CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216743Orig1s000

CLINICAL REVIEW(S)

FDA CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF DIABETES, LIPID DISORDERS, AND OBESITY
Clinical Memorandum

Date	October 30, 2023
From	Justin Penzenstadler, PharmD (primary clinical reviewer)
NDA # / Sequence #:	NDA 216743 S-0006
Applicant	Zydus Worldwide DMCC
Date of Submission Receipt	December 31, 2022
PDUFA Goal Date	November 3, 2023
Proprietary Name / Established (USAN) names	Sitagliptin + Metformin hydrochloride (HCl)
(Proposed) Trade name	ZITUVIMET
Dosage forms / Strength	The Applicant is seeking approval of film-coated tablets containing the following sitagliptin/metformin hydrocholoride dosage strengths: • 50 mg/500 mg • 50 mg/1000 mg
Recommended Action	Approval
New Recommended Indication(s)/Populations(s)	As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
Documents Reviewed	Draft Labeling Fasting Study Report Fed Study Report

On December 31, 2022, Zydus submitted a New Drug Application (NDA) under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act seeking approval for sitagliptin (as free base)/metformin (HCL) 50mg/500mg and 50mg/1000mg tablets to improve glycemic control in adults with type 2 diabetes mellitus.

In this 505(b)(2) NDA, the applicant proposed to rely on FDA's finding of safety and effectiveness for Janumet (Sitagliptin phosphate monohydrate and metformin hydrochloride tablet, NDA 022044), marketed by Merck Sharp & Dohme Corp. The development program for this application is based on demonstration of bioequivalence (BE) to the listed drug Janumet. The applicant conducted two pivotal clinical pharmacology studies: a relative bioavailability using Janumet tablets as the reference under fasting conditions; and a relative bioavailability using Janumet tablets as the reference under fed conditions. Assuming bioequivalence is met, it is acceptable to rely on previous findings of safety, efficacy, and drug labeling from the Janumet for the proposed product. Therefore, the proposed regulatory pathway and the submitted clinical pharmacology data to support this application are reasonable from a clinical perspective.

I have reviewed:

(1) the adverse event, clinical laboratory, and vital sign data from the two BE studies. I did not identify any concerns with the methods of ascertainment, analysis, or findings.

(2) proposed labeling. The proposed labeling has minor differences in naming conventions and format but is identical in medical content to the Janumet label, except for the removal of a description of pediatric studies conducted by Merck Sharpe and Dohme Corp (submitted under NDA021995/S047) in section 8.4. This language is omitted in the proposed label due to a 3 and one-half year exclusivity period granted to Merck Sharpe and Dohme. The appropriateness of this omission was determined to be acceptable by DPMH in consultation with OCC.

(3) Financial disclosure information (form 3454) submitted for both pivotal bioequivalence studies. The applicant stated that no clinical investigators had financial interests in the outcome of the study.

There are no outstanding clinical issues. Based on review of these items, I recommend this Application for approval from the clinical perspective.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JUSTIN A PENZENSTADLER
10/31/2023 03:55:22 PM