Food and Drug Administration

Center for Drug Evaluation and Research (CDER)

Arthritis Advisory Committee

June 3, 2004

Questions to the Committee

Individuals with acute gout often experience significant pain. Although standard treatments include NSAIDs, colchicine and glucocorticoids, none of these agents have been demonstrated to be efficacious in placebo-controlled, randomized double-blind studies. Therefore, it is important to carefully assess any new therapy for efficacy.

I. Please discuss whether gout is considered a unique clinical entity or a model of acute pain?

II. Please comment on the use of the following clinical measures: pain intensity, pain relief, time to onset of analgesia, time to re-medication
- Are there additional endpoints that should be considered for these clinical trials such as evidence of local inflammation, erythema, sensitivity to touch, assessment of function, patient/physician global assessment?
- Please discuss the value of an endpoint such as time to good or excellent pain relief in a defined period of time (a responder analysis).

III. Attacks of gout may be self limited and resolve spontaneously over 1-2 weeks.
- Please discuss the duration of a trial for acute gout.
- What is the value of a demonstration of efficacy within the first 8 hours? The first day?
- Is there clinical meaning in an analysis of average of pain over several days? How many days?

IV. The onset and duration of an acute attack is unpredictable and the extent of pain during an acute attack of gout is variable.
- Please discuss the clinical trial implications of enrollment of patients who have already had symptoms of an acute attack for a period of time (for example 48 hours).
- Please discuss the clinical trial implications of enrolling patients who may be untreated or partially treated.

V. Considering the extent of pain and duration of attacks at trial entrance, please discuss the advantages and disadvantages of placebo-controlled studies vs. active-controlled trials. If placebo-controlled studies are not recommended, are there data from studies of existing therapies sufficient to define a margin of non-inferiority?

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Questions to the Committee (cont.)

VI. Please discuss the following clinical trial issues:

- Use of concomitant medications such as diuretics or low dose ASA
- Entry (inclusion) criteria for an acute gout trial, particularly the need for documentation of the presence of crystals.
- Enrollment of patients with polyarticular gout
    - Should the trials be stratified by this factor?
    - Please comment on other factors to consider for stratification