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)
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
April 24-25, 2018

QUESTIONS

PRECISION Trial

1. **DISCUSSION:** Discuss whether the data from the PRECISION trial support a conclusion of cardiovascular safety for celecoxib relative to ibuprofen and naproxen, taking into consideration the outcomes of cardiovascular thrombotic events (Anti-Platelet Trialists' Collaboration [APTC] endpoint) and hypertension.

2. **DISCUSSION:** Discuss limitations of the PRECISION trial that may interfere with interpretability of the cardiovascular outcome results, including the comparability of the dosing regimens, and any other concerns regarding study design or conduct.

3. **VOTE:** Has the PRECISION trial demonstrated comparable cardiovascular safety for celecoxib as compared to naproxen and ibuprofen? Please provide an explanation for your vote.

4. **DISCUSSION:** Discuss whether the secondary and tertiary endpoints of the trial (e.g., clinically significant GI or renal events, all-cause mortality) can be relied upon for comparing the risk across celecoxib, ibuprofen, and naproxen given the definitions used and the lack of a pre-specified hierarchical statistical plan.

Interaction Between Aspirin and Non-aspirin NSAIDs

5. **DISCUSSION:** Discuss whether there is a clinically significant interaction between aspirin and celecoxib, aspirin and ibuprofen, or aspirin and naproxen.

6. **DISCUSSION:** If you have concluded that there is a clinically significant interaction with aspirin for one or more of the non-aspirin NSAIDs presented, discuss whether there are patient populations (e.g., patients with recent MI, revascularization, stent placement) for whom the risks of the aspirin-NSAID interaction potentially outweigh the benefits of the non-aspirin NSAID.

7. **DISCUSSION:** Discuss whether any of the interactions between aspirin and non-aspirin NSAIDs are of sufficient clinical significance to warrant description in prescription labeling.

QUESTIONS (cont.)

8. **VOTE:** Which of the following regulatory actions, based on the material presented and discussed at this Advisory Committee meeting, should be taken with respect to naproxen nonprescription labeling and comment on your rationale.
    a. No change to the current naproxen Drug Facts label (See FDA Briefing Document Appendix 1 for example.)
    b. Include a warning regarding the interaction between aspirin and naproxen
    c. Include a contraindication of use for naproxen when taken with aspirin

9. **VOTE:** Which of the following regulatory actions, based on the material presented and discussed at this Advisory Committee meeting, should be taken with respect to ibuprofen nonprescription labeling and comment on your rationale.
    a. No change to the current ibuprofen Drug Facts label (See FDA Briefing Document Appendix 3 for example.)
    b. Include a contraindication of use for ibuprofen when taken with aspirin