

**FOOD AND DRUG ADMINISTRATION (FDA)**  
Center for Drug Evaluation and Research (CDER)

*Joint Meeting of the Arthritis Advisory Committee (AAC) and the  
Drug Safety and Risk Management Advisory Committee (DSaRM)*  
College Park Marriott Hotel and Conference Center, General Vessey Ballroom  
3501 University Blvd. East, Hyattsville, Maryland  
January 11, 2019

**QUESTIONS**

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1. **Discussion:** Discuss the results of the “Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Gout and Cardiovascular Morbidities (CARES)” study, particularly major adverse cardiovascular events (MACE) and cardiovascular (CV) mortality. Please consider the following in your discussion:
  - a. Biological plausibility of CV mortality
  - b. Strength of the findings for CV mortality, considering the totality of available data
2. **Discussion:** Discuss the benefits of febuxostat for the treatment of hyperuricemia in patients with gout.
3. **Discussion:** Given the results of the CARES study, discuss whether the benefit-risk profile of febuxostat for the treatment of hyperuricemia in patients with gout has changed. Address the following in your discussion:
  - a. Discuss any patient populations in which the benefits outweigh the risks of the use of febuxostat
  - b. Discuss any patient populations in which the benefits do not outweigh the risks of the use of febuxostat
4. **Discussion:** Discuss the following potential regulatory activities in response to the results of the CARES study.
  - a. Update existing warning regarding Cardiovascular Events in the febuxostat product label
  - b. Addition of a boxed warning for cardiovascular death to the febuxostat product label
  - c. Modify labeling to limit use of febuxostat to second line therapy (e.g. 2<sup>nd</sup> line therapy in patients who have failed allopurinol)
  - d. Withdrawal of febuxostat from the market
5. **Vote:** Based upon the available data, is there a patient population in which the benefit-risk profile for febuxostat is favorable for the treatment of hyperuricemia in patients with gout? (Y/N)
  - If you voted “Yes”, describe the patient population with a favorable benefit-risk profile for use of febuxostat. Also, describe any other recommendations (e.g. labeling changes) you may have for use of febuxostat in this population.
  - If you voted “No”, discuss your rationale, the impact of this recommendation, and any other recommendations you may have.