OPTUMRx®

## Tibsovo® (ivosidenib) – New orphan drug approval

- On July 20, 2018, Agios announced the FDA approval of Tibsovo (ivosidenib), 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.
    - The FDA has approved the RealTime IDH1 Assay, a companion diagnostic that can be used to detect this mutation.
    - Information on FDA-approved tests is available here.
- AML is a rapidly progressing cancer involving the blood and bone marrow. It is the most common acute leukemia affecting adults, with approximately 20,000 new cases each year in the U.S.
    - The majority of patients with AML eventually relapse. Relapsed and refractory AML cases have a poor prognosis.
    - An estimated 6% – 10% of AML patients have an IDH-1 mutation.
- Tibsovo is an IDH-1 inhibitor that works by decreasing abnormal production of the oncometabolite 2-hydroxyglutarate (2-HG), which leads to the differentiation of malignant cells.
- The efficacy and safety of Tibsovo were based on an open-label, single-arm trial involving 174 adults with relapsed or refractory AML with an IDH-1 mutation. Efficacy was established based on the rate of complete remission (CR) plus CR with partial hematologic recovery (CRh), the duration of CR plus CRh, and the rate of conversion from transfusion dependence to transfusion independence.
    - The CR plus CRh rate was 32.8% (95% CI: 25.8, 40.3).
    - The median duration of CR plus CRh was 8.2 months (95% CI: 5.6, 12).
    - Of the 110 patients who required transfusions at baseline, 37.3% became independent of transfusions during any 56-day post-baseline period.
- Tibsovo carries a boxed warning regarding differentiation syndrome.
- Other warnings and precautions include QTc interval prolongation and Guillain-Barré syndrome.
- The most common adverse reactions (≥ 20%) with Tibsovo use were fatigue, leukocytosis, arthralgia, diarrhea, dyspnea, edema, nausea, mucositis, electrocardiogram QT prolonged, rash, pyrexia, cough, and constipation.
- The recommended dose of Tibsovo is 500 mg orally once daily until disease progression or unacceptable toxicity. Patients without disease progression or unacceptable toxicity should be treated for a minimum of 6 months to allow time for clinical response.
    - Patients should be selected based on the presence of IDH-1 mutations in the blood or bone marrow. Patients without IDH-1 mutations at diagnosis should be re-tested at relapse because a mutation in IDH1 may emerge during treatment and at relapse.
    - Tibsovo should not be administered with a high-fat meal because of an increase in ivosidenib concentration.

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    - Tibsovo tablets should not be split or crushed.

- Agios' launch plans for Tibsovo are pending. Tibsovo will be available as 250 mg tablets.