Draft Questions for Lotronex Advisory Committee
April 16, 2002

2:45 p.m.

Questions:

1. Should Lotronex be made available to patients with irritable bowel syndrome (IBS) through restricted marketing?
   a. If yes, describe the patient population for which the benefits of the drug outweigh the risks. For example: Should the degree of disability, severity of symptoms, chronicity of IBS, failure of conventional IBS therapies, or sex be taken into account? If so, how?

   b. If no, clarify whether Lotronex should be withheld completely from the market or if marketing of Lotronex without restrictions is acceptable. Explain your rationale.

2. Process controls for **patients** prescribed Lotronex
   a. Should patient registration be a part of a risk-management program? Why or why not?
   b. GlaxoSmithKline (GSK) has proposed a utilization study of the UnitedHealthcare Research Database (UHC) as a mechanism to audit whether appropriate patients are being prescribed Lotronex. Is this auditing mechanism adequate to achieve this goal? If not, please describe an appropriate auditing mechanism.
   a. GSK has proposed a pharmacy-based study using the Slone Epidemiology Unit and Eckerd Corporation to audit patients' knowledge and awareness of the risks and benefits of Lotronex. Is this auditing mechanism adequate to achieve this goal? If not, describe an appropriate auditing mechanism.
   b. Define adequate performance on the knowledge survey.

3. Process controls for **physicians** prescribing Lotronex:
   a. Should the risk-management plan limit prescribing to certain physicians? If so, what types of physicians and what qualifications are needed?
   b. Should physician registration be a component of a risk-management plan? Why or why not?
   c. GSK has proposed a plan in which physicians self-attest to their qualifications by signing the "Section for the Physician" on the Patient-Physician Agreement. This agreement is then filed in the patient's medical record. The agreement is not filed at a central location. Is this proposal adequate to evaluate physician adherence to the program (e.g., the extent of Lotronex prescribing outside of the program)? Why or why not? In not, describe an appropriate auditing mechanism.
   d. Define an adequate level of adherence to the program by physicians.

4. Process controls for **pharmacists** dispensing Lotronex:
   GSK has proposed that pharmacists accept only written prescriptions with an affixed sticker and that the pharmacists dispense a Medication Guide when the prescription is

filled or refilled. Is this proposal adequate to evaluate pharmacist adherence to the program? Why or why not? If not, describe an appropriate auditing mechanism.

5. Evaluation of safety outcomes:
   a. Should clinical outcomes (e.g., ischemic colitis, severe constipation, and death) be used to assess the success of the risk-management program? For example, should the rates and/or degree of severity of ischemic colitis and constipation be monitored with the specific goal of evaluating the effectiveness of the program? Why or why not?
   b. If so, specify the adverse events that should be assessed. Describe acceptable rates for these adverse events and/or acceptable degrees of severity.

6. Please provide any additional comments that you may have about a Lotronex risk-management program, such as the need for additional studies.