CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

207174Orig1s000

SUMMARY REVIEW

Summary Review for Regulatory Action

Date	2/4/16
From	
Subject	Division Director Summary Review
NDA/BLA # Supplement #	207174
Applicant Name	Accord Healthcare Inc.
Date of Submission	5 August 2015
PDUFA Goal Date	5 February 2015
Proprietary Name / Established (USAN) Name	None/Paricalcitol Injection
Dosage Forms / Strength	Solution for Injection/2 mcg per mL and 5 mcg per mL
Proposed Indication(s)	1. For the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5
Action/Recommended Action for NME:	Approval

1. Introduction

Accord Health Inc., submitted a new drug application pursuant to Section 505(b)(2) of the Food Drug and Cosmetic Act for paricalcitol injection. The drug product is a solution containing paricalcitol, an active vitamin D2 analog. Two product presentations [i.e., a 1 mL single dose vial and a 10 mL multiuse vial] and two dose strengths [i.e., 2 and 5 mcg/mL] are submitted with this application.

The proposed adult indication is for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease (CKD) Stage 5.

2. Background

The applicant relies in part on the Agency's previous findings of safety and effectiveness for the listed drug Zemplar (NDA# 020819), manufactured by AbbVie Inc to support approval of their product. The active ingredient, route of administration, dosage form and strength of the proposed drug product are the same as those of the listed product Zemplar. The two product formulations differ only in their ethanol content with the new product containing 35% ethanol and Zemplar containing 20% ethanol. The new product was not submitted through the 505(j) pathway because of this difference.

The scientific justification to support that reliance on the Agency's previous findings of safety and effectiveness for Zemplar was appropriate included comparative analytic data on impurity profiles between the two drug products (reviewed by Dr. Ysern), a four week toxicity study comparing the the new formulation and listed drug formulation (reviewed by Dr. Espandiari) and a biowaiver request (reviewed by Dr. Riviere) were submitted.

The NDA received a Complete Response action on January 29 2015 because of good manufacturing practices deficiencies at the testing site (b) (4) . The resubmission includes information for a new testing site (b) (4)

3. CMC/Device

No CMC deficiencies that would preclude approval were identified. Dr. Ysern reviewed data on product identity, purity, potency and stability. The applicant also submitted comparative analytic data between the listed drug and paricalcitol injection. He concludes that these comparative analyses reveal no differences among impurity profiles. Stability studies support a 24 months shelf-live when the product is stored at 25 ^{o}C protected from light. In use study for the multi-dose presentation support a conclusion that the product in this presentation is stable for at least (b) (4) days. The new testing site proposed to address the deficiency highlighted in the January 29 2015 complete response letter was found acceptable by the Office of Pharmaceutical Quality on 12 January 2016.

For a detailed discussion of CMC findings and testing site inspection recommendations refer to Drs. Ysern and Tran's respective reviews.

4. Nonclinical Pharmacology/Toxicology

No nonclinical pharmacology/toxicology deficiencies that would preclude approval were identified. The Sponsor conducted a 4-week repeat-dose toxicity study in rats with a 2-week recovery period to assess for potential differences in toxicity between the new formulation and the listed drug being relied upon. Dr. Parvaneh Espandiari concludes that the results of the nonclinical study suggest similar toxicokinetic and/or toxicity profile between the new formulation and the listed drug formulation. Refer to her review for full details.

5. Clinical Microbiology

There are no outstanding clinical microbiology or sterility issues that preclude approval.

6. Clinical Pharmacology/Biopharmaceutics

The applicant submitted a request to have the requirements to conduct an *in vivo* bioequivalence study waived. The waiver request was reviewed by Dr. Riviere and she recommends that the waiver be granted on the following basis;

- The proposed product is a parenteral solution intended solely for administration by injection.
- The proposed product contains the same active ingredient in the same concentration as the reference product, Zemplar (paricalcitol) Injection.
- The difference in concentration of the inactive ingredients in the proposed product and the reference product, Zemplar (paricalcitol) Injection, should not affect the safety and/or effectiveness of paricalcitol as demonstrated by the similar pH and osmolality data.

7. Clinical/Statistical-Efficacy

The applicant did not submit clinical efficacy data in this application.

8. Safety

The applicant did not submit safety data in this application.

9. Advisory Committee Meeting

No efficacy or safety issues requiring the input from an advisory panel was needed for this application. Therefore no advisory committee was convened.

10. Pediatrics

This application does not trigger the pediatric study requirements of the Pediatric Research Equity Act.

11. Other Relevant Regulatory Issues

No other relevant regulatory issues were identified.

12. Labeling

Labeling will be consistent with current Zemplar labeling as sufficient similarity between the the new product and Zemplar have been established.

13. Decision/Action/Risk Benefit Assessment

- Regulatory Action

I recommend approval.

- Risk Benefit Assessment

I agree with all review disciplines that the applicant has provided sufficient CMC, nonclinical and biopharmaceutics information to conclude that paricalcitol injection is sufficiently similar to Zemplar to support a conclusion that reliance on the Agency's previous findings of safety and effectiveness for Zemplar to approve paricalcitol injection is appropriate.

- Recommendation for Postmarketing Risk Evaluation and Mitigation Strategies

No new safety findings from this clinical development program prompt the need for a postmarketing risk evaluation and management strategies.

- Recommendation for other Postmarketing Requirements and Commitments

No new safety findings from this clinical development program prompt the need for a postmarketing requirements and commitments.

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/s/

JEAN-MARC P GUETTIER
02/04/2016