disintegrating Tablets by Amici Pharmaceuticals, LLC
Drug Substance	Diclofenac Potassium USP	
Dosage Strengths	25mg and 50 mg	
Dosage Form	Film-coated tablets	Orally disintegrating tablets
Route of Administration	Oral	
Indication	• For treatment of primary dysmenorrhea • For relief of mild to moderate pain • For relief of the signs and symptoms of osteoarthritis • For relief of the signs and symptoms of rheumatoid arthritis	
Method of administration (Dosing Information)	Diclofenac Potassium Tablets should be taken with water and swallowed whole. It can be administered with or without food.	Diclofenac Potassium Orally Disintegrating Tablets should be taken orally and shouldbe 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 requirement.*

The proposed labeling for Amici's Diclofenac Potassium 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.*

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

- ODT do 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 and inflammation need a quick onset of action, where an ODT would provide that without the administration of water.

Considering the formulation release properties and the desired bioequivalence to the RS formulation, the bioavailability of the 50 mg dosage strength of orally disintegrating tablets shall be studied against the 50 mg dosage strength of RK PHARMA's Diclofenac Potassium Tablets, 50 mg film-coated tablets as this is specified as the reference standard (RS) against which in vivo bioequivalence must be established. Thus, within the scope of the proposed ANDA approach, the drug product orally disintegrating tablets shall demonstrate bioequivalence (90% CI) against the RS in the two bioavailability studies (fasting and fed conditions) required by the Office of Generic Drug (OGD) Product-Specific Guidance for Generic Drug Development for bioequivalence studies of Diclofenac Potassium tablets, as provided in **Attachment 4**.

Therefore, the petitioner's request for the Commissioner to find that a change in dosage for (from Film coated tablets to ODT) in strengths of 25 mg and 50 mg (consistent with the approved RLD strengths) 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:

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(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.

As per the information given in the approved labeling, "The pharmacokinetics of diclofenac potassium tablets have not been investigated in pediatric patients." Based on this information, it is believed that it is not likely that this product would, nor should, 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 has been studied 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. A copy of a US Regulatory Agent can be found in **Attachment 5**.

Sincerely,

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