CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208216Orig1s000

PHARMACOLOGY REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PHARMACOLOGY/TOXICOLOGY NDA REVIEW AND EVALUATION

Application number:	208216
Supporting document/s:	1
Applicant's letter date	June 30, 2015
CDER stamp date:	June 30, 2015
Product:	Azacitidine
Indication:	French-American-British (FAB) myelodysplastic syndrome (MDS) subtypes
Applicant:	Actavis LLC
Review Division:	Division of Hematology Oncology Toxicology (for Division of Hematology Products)
Reviewer:	Ramadevi Gudi, PhD
Supervisor/Team Leader:	Christopher M. Sheth, PhD
Division Director:	John Leighton, PhD, DABT Ann Farrell, MD (DHP)
Project Manager:	Tracy L. Cutler, MPH, CCRP, CIP

Disclaimer

Except as specifically identified, all data and information discussed below and necessary for approval of NDA 208216 are owned by Actavis or are data for which Actavis has obtained a written right of reference. Any information or data necessary for approval of NDA 208216 that Actavis does not own or have a written right to reference constitutes one of the following: (1) published literature, or (2) a prior FDA finding of safety or effectiveness for a listed drug, as reflected in the drug's approved labeling. Any data or information described or referenced below from reviews or publicly available summaries of a previously approved application is for descriptive purposes only and is not relied upon for approval of NDA 208216.

1 Executive Summary

1.1 Introduction

The 505(b)(2) NDA 208216 was submitted on June 30, 2015 by Actavis LLC for Azacitidine for Injection for SC or IV use, 100 mg/vial. Actavis LLC is relying on the FDA's previous findings of safety and effectiveness for the listed drug VIDAZA (NDA 050794), in addition to published literature and results from studies they have conducted comparing their product to VIDAZA in tests of bioequivalence, dissolution and other quality attributes.

No nonclinical study reports are provided with this application. Azacitidine is a nucleoside analog with a ribose structure that is incorporated into RNA and requires the activity of ribonucleotide reductase to be incorporated to deoxyribonucleic acid (DNA). Azacitidine is indicated for the treatment of patients with the following French-American-British (FAB) myelodysplastic syndrome (MDS) subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL).

The approved dosage and schedule for VIDAZA for all patients regardless of baseline hematology values is 75 mg/m^2 daily for 7 days to be administered by subcutaneous (SC) injection or intravenous (IV) infusion. After 2 cycles, the dose may be increased to 100 mg/m^2. The proposed indications are identical to the VIDAZA.

1.3 Recommendations

1.3.1 Approvability

No new nonclinical data was submitted. Actavis LLC's azacitidine for injection 505(b)(2) NDA 208216 is approvable from the perspective of pharmacology/toxicology.

1.3.2 Additional Non Clinical Recommendations

None

1.3.3 Labeling

The Applicant proposed PLLR labeling changes to the prescribing information. The finalized PLLR update has been reviewed by and is agreeable to the NDA review team, the Division of Pediatric and Maternal Health, and Actavis LLC.

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

/s/

RAMADEVI GUDI
04/01/2016

CHRISTOPHER M SHETH
04/01/2016