Uloric® (febuxostat) – Safety communication and updated indication

- On February 21, 2019, the FDA announced that there is an increased risk of death with Uloric (febuxostat) use compared to allopurinol. This conclusion was based on an in-depth review of results from a safety clinical trial that found an increased risk of heart-related death and death from all causes with Uloric.
    - As a result of the findings, a boxed warning for cardiovascular (CV) death was added to the Uloric drug label and a new patient Medication Guide.
    - The indication for Uloric was also updated to chronic management of hyperuricemia in adult patients with gout who have an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.
    - Uloric is not recommended for the treatment of asymptomatic hyperuricemia.

- Uloric was previously approved for chronic management of hyperuricemia in patients with gout.

- Patients should tell their health care professional if they have a history of heart problems or stroke and discuss the benefits and risks of using Uloric. Patients should seek emergency medical attention right away if they experience the following symptoms while taking Uloric:
    - Chest pain
    - Shortness of breath
    - Rapid or irregular heartbeat
    - Numbness or weakness on one side of the body
    - Dizziness
    - Trouble talking
    - Sudden severe headache.

- Patients should not stop taking Uloric without first talking to their health care professional, as doing so can worsen their gout.

- Health care professionals should reserve Uloric for use only in patients who have failed or do not tolerate allopurinol. Patients taking Uloric should be monitored for CV signs and symptoms. In addition, patients should be counseled about the CV risk with Uloric and they should be advised to seek medical attention immediately if they experience the symptoms listed above.

- The labeling update is based on CARES, a large, double-blind, postmarketing study that evaluated the CV safety of Uloric. The study evaluated 6,190 patients with gout treated with either Uloric or allopurinol. The primary endpoint was a composite of major adverse CV events (MACE): CV death, nonfatal myocardial infarction, nonfatal stroke, and unstable angina with urgent revascularization. Secondary endpoints included the individual components of the MACE composite as well as death from any cause.
    - Results showed that although the study met the pre-specified noninferiority margin, there was a significant increase in CV deaths in patients treated with Uloric (134 deaths [4.3%]; 1.5 per 100 patient-years) compared to patients treated with allopurinol (100 deaths [3.2%]; 1.1 per 100 patient-years) (Hazard Ratio [HR]: 1.34; 95% CI: 1.03, 1.73).

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— In addition, all-cause mortality was higher in the Uloric group (243 deaths [7.8%]; 2.6 per 100 patient-years) than the allopurinol group (199 deaths [6.4%]; 2.2 per 100 patient-years) (HR: 1.22; 95% CI: 1.01, 1.47), due to a higher rate of CV deaths.

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