

Questions for PCNS Discussion

Xyrem®, Orphan Medical, Inc.

June 6, 2001

1. **Has the sponsor demonstrated efficacy of Xyrem® for the proposed indication to treat cataplexy and excessive daytime sleepiness in patients with narcolepsy?**
 - a. If no, is there any reasonable claim for which the sponsor has presented substantial evidence of effectiveness?
2. **Has the sponsor established the safety of Xyrem® when used for the proposed indication for which substantial evidence of effectiveness has been submitted?**
3. **Is the adoption of a risk management plan necessary for the safe use of Xyrem®?**

Please evaluate the following components of the Risk Management Program:

4. Safe Use in Home

- a. Should there be a requirement for additional safeguards in patient's homes, e.g., keeping drugs in a locked storage space?
- b. Should there be additional warnings on the labeling of the dose cups and/or bottle of GHB?
- c. Is there any special concern or advice regarding limitations on the quantity of Xyrem supplied at any one time?
- d. What special concerns should be communicated in the product label and other printed materials?

5. Safe Use by Patient

- a. Should patients sign an informed consent form before receiving the initial shipment of the drug?
- b. Should patients be required to return a registry form before receiving the first shipment?

6. Appropriate Prescribing

- a. Should physicians document that they read the materials sent to them before the pharmacy fills the initial prescription?
- b. Should physicians be required to demonstrate safe use and appropriate dosage preparation to patients before the first prescription and be required to document that it has been accomplished?
- c. Should there be restricted prescribing for the product? (e.g., only to those who have a diagnosis of cataplexy)
- d. Does the Risk Management Program assure appropriate prescribing or sufficiently reduce the risks of misuse or overdose from Xyrem?
- e. Should certification of physicians for prescribing Xyrem be required?

7. Central Pharmacy

- a. Is the institution of the sponsor's central pharmacy adequate?
- b. Should the central pharmacy be described in the product labeling, as well as educational and promotional material?

8. Post Market Surveillance

- a. Should there be a requirement for post-marketing reporting of cases of misuse, abuse, overdose, dependence, and diversion?
- b. Should the role of the central pharmacy include providing post-marketing and surveillance reports to the Agency in addition to the sponsor?
- c. Should these reports be provided on a regular basis and include monitoring prescribing and dispensing patterns?

9. Other recommendations

- a. Any other recommendations on how to protect the family of the patient, on the handling, storage, and disposal of GHB, on labeling and on post market follow-up for misuse and overdose?