Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

Peripheral and Central Nervous System Drugs Advisory Committee

August 4, 2005

CDER Advisory Committee Conference Room
5630 Fishers Lane, Rockville, Maryland

FINAL QUESTIONS

1. Pozen estimated an annual incidence of tardive dyskinesia (TD) of up to 0.038% for metoclopramide at a daily dose of 30-40 mg/day for 72 days/year (which corresponds to up to 380 cases of TD per million patients per year).

   - Do you think that this is a reasonable estimate?

   - If MT100 were to carry the same risk, would such a risk level be acceptable if the only contribution of metoclopramide is a 5-10% improvement on sustained headache relief (with no effect on 2-h endpoints)?

   - Is any risk of tardive dyskinesia acceptable for a migraine population?

2. Is there sufficient evidence that the chronic-intermittent administration of metoclopramide does not carry a risk of tardive dyskinesia?

   - Is it possible to define a maximum recommended number of monthly doses of MT100 to avoid the risk of tardive dyskinesia?

3. Do you believe that, based on the existing data on medication-overuse headache, there is evidence that a proportion of patients prescribed MT100 will likely take a number of monthly doses higher than recommended?

4. All currently approved acute treatments of migraine are indicated without restriction regarding the presence or absence of nausea at baseline.

   - Given that patients may have nausea at some attacks and no nausea at others, does an indication limited to the subpopulation of migraine patients with no nausea at baseline represent a clinically meaningful and acceptable indication?

5. If Pozen shows prospectively in a new clinical study in migraine patients with no nausea at baseline:
   - a significant contribution of metoclopramide on sustained headache pain relief of 5-10%
   - no contribution of metoclopramide at 2-hours
   - no contribution of metoclopramide on relapse rate or rescue medication use in the 2-24 hour period,

   - Would the demonstrated benefit outweigh the risks related to tardive dyskinesia?

   - If not, what additional data (or desired primary outcome, or desired effect on sustained relief) could provide evidence of safety and efficacy?