Questions to the Committee

Arthritis Advisory Committee

April 12, 2007

Discussion Points

- Has the safety profile of etoricoxib been sufficiently characterized? If not, what other studies would you recommend?
  - Discuss the cardiovascular safety findings based on the data presented (in particular, from the large outcome trials in comparison to diclofenac). Specifically, address:
    - Cardiovascular thrombotic events
    - Edema/congestive heart failure and hypertensive effects
  - Discuss the gastrointestinal safety findings based on the data presented (in particular, from the large outcome trials in comparison to diclofenac), e.g. the "complicated" versus the "complicated and not complicated" events analyses.

Discussion Points, Cont'd.

1. Discuss the efficacy data for etoricoxib, particularly as it relates to appropriate dosing.

Committee Vote

- Do you recommend approval of etoricoxib for "relief of the signs and symptoms of osteoarthritis?"
- If not, are there additional studies that might provide support for approval?
- If yes:
  - Is there a need for labeling beyond the NSAID template language to address the findings of hypertension and CHF?
  - Do the GI safety findings warrant a reduction in the gastrointestinal warnings in the product label?
  - Do the GI findings support an affirmative GI safety claim relative to other NSAIDs?
  - Is there a need for specific risk management beyond labeling, e.g. deterrence of dosing above the recommended dose? If yes, what specific measures should be implemented?