information regarding the proper handling of the drug with an outline of precautions to be taken against diversion

- If a patient has prescription drug coverage, [redacted] will then contact the patient's insurance company to obtain coverage. [redacted] will notify the patient of his/her approval status

10.1.1.3 Patient Services

- All patient assignment forms and registry information will need to be signed and sent back to the pharmacy before the initial prescription can be filled
- Comprehensive printed and video materials (see Xyrem® Patient Success Program below) that also contain information regarding the proper handling of the drug with an outline of precautions to be taken against diversion will be provided to the patient in advance of shipment.
- Once approval has been established, [redacted] will verify the patient's home address and availability for shipping and arrange shipment through Federal Express RapidTrac or a similar carrier
- Receipt of the initial drug shipment will be ensured through the following
  - A phone call by the pharmacy to the patient, no more than 24 hours after the shipment is delivered, to verify that the medication and educational materials have been received
  - The courier service's own tracking system for shipments which requires a signature by the patient
- If the patient or their designee is unavailable to accept a shipment of Xyrem® and execute the required receipt after two delivery attempts, the package will be returned to the pharmacy.
- If a shipment is lost, an investigation will be launched to find it.
- If required by the patient's insurance company the product may be shipped by [redacted] to another pharmacy for patient pick-up. The sponsor anticipates that this will be an unusual occurrence and has a mechanism for verifying the second pharmacy's ability to protect against diversion of sodium oxybate before shipping the drug there through NTIS and State Boards of Pharmacy

10.1.1.4 Registry

- Every patient and prescribing physician will be registered with [redacted] in a secure database. The database will contain the physician's name, address, telephone and facsimile numbers, DEA and state license numbers and prescribing frequency. The database will be made available for review by the DEA as well as other federal and state agencies upon request. From this database it will be possible to obtain the following information
  - Prescriptions by physician specialty
  - Prescriptions by patient name
  - Prescriptions by volume (frequency)
  - Prescriptions by dose
- Prescription refills will be permitted in the number specified in the original prescription. In addition

- If a prescription refill is requested by the patient prior to the anticipated due date, such refills will be questioned by the pharmacist
- A lost, stolen, destroyed, or spilled prescription/supply will be documented and the prescription replaced to the extent necessary to honor the original prescription (e.g., a destroyed or spilled bottle will reduce the prescription refill amount). The pharmacist has the discretion to grant or not grant refill requests under those circumstances and at a minimum will contact the prescribing physician to determine if the physician has any special concerns in regard to that refill request. New supplies of Xyrem® will be sent to the patient only if the pharmacist and physician are in agreement.
- Repeat instances of lost, stolen, destroyed, or spilled prescriptions/supplies will be flagged for monitoring and future instances thoroughly questioned
- With the first prescription it is planned to provide the patient with only one month's supply of Xyrem®.
- Following further contact between the pharmacy and patient, and verification that the patient understands the material in the Xyrem® Patient Success Program, supplies of Xyrem® that are intended to last longer than a month may be shipped
- The quantity of drug shipped to the patient with each refill may also be regulated based on the requirements of the patient's health insurance plan and the terms of the prescription itself
- It is anticipated that the majority of patients will receive only one month's shipment at a time and never more than 3 months' supply per shipment.

10.1.2 Drug Product Kit

The drug product kit will consist of

- The drug product, a clear solution, in a 180 mL amber bottle with a closure mechanism that is child-resistant
- The Press-In-Bottle-Adapter (PIBA Well) which will be inserted into the bottle by the pharmacist
- An Exacta-Med Dispenser which allows the patient to withdraw the appropriate dose of drug
- Two child-resistant dosing cups, one for each of 2 nightly doses. The first dose will be consumed just prior to lying down at bedtime and the second dose will be placed at the bedside, and sealed with a childproof lid until consumed by the patient 2.5 to 4 hours later.
- A package insert which includes a Medication Guide

Every box of Xyrem® shipped to the patient will contain all the above items

10.1.3 Xyrem® Physician Success Program

This program consists of a videotape and printed material(s) to educate physicians about the features of Xyrem®. When a physician prescribes the drug for the first time, he/she will be mailed the program; the mailing will be documented as will a follow-up phone call to the physician confirming receipt and

the physician must verify that they have read the materials before the medication will be sent to the patient

10.1.4 Xyrem® Patient Success Program

This program consists of a videotape and printed educational material. The patient will receive this material prior to the first shipment of drug.

10.2 Proposed Physician Success Program

The components of this section are as follows

10.2.1 Dear Doctor Letter

In this letter the following are outlined

- Indication for which Xyrem® is approved
- Active ingredient in Xyrem®
- Reason for Xyrem® being marketed under a restricted distribution program
- Patient responsibilities and requirements
- Physician responsibilities and requirements
- That monitoring patients for efficacy and safety is a condition for approval. For that purpose evaluation forms have been provided which the physician has been asked to fill in every 3 months for the first 6 months.
- A toll-free number for the Xyrem® Physician Success Program

10.2.2 Booklet

The booklet has the following headings

- Prescribing Xyrem® - A Brief Guide
- Prescription and Enrollment Form
- Suggested Guidelines for Titrating Xyrem®
- Information You Need To Know About Xyrem®
- Contact Information
- Package Insert (copied below)

APPEARS THIS WAY
ON ORIGINAL

Prescription and Enrollment Form

Prescriber Information

Prescriber's Name: _____ Office Contact: _____
Street Address: _____
City: _____ State: _____ Zip: _____
Phone: _____ Fax: _____
License Number: _____ DEA Number: _____
MD Specialty: ☐ N ☐ PUD ☐ IM ☐ FP ☐ GP ☐ Other _____

Prescription Form

Patient Name: _____ SS#: _____ DOB: ____ Sex: M / F
Address: _____
City: _____ State: _____ Zip: _____
Rx: Xyrem Oral Solution (500 mg/mL) Quantity: ____ One Month's Supply
Sig: Take ____ gms p.o. diluted in 60mL water at h.s. and then again 2 1/2 to 4 hours later.
Refills (circle one): 1 2 3 (maximum of 3 month supply)
_____ Date: ____/____/____
Prescriber's Signature

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 by FDA only for the treatment of cataplexy in patients with narcolepsy

Patient Information

Best time to contact patient: ☐ Day ☐ Evening
Day #: _____ Evening #: _____
Insurance Company Name: _____ Phone #: _____
Insured's Name: _____ Relationship to Patient: _____
Identification Number: _____ Policy/Group Number: _____
Prescription Card: ☐ No ☐ Yes If Yes, Carrier: _____ Policy #: _____ Group: _____
Please attach copies of patient's insurance cards

Statement of Medical Necessity

Anticipated Start Date: _____ (Xyrem Success Program will call to verify date)
Pertinent medical history and clinical course: _____
_____
Diagnosis: _____
Previous Treatments Tried and Failed: _____
_____

- Medication Guide

10.2.3 Video

The sponsor states that

- A storyboard and proposed text has previously been submitted to the NDA
- A prototype video has been submitted to the briefing booklet for the FDA Advisory Panel meeting
- A new video will be prepared once final labeling is arrived at and agreed upon

10.2.4 Patient Evaluation Program

This section contains the following components

10.2.4.1 Dear Doctor Letter

This explains

- The purpose of the Program which is fulfil a commitment made as a condition for approval to provide data on the first 6 months of Xyrem® therapy for 1000 patients to the FDA
- What the physician needs to do to fulfil this requirement: complete the Xyrem® Post-Marketing Evaluation Form at repeat visits every 6 months during the first 6 months of treatment (i.e., the form must be completed twice); and whenever any adverse event occurs

10.2.4.2 Instructions For Completion Of Xyrem® Post-Marketing Evaluation Form

10.2.4.3 Xyrem® Post-Marketing Evaluation Form

This 2-page form is copied below

Patient Information: Gender (✓ one): ☐ Male ☐ Female; Initials: ☐☐☐; Date of birth: Month / Day / Year; Weight: ☐☐☐ ☐ lb ☐ kg

Relevant history, including pre-existing medical conditions

Xyrem® Oral Solution: Total nightly dose: ______

Xyrem® Therapy Start Date: Month / Day / Year

Relevant Tests/ Laboratory Data, including dates

Concomitant medical products and therapy dates

Lot # (if known): ______ **Expiration Date (if known):** Month / Day / Year

Ask patient if they've had any medical events or symptoms over the last 3 months that they would like to report. ☐ None

Adverse Event (Diagnosis or syndrome if known or signs/symptoms)	Is Event Serious? (See criteria below) Yes No	Is Event Unexpected? (Not listed in current label.) Yes No	Date of Onset (Day/Month/Year)	Stop Date (Day/Month/Year)	Nightly Dosage at Onset	Event abated after drug stopped or dose reduced Yes No	Event reappeared after reintroduction Yes No	Frequency	Severity	Relationship to Xyrem®	Action Taken with Xyrem®
	☐ ☐	☐ ☐	/ /	/ /		☐ ☐	☐ ☐				
	☐ ☐	☐ ☐	/ /	/ /		☐ ☐	☐ ☐				
	☐ ☐	☐ ☐	/ /	/ /		☐ ☐	☐ ☐				
	☐ ☐	☐ ☐	/ /	/ /		☐ ☐	☐ ☐				
	☐ ☐	☐ ☐	/ /	/ /		☐ ☐	☐ ☐				

→ YES, please indicate which criteria apply

Serious Adverse Event Reporting Information: All SERIOUS and UNEXPECTED events must be reported. Call the Medical Monitor at Orphan Medical at 888-867-7426 within 24 hours for any Adverse Event resulting in the following outcomes:

- ☐ Death
- ☐ A life-threatening adverse drug experience
- ☐ Inpatient hospitalization or prolongation of existing hospitalization
- ☐ A persistent or significant disability/incapacity
- ☐ A congenital anomaly/birth defect
- ☐ Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when they may jeopardize the patient and require medical or surgical intervention to prevent one of the outcomes listed previously.

Name/Address of Reporter: (please PRINT)

Phone number: ( ) -

Signature:

Date: Month / Day / Year

Ask the patient if they ever had this symptom?	Yes	No	Had it in the last 3 months? Yes	No	Has it changed since Xyrem® treatment? Better	Unchanged	Worse
Vomiting	☐	☐	☐	☐	☐	☐	☐
Incontinence	☐	☐	☐	☐	☐	☐	☐
Sleepwalking	☐	☐	☐	☐	☐	☐	☐
Confusion	☐	☐	☐	☐	☐	☐	☐
Convulsions	☐	☐	☐	☐	☐	☐	☐

If selected, complete above.

(For sponsor completion only.) **Manufacturer report number:** ______ **Date rec'd by manufacturer:**

Report Type: ☐ 15-day ☐ Initial ☐ Periodic ☐ 5-day ☐ Follow-up # ______

If patient discontinued please state reason for discontinuation: ______ If stopped: ☐☐ ☐☐ ☐☐☐☐

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