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Approval Package for:

APPLICATION NUMBER:

211192Orig1s000

Trade Name: Tibsovo® tablets; 250 mg

Generic or Proper Name: ivosidenib

Sponsor: Agios Pharmaceuticals, Inc.

Approval Date: July 20, 2018

Indication: For the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

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APPROVAL LETTER



NDA 211192

NDA APPROVAL

Agios Pharmaceuticals, Inc.
Attention: Jamie Cohen, PhD
Director, Regulatory Affairs
88 Sidney Street
Cambridge, MA 02139

Dear Dr. Cohen:

Please refer to your New Drug Application (NDA) dated December 21, 2017, received December 21, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tibsovo[®] (ivosidenib) tablets; 250 mg.

This new drug application provides for the use of Tibsovo[®] (ivosidenib) tablets for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the prescribing information and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the carton and immediate container labels submitted on May 16, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to

the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 211192.**” Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for ivosidenib was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of long-term toxicities of ivosidenib or assess a signal of excessive drug toxicity from impaired hepatic function on the pharmacokinetics of ivosidenib.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess these risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following trials:

- PMR 3444-1 Characterize the long-term safety of ivosidenib in patients with relapsed or refractory acute myeloid leukemia (AML). Submit the final study report and data set with 3 years of follow-up from ongoing Study AG120-C-001, *A Phase I, Multicenter, Open-Label, Dose-Escalation and Expansion, Safety,*

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