Idhifa® (enasidenib) – Safety communication

- On November 29, 2018, the FDA announced that signs and symptoms of a life-threatening side effect called differentiation syndrome are not being recognized in patients receiving Idhifa (enasidenib).

- Idhifa is approved for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.

- Idhifa carries a boxed warning for differentiation syndrome and information is in the patient medication guide. However, the FDA has become aware of cases of differentiation syndrome not being recognized and patients not receiving the necessary treatment.

- Differentiation syndrome has occurred as early as 10 days and up to 5 months after starting the medicine. Differentiation syndrome may be life-threatening or fatal if not treated quickly.

    - A recent systematic analysis by the FDA identified a differentiation syndrome incidence with Idhifa of 19%, with 5% of these cases fatal.

- In the manufacturer's latest Idhifa quarterly safety report (May 1, 2018 to July 31, 2018), there were five cases of death associated with differentiation syndrome in patients treated with the drug.

    - In two cases, differentiation syndrome was listed as the only cause of death, while the three other cases were confounded by hemorrhagic stroke, pneumonia and sepsis, and sepsis alone.
    - One patient received systemic corticosteroids without delay, however may possibly have died of sepsis during the hospitalization.
    - Another patient died after a delay in diagnosis and treatment, and treatment details are unavailable for the remaining three patients.

- If patients experience unexplained respiratory distress or other symptoms, a diagnosis of differentiation syndrome should be considered and treatment with oral or intravenous corticosteroids should be given promptly.

    - Other symptoms of differentiation syndrome include acute respiratory distress represented by dyspnea and/or hypoxia and a need for supplemental oxygen; pulmonary infiltrates and pleural effusion; fever; lymphadenopathy; bone pain; peripheral edema with rapid weight gain; pericardial effusion; and hepatic, renal, and multiorgan dysfunction.

- Tibsovo® (ivosidenib), another drug FDA-approved for AML with a specific genetic mutation called IDH-1, also carries a risk of differentiation syndrome.

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— Health care professionals should be vigilant in monitoring for differentiation syndrome when prescribing Tibsovo and patients should alert their health care professional of any symptoms.
— Tibsovo carries a boxed warning for differentiation syndrome.

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