In reviewing each of these documents, I have edited them. Each of the edited documents is separate from this review.

Key changes to each of these documents are addressed below

11.1 Risk Management Program Proper

Key changes to the program have been to the following components and are acceptable to the reviewer.

- The names of the manufacturer and distributor have been deleted based on advice that the sponsor has received from law enforcement bodies. The central pharmacy distributing the drug has been referred to as such, rather than as

- The Risk Management Program summary that accompanied the Approvable Letter of 4/9/02 specifically stated that "all patient assignment of benefit forms and registry information would need to be signed and sent back to the central pharmacy before the first prescription is filled." The sponsor has altered this section to
  - Delete "assignment of benefits" forms from this statement. The sponsor justifies this deletion on the basis that these forms are a legal contract between the pharmacy and patient which will be mailed out as a separate step for insurance billing purposes, if needed, and that it is not necessary for the form to be returned in order for a prescription to be filled unless the central pharmacy deems it necessary
  - State that registry information will need only to be verified (and not signed and sent back to the pharmacy) before the first prescription is filled. The Xyrem® Patient Success Program materials do not contain any registry information.

- Under the "Drug Product Kit" heading the sponsor has deleted the following statement from the summary

11.2 Xyrem® Physician Success Program Elements

Only key changes are addressed below

11.2.1 Letter To Physician

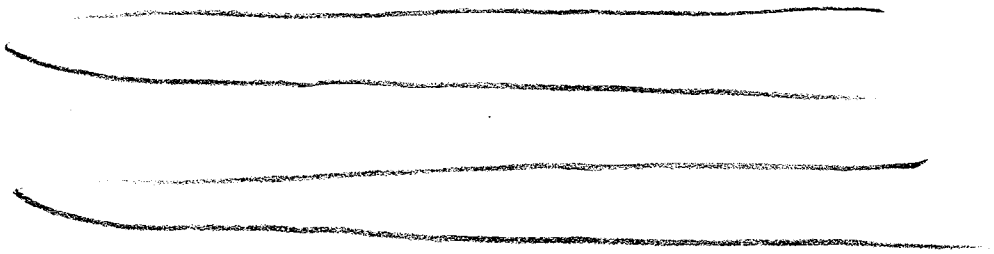
Changes to this letter made by the sponsor are minor and acceptable. I have not made any changes to the document submitted by the sponsor.

11.2.2 Physician Booklet ("Doctor Book")

The physician declaration that accompanied the Approvable Letter of 4/9/02 read as follows

Physician Declaration – Please initial each box	To be completed at initial prescription only
☐ I have read the materials in the Xyrem Physician Success Program	
☐ I verify that the patient has been educated with respect to Xyrem preparation, dosing and scheduling	
☐ I understand that Xyrem is approved for the treatment of cataplexy in patients with narcolepsy	
☐ I understand that Xyrem has not been shown to be effective or safe for any other indication. I also understand that there is not evidence that doses greater than 9 gm/day are safe.	

In this submission the sponsor has edited the declaration to read as follows:



These and other, more minor, changes to the label are acceptable. I have not made any changes to the document submitted by the sponsor.

11.3 Xyrem® Patient Success Program Elements

11.3.1 Letter To Patient

The sponsor has made only very minor changes to this document. I have not made any changes to the document submitted by the sponsor.

11.3.2 Patient Booklet ("Patient Book")

Key changes to this document as made by the sponsor are summarized below

- Under the heading "How soon might I see a change in my symptoms" the text that accompanied the Approvable Letter of 4/9/02 contained the following statement: "You can expect to see some improvement within the first weeks."

The sponsor has edited this statement to read as follows:

You can expect to see some improvement within the first weeks of Xyrem® therapy, however, may take up to 8 weeks.

I have further edited this statement so as to use language that might be understood by a lay person (see edited document for full details).

- Under the heading "What should I avoid while taking Xyrem®" the text that accompanied the Approvable Letter of 4/9/02 contained the following statement

What should I avoid while taking Xyrem?

11.3.3 Patient Video

The sponsor has submitted the script of a video that that is intended to instruct patients regarding the following

- Preparation and use of Xyrem®
- Precautions needed to ensure the in-home safety of Xyrem®
- Laws governing, and precautions to be taken against, the misuse of Xyrem®

I have read the script of the video and found it acceptable.

11.4 Post-Marketing Program Elements

This program consists of the post-marketing safety evaluation form and accompanying documents.

11.4.1 Instructions

- Changes made by the sponsor to the document that accompanied the Approvable letter of 4/9/02 are minor and do not warrant further comment
- I have not made any changes to the document submitted by the sponsor.

11.4.2 Letter

- Changes made to the document that accompanied the Approvable letter of 4/9/02 are acceptable and do not warrant further comment
- I have not made any changes to the document submitted by the sponsor.

11.4.3 Outline

The sponsor has not made any changes to the form that accompanied the Approvable letter of 4/9/02

11.4.4 Form

- Changes made to the document that accompanied the Approvable letter of 4/9/02 are acceptable and do not warrant further comment
- I have not made any changes to the document submitted by the sponsor.

11.4.5 Additional Item

In the cover letter, the sponsor has asked the following question

"It is our understanding from the language you placed in the letter to doctors that that safety information on 1000 patients followed for 6 months on Xyrem® therapy will fulfill our obligations for this program. Can you please confirm our agreement?"

The answer to this question is, I believe, that the sponsor's understanding is correct.

12. Proposed Labeling

This has been submitted in 3 separate formats: Microsoft Word, PDF (annotated) and PDF ("clean")

The key changes made to the label, that accompanied the Approvable action letter of 4/9/02, were to the following sections of the label. More minor changes are acceptable and are not reviewed below. I have edited the label submitted by the sponsor in a separate document.

15 page(s) of revised draft labeling has been redacted from this portion of the review.

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Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

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Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.