GLAND PHARMA LIMITED

Date: 07 September 2020

To

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

SUITABILITY PETITION

Dear Sir/Madam:

The undersigned hereby submits this petition pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("FDC Act"), and 21 C.F.R. § 314.93, and in accordance with 21 C.F.R. § 10.20 and 21 C.F.R. § 10.30, requesting Food and Drug Administration ("FDA") to declare that the drug product, Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL) is suitable for review as a Prior Approval supplement (PAS) to already approved ANDA of Doxercalciferol Injection, 4 mcg/2 mL – 2 mL Multi-dose vial.

A. Action Requested

The Petitioner requests that FDA declare that the drug product, Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL) is suitable for submission and review as a Prior Approval supplement (PAS) for already approved ANDA pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, as amended.

The reference listed drug upon which this petition is based, is Hectorol (doxercalciferol) Injection, 4 mcg/2 mL as registered by SANOFI GENZYME (NDA # N021027). Hectorol (doxercalciferol) Injection, 4 mcg/2 mL is having RLD status as per current orange book (please refer Attachment-I). Petitioner seeks an additional strength from that of the Reference listed drug product, from Hectorol (doxercalciferol) Injection, 4 mcg/2 mL to **Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL)**. This would be a change in total drug content only and not in concentration. In other words, Applicant is proposing an additional fill presentation of 5 mL without changing the concentration (i.e. 2 mcg/mL).

B. Statement of Grounds

FDC Act § 505(J) (2) (A) permits the submission of an ANDA for a drug product that differs in strength from a listed drug after FDA has approved a petition submitted pursuant to FDC Act§ 505(J)(2)(C).

The RLD, Hectorol (doxercalciferol) Injection, 4 mcg/2 mL is a clear, colorless solution administrated by intravenously. Petitioner proposes new additional strength of Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL).

The proposed drug product would be a sterile solution for intravenous injection with a formulation that is qualitatively and quantitatively the same as the Reference listed drug, but would contain 10 mcg/5 mL (2 mcg/mL) in multidose vial. There is no change in the dosage form and administration route. There would be a change in total drug content only i.e. fill volume, with no change in concentration per mL.

Importantly, the proposed dosage strengths are consistent with, and already contemplated by, the dosing recommendations reflected in the RLD's approved labeling (Refer Attachment – II). Specifically, the labeling of RLD, Hectorol (doxercalciferol) Injection, states that

"Initiate HECTOROL injection at a dose of 4 mcg given by bolus intravenous administration three times weekly at the end of dialysis (no more frequently than every other day). Target the maintenance dose of HECTOROL to intact parathyroid hormone (PTH) levels within the desired therapeutic range and serum calcium within normal limits. Monitor serum calcium, phosphorus, and intact PTH levels weekly after initiation of therapy or dose adjustment. Titrate the dose of HECTOROL injection based on intact PTH. The dose may be increased at 8-week intervals by 1 mcg to 2 mcg if intact PTH is not lowered by 50% and fails to reach the target range. The maximum dose is 18 mcg weekly. Prior to raising the dose, ensure serum calcium is within normal limits. Suspend or decrease the dose if intact PTH is persistently and abnormally low to reduce the risk of adynamic bone disease *[see Warnings and Precautions (5.4)]* or if serum calcium is consistently above the normal range to reduce the risk of hypercalcemia *[see Warnings and Precautions (5.1)]*. If suspended, the drug should be restarted one week later at a dose that is at least 1 mcg lower."

Therefore, patient would generally require a dose of 12 mcg to 18 mcg weekly. The maximum daily dose is 6 mcg per day. Currently, healthcare practitioners must use two vials of Doxercalciferol Injection, 4 mcg/2 mL in order to administer 6 mcg per day. **Therefore, the proposed drug product, Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL) will provide additional dosing flexibility with less waste.** Further, it may reduce the risk of medication error as 6 mcg of dose can be collected from one vial of proposed drug product i.e. Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL). Below are the details of RLD product and proposed drug product.

TABLE 1: DETAILS OF THE RLD AND PROPOSED DRUG PRODUCT

Product	Dosage Form	Route of Administration	Strength
RLD			
Hectorol (doxercalciferol) Injection	Injection	Intravenous	4 mcg/2 mL (2 mcg/mL)
Proposed drug product			
Doxercalicferol Injection	Injection	Intravenous	10 mcg/5 mL (2 mcg/mL)

There are no proposed changes in labeling except the change in strength sought in this Petition and the associated permissible changes. The active ingredient, dosage form, and route of administration are the same as that of the Reference listed drug. The indications, warnings, directions for use, and all other conditions of use described in the RLD labeling will remain the same. Draft labeling for the proposed product, Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL) is provided in **Attachment III**.

For the reasons stated above, Agency should find that the proposed strengths do not pose any safety or efficacy issues or concerns that would warrant the conduct of clinical trials. Petitioner requests FDA to approve this petition in order to submit proposed additional dosage strength as Prior Approval supplement (PAS) for already approved ANDA.

C. Environmental Impact

A claim for categorical exclusion of the requirements for an environmental assessment is made pursuant to 21 CFR § 25.31.

D. Economic Impact Statement

Pursuant to 21 CFR § 10.30(b), Gland Pharma 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 that are unfavorable to the Petition.

Sincerely,

Renuka

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Enclosures:

Attachment - I:
Copy of Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing current through September 2020 for the subject drug product.

Attachment - II:
Copy of the current RLD, Hectorol (doxercalciferol) Injection, 4 mcg/2 mL package insert

Attachment - III:
Copy of Draft labeling (Carton, container Label and Package Insert) for the proposed drug product, Doxercalicferol Injection, 10 mcg/5 mL (2 mcg/mL).