DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-196/S-005

Orphan Medical, Inc.
(A Subsidiary of Jazz Pharmaceuticals)
13911 Ridgedale Drive, Suite 250,
Minnetonka, MN 55305

Dear Dr. Reardan:

Please refer to your supplemental new drug application dated January 14, 2005, received January 18, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Xyrem ® (sodium oxybate) oral solution.

We also refer to your new drug application for this drug product, which was reviewed and approved under the restricted distribution regulations contained in 21 CFR 314.500 (Subpart H) to assure safe use of the product.

We acknowledge receipt of your additional submissions to this supplemental application dated March 15, 2005, April 4, 2005, and November 7, 2005.

This supplemental new drug application provides for the use of Xyrem ® (sodium oxybate) oral solution for the treatment of excessive daytime sleepiness in patients with narcolepsy.

We have completed our review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed, agreed-upon labeling text. Accordingly, this application is approved, effective on the date of this letter.

Final Printed Labeling

The final printed labeling (FPL) must be identical to the enclosed agreed upon labeling text for the Product Package Insert, Medication Guide, Xyrem® Success Program For Physicians (Book, Letter and Registration Form), and Xyrem® Success Program For Physicians (Book, Letter, and Patient Prescription & Enrollment Form).

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 21-196/S-005**." Approval of this submission by FDA is not required before the labeling is used.

Request for Removal of the Pre-submission Requirement for Promotional Materials

We note that in your January 14, 2005 submission, you request FDA to withdraw the 30-day promotional pre-submission requirement (21 CFR Part 314.550) as allowed under 21 CFR 314.560 for Xyrem (sodium oxybate) oral solution, NDA 21-196. We are denying your request. We believe that it is important for the Division of Drug Marketing, Advertising, and Communications (DDMAC) to review the proposed materials before their dissemination to ensure the continued appropriateness of the advertising campaign.

Accordingly, as required by 21 CFR 314.550, please continue to submit three copies of all promotional materials including promotional labeling and advertisements at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement with a cover letter requesting advisory comment. Send one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

Fulfillment of Postmarketing Commitment

We note that, in the supplemental application, you propose to discontinue the Xyrem® Post-Marketing Evaluation Program, which was intended to collect solicited safety data on an additional 1000 patients following the approval of Xyrem® and was specified as Postmarketing Study Commitment #3 in the original Xyrem® approval letter dated July 17, 2002.

We have reviewed your arguments regarding the discontinuation of this program and agree that it may be stopped. Therefore, we also conclude that Postmarketing Study Commitment #3 has been fulfilled.

Please note, however, that Postmarketing Study Commitment #2 (Conduct a clinical study in subjects with respiratory compromise), acknowledged in our July 17, 2002 letter, is still open.

Dear Health Care Professional Letter

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Building 22 Mail Stop 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80, 314.81, 314.520, 314.550 and 314.560.

If you have any questions, call Jacqueline H. Ware, Pharm.D., Senior Regulatory Project Manager, at (301) 796-2050.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosures:
Package Insert
Patient MedGuide
Risk Management Plan
Xyrem® Success Program For Physicians (Book, Letter and Registration Form)
Xyrem® Success Program For Physicians (Book, Letter, and Patient Prescription & Enrollment Form)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Russell Katz
11/18/2005 04:09:04 PM