Symptoms of a Serious Condition Not Being Recognized With Leukemia Med

The life-threatening side effect, called differentiation syndrome, is related to the acute myeloid leukemia medicine Idhifa (enasidenib).

November 29, 2018 By Food and Drug Administration (FDA)

FDA warns that symptoms of a serious condition affecting the blood cells are not being recognized with the leukemia medicine Idhifa (enasidenib)

The U.S. Food and Drug Administration (FDA) is warning that signs and symptoms of a life-threatening side effect called differentiation syndrome are not being recognized in patients receiving the acute myeloid leukemia medicine Idhifa (enasidenib). The Idhifa prescribing information and patient Medication Guide already contain a warning about differentiation syndrome. However, we have become aware of cases of differentiation syndrome not being recognized and patients not receiving the necessary treatment.

As a result, we are alerting health care professionals and patients about the need for early recognition and aggressive management of differentiation syndrome to lessen the likelihood of serious illness and death. We are continuing to monitor this safety concern.

Health care professionals should describe to patients the symptoms of differentiation syndrome listed in the Medication Guide when starting Idhifa and at follow-up visits, and inform them to call their health care professional if such symptoms occur. Differentiation syndrome has occurred as early as 10 days and up to 5 months after starting the medicine. If patients experience unexplained respiratory distress or other symptoms, consider a diagnosis of differentiation syndrome and treat promptly with oral or intravenous corticosteroids (See Additional Information for Health Care Professionals).

Patients should contact your health care professional or go to the nearest hospital emergency room right away if you develop any of the following symptoms of differentiation syndrome while you are taking Idhifa:

- Fever
- Cough
- Shortness of breath

- Swelling of arms and legs
- Swelling around the neck, groin, or underarm area
- Fast weight gain of more than 10 pounds within a week
- Bone pain
- Dizziness or feeling lightheaded

Idhifa was approved in August 2017 to treat patients with acute myeloid leukemia (AML) with a specific genetic mutation called isocitrate dehydrogenase (IDH)-2 whose disease has come back or has not improved after treatment with other chemotherapy medicines. AML is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of abnormal white blood cells. Idhifa works by blocking several enzymes that promote this abnormal blood cell growth.

In the clinical trial conducted for Idhifa's approval, at least 14 percent of patients experienced differentiation syndrome. The manufacturer's safety report, which included the period of May 1, 2018 to July 31, 2018, reported five cases of death associated with differentiation syndrome in patients taking Idhifa (See Data Summary). Until Idhifa was approved, differentiation syndrome had been associated only with induction chemotherapy in patients with a rare form of cancer called acute promyelocytic leukemia. Health care professionals and patients may not recognize the signs and symptoms of differentiation syndrome associated with Idhifa. Another recently approved drug for AML with a specific genetic mutation called isocitrate dehydrogenase (IDH)-1, Tibsovo (ivosidenib), also carries a risk of differentiation syndrome. Health care professionals should also be vigilant in monitoring for differentiation syndrome when prescribing Tibsovo and patients should alert their health care professional of any symptoms.

To help FDA track safety issues with medicines, we urge patients and health care professionals to report side effects involving Idhifa or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

This announcement was originally published on the Food and Drug Administration website on November 29, 2019.

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