CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208614Orig1s000

CLINICAL REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Memorandum

Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

Date: July 18, 2018

From: Marina Zemskova M.D., Team Leader, Division of Metabolism and Endocrinology Products

Through: William H Chong, M.D., Acting Division Director, Division of Metabolism and Endocrinology Products

Subject: NDA 208614, Doxercalciferol Injection, 4 mcg/2 mL and 10 mcg/5 mL multi dose vials resubmission

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On January 26, 2018, Hospira resubmitted a New Drug Application (NDA) for Doxercalciferol Injection, 4 mcg/2 mL and 10 mcg/5 mL multi dose vials under Section 505(b) (2) of the Federal Food, Drug, and Cosmetic Act.

This NDA was originally submitted to the Agency on 11/30/2016. The Agency reviewed submitted data and issued a Complete Response (CR) action letter due to the following deficiencies (refer to CR letter from 9/14/2017 in DARRTS):

"During recent inspections of the drug product manufacturing facility - Hospira (FEI# 1925262) and testing facility - Hospira (b) (4) OPQ field investigators observed objectionable conditions at the facilities and conveyed that information to the representatives of the facilities at the close of the inspections. Satisfactory resolution of the observations is required before this application may be approved".

No clinical study was conducted with the new product and no new clinical efficacy and/or safety data essential for the risk/benefit assessment of Doxercalciferol was included in this application.

Doxercalciferol is a synthetic vitamin D_2 analog. The proposed indication is treatment of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) on dialysis.

FDA's findings for use of Hectorol (doxercalciferol) Injection (NDA 021027, Genzyme Corp) in treatment of SHPT in patients with CKD on dialysis are relied upon by the applicant as permitted under 505(b)(2). Both products have the same active ingredient and excipients (i.e., same qualitative and quantitative composition). The only difference between the two NDAs is the additional larger fill size of 5 mL in the new NDA.

A biowaiver was granted based on 21 CFR 320.22(b)(1) requirements: the new product and HECTOROL have the same qualitative and quantitative composition, and both are solutions for IV use (self-evident bioavailability).

The Office of Pharmaceutical Quality (OPQ) review recommends Approval (refer to the review from 6/11/2018). The deficiencies identified with the original submission have been adequately addressed. The reviewers indicated:

"As per the attached Facilities review, recent inspections of Hospira at 1776 N. Centennial Drive, McPherson KS 67460 (FEI# 1925262) in October of 2017 and February of 2018 resulted in a Voluntary Action Indicated classification and a No Action Indicated classification, respectively, which led to the current OPQ recommendation for Approval.

As per the attached Facilities review, Hospira (b) (4) was recently inspected in (b) (4) with GMP observations issued in a 483; FDA's evaluation of the inspection results is ongoing. Any risk related to the GMP observations is mitigated by the lack of application-specific deficiencies, apparent lack of impact on application data, and lack of any commercial function in this application".

In conclusion, I concur with the OPQ recommendations that recommend Approval.

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/s/

MARINA ZEMSKOVA
07/18/2018

WILLIAM H CHONG
07/18/2018

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Memorandum

Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

Date: September 13, 2017
From: Marina Zemskova M.D., Team Leader, Division of Metabolism and Endocrinology Products
Through: Jean-Marc Guettier, M.D., Division Director, Division of Metabolism and Endocrinology Products

Subject: Doxercalciferol Injection, 4 mcg/2 mL and 10 mcg/5 mL multi dose vials
To: File (NDA 208614)

On November 30, 2016, Hospira submitted a New Drug Application (NDA) for Doxercalciferol Injection, 4 mcg/2 mL and 10 mcg/5 mL multi dose vials under Section 505(b) (2) of the Federal Food, Drug, and Cosmetic Act.

Doxercalciferol is a synthetic vitamin D_2 analog. The proposed indication is treatment of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) on dialysis.

FDA's findings for use of Hectorol (doxercalciferol) Injection (NDA 021027, Genzyme Corp) in treatment of SHPT in patients with CKD on dialysis are relied upon by the applicant as permitted under 505(b)(2). Both products have the same active ingredient and excipients (i.e., same qualitative and quantitative composition). The only difference between the two NDAs is the additional larger fill size of 5 mL in the new NDA.

No clinical study was conducted with the new product and no new clinical efficacy and/or safety data essential for the risk/benefit assessment of Doxercalciferol was included in this application.

A biowaiver was granted based on 21 CFR 320.22(b)(1) requirements: the new product and HECTOROL have the same qualitative and quantitative composition, and both are solutions for IV use (self-evident bioavailability).

The Office of Pharmaceutical Quality (OPQ) review recommends Complete Response (CR). During recent inspections of the drug product manufacturing facility - Hospira (FEI# 1925262) and testing facility - Hospira (b) (4), OPQ field investigators observed objectionable conditions at the facilities and conveyed that information to the representatives of the facilities at the close of the inspections. Satisfactory resolution of the observations is required before this application may be approved.
There are no other deficiencies identified by the other review members of the OPQ team.

In conclusion, I concur with the OPQ recommendations that recommend CR.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MARINA ZEMSKOVA
09/13/2017

JEAN-MARC P GUETTIER
09/13/2017
I concur with the recommendations.