CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

212690Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document

XYWAV (calcium, magnesium, potassium, and sodium oxybates) and XYREM (sodium oxybate) REMS Program

I. Administrative Information

Application Numbers: NDA 21196; NDA 212690
Application Holder: Jazz Pharmaceuticals, Inc (NDA 21196); Jazz Pharmaceuticals Ireland, Ltd. (NDA 212690)
Initial REMS Approval: 02/2015
Most Recent REMS Update: [07/2020]

II. REMS Goal

The goal of the XYWAV and XYREM REMS is to mitigate the risks of serious adverse outcomes resulting from inappropriate prescribing, misuse, abuse, and diversion of XYWAV and XYREM by:

1. Informing prescribers, pharmacists, and patients of:
    a. The risk of significant CNS and respiratory depression associated with XYWAV and XYREM
    b. The contraindication of use of XYWAV and XYREM with sedative hypnotics and alcohol
    c. The potential for abuse, misuse, and overdose associated with XYWAV and XYREM
    d. The safe use, handling, and storage of XYWAV and XYREM
2. Ensuring that pharmacy controls exist prior to filling prescriptions for XYWAV and XYREM that:
    a. Screen for concomitant use of sedative hypnotics and other potentially interacting agents
    b. Monitor for inappropriate prescribing, misuse, abuse, and diversion of XYWAV and XYREM
    c. Notify prescribers when patients are receiving concomitant contraindicated medications or there are signs of potential abuse, misuse, or diversion

III. REMS Requirements

Jazz Pharmaceuticals must ensure that healthcare providers, patients, and the pharmacy comply with the following requirements:

1. Healthcare providers who prescribe XYWAV and XYREM must:	
To become certified to prescribe	1. Review the XYWAV and XYREM Prescribing Information. 2. Review the following: Prescriber Brochure. 3. Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS Program.
Before treatment initiation (first dose)	4. Assess the patient's health status to determine if XYWAV or XYREM is medically appropriate by screening for history of alcohol or substance abuse, sleep-related breathing disorders, compromised respiratory function, and depression or suicidality.

1. Healthcare providers who prescribe XYWAV and XYREM must:	
	5. Assess the patient's health status to determine if XYWAV or XYREM is medically appropriate by screening for concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents. Document and submit to the REMS Program using the product-specific Prescription Form. 6. Counsel the patient on the serious risks associated with XYWAV and XYREM safe use, handling, and storage using the XYWAV Patient Quick Start Guide, XYREM Patient Quick Start Guide, XYWAV Brochure for Pediatric Patients and their Caregivers, or XYREM Brochure for Pediatric Patients and their Caregivers. 7. Enroll the patient by completing and submitting the Patient Enrollment Form to the REMS Program. 8. Order the prescription using either the XYWAV Prescription Form or XYREM Prescription Form and submit it to the REMS Program.
Before treatment re-initiation	9. For patients dis-enrolled for suspicion of abuse, misuse or diversion: communicate with the pharmacy and agree it is appropriate to re-enroll the patient. 10. For patients with a lapse in treatment of 6 months or longer: order the prescription using either the XYWAV Prescription Form or XYREM Prescription Form and submit it to the REMS program.
During treatment; within the first 3 months of starting treatment and recommended every 3 months thereafter	11. Assess the patient for: concomitant use of sedative hypnotics, other CNS depressants, or potentially interacting agents; serious adverse events; and signs of abuse and misuse including an increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, and drug-seeking behavior.
At all times	12. Report all potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, and death, and any cases of suspected abuse, misuse, or diversion to Jazz Pharmaceuticals.

2. Patients who are prescribed XYWAV and XYREM:

Before treatment initiation	1. Review the XYWAV Patient Quick Start Guide, XYREM Patient Quick Start Guide, XYWAV Brochure for Pediatric Patients and their Caregivers, or XYREM Brochure for Pediatric Patients and their Caregivers. 2. Receive counseling from the prescriber on the serious risks associated with XYWAV and XYREM and safe use, handling, and storage of XYWAV and XYREM using the XYWAV Patient Quick Start Guide, XYREM Patient Quick Start Guide, XYWAV Brochure for Pediatric Patients and their Caregivers, or XYREM Brochure for Pediatric Patients and their Caregivers. 3. Enroll in the REMS Program by completing the Patient Enrollment Form with the prescriber. Enrollment information will be provided to the REMS Program. 4. Complete the Patient Counseling Checklist with the pharmacist.
During treatment	5. Adhere to the safe use conditions described in the XYWAV Patient Quick Start Guide, XYREM Patient Quick Start Guide, XYWAV Brochure for Pediatric Patients and their Caregivers, or XYREM Brochure for Pediatric Patients and their Caregivers. 6. Complete the Patient Counseling Checklist with the pharmacist based on changes in your medication and/or medical history.
During treatment; within the first 3 months of starting treatment and recommended every 3 months thereafter	7. Be monitored for concomitant use of sedative hypnotics, other CNS depressants, or potentially interacting agents; serious adverse events; signs of abuse and misuse including an increase in dose or frequency of dosing; reports of lost, stolen, or spilled medication; and drug-seeking behavior.
Before treatment re-initiation, after lapse in treatment for 6 months or longer	8. Complete the Patient Counseling Checklist with the pharmacist.
At all times	9. Inform your prescriber and the pharmacy about any new medications you may be taking or medical conditions you may have.

3.The pharmacy that dispenses XYWAV and XYREM must:

To become certified to dispense	1. For all relevant staff involved in dispensing: review the Pharmacy Training Program – Module A. 2. For all relevant staff involved in dispensing: successfully complete the Module A Knowledge Assessment and submit it to the REMS Program. 3. For all pharmacists involved in dispensing: review the Pharmacy Training Program – Module A and B. 4. For all pharmacists involved in dispensing: successfully complete the Module A Knowledge Assessment and Module B Knowledge Assessment and submit it to the REMS Program. 5. Train all pharmacists involved in dispensing per the requirements of the Pharmacy Training Program – Module B. 6. Establish processes and procedures to verify the following: the patient and prescriber are enrolled, the patient has no other active XYWAV or XYREM prescriptions. 7. Establish processes and procedures to verify all the prescription information including patient name and two additional identifiers, prescriber name and information, dose, titration information (if applicable), number of refills, dosing directions, total quantity (days' supply), and concomitant medications. 8. Establish processes and procedures to assess the patient's concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents that either are unknown to the prescriber or pose a high risk of serious interaction. 9. Establish processes and procedures to provide 24-7 toll-free access to a XYWAV and XYREM REMS Program pharmacist; to dispense no more than a one-month supply for the initial shipment and no more than a three-month supply for subsequent shipments; and to ship, track, and verify receipt of XYWAV and XYREM to the patient or patient-authorized adult designee using an overnight service.

Before dispensing	10.	For new patients and existing patients who restart treatment after not receiving XYWAV or XYREM for 6 months or longer: Counsel the patient using the Patient Counseling Checklist. Document and submit to the REMS Program using the Central Database.
	11.	For patients who report a change in their medication use or medical history: document and submit to the REMS Program using the Central Database.
	12.	Assess the patient's concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents that either are unknown to the prescriber or pose a high risk of serious interaction using the processes and procedures established as a requirement of the REMS Program.
	13.	Verify in the Central Database that the patient and prescriber are enrolled and that the patient has no other active XYWAV or XYREM prescriptions through the processes and procedures established as a requirement of the REMS Program.
	14.	For patients previously dis-enrolled for suspicion of abuse, misuse or diversion: communicate all relevant patient history to the prescriber and re-enroll the patient if the prescriber and pharmacist agree.
	15.	Verify the patient's prescription information, including patient name and two additional identifiers, prescriber name and information, dose, titration information (if applicable), number of refills, dosing directions, total quantity (days' supply), and concomitant medications through the processes and procedures established as a requirement of the REMS Program.
	16.	Assess the patient's potential for abuse, misuse, and diversion by reviewing the alerts and Risk Management Report history in the Central Database.
	17.	For patients who request an early refill or if abuse, misuse or diversion is suspected: Discuss the request or concern with the prescriber.
	18.	Dispense no more than a one months' supply for the initial shipment.
	19.	Dispense no more than a three months' supply for subsequent shipments.
Before Shipping	20.	Verify the patient's shipping address and that the patient or patient-authorized adult designee will be available to receive the shipment through the processes and procedures established as a requirement of the REMS.
	21.	Ship XYWAV and XYREM directly to each patient or a patient-authorized adult designee through the processes and procedures established as a requirement of the REMS.
	22.	Provide the patient with the XYWAV Patient Quick Start Guide, XYREM Patient Quick Start Guide, XYWAV Brochure for Pediatric Patients and their Caregivers, or XYREM Brochure for Pediatric Patients and their Caregivers with the first shipment.

After Shipping	23.	Track and verify receipt of each shipment of XYWAV and XYREM through the processes and procedures established as a requirement of the REMS.
	24.	Document and submit the shipment and receipt dates to the Central Database.
To Maintain Certification to Dispense, Every Year	25.	For all relevant staff involved in dispensing: review the Pharmacy Training Program – Module A.
	26.	For all relevant staff involved in dispensing: successfully complete the Module A Knowledge Assessment and submit it to the REMS Program.
	27.	For all pharmacists involved in dispensing: review the Pharmacy Training Program – Modules A and B.
	28.	For all pharmacists involved in dispensing: successfully complete the Module A Knowledge Assessment and Module B Knowledge Assessment and submit it to the REMS Program.
	29.	Train all pharmacists involved in dispensing on the requirements of the REMS Program using Pharmacy Training Program – Module B.
At all times	30.	Provide 24-7 toll-free access to a XYWAV and XYREM REMS Program pharmacist.
	31.	Ship XYWAV or XYREM directly to the patient or a patient-authorized adult designee using an overnight service.
	32.	Document and report all potential adverse events reported by all sources, including any CNS depression, respiratory depression, loss of consciousness, coma, and death to Jazz Pharmaceuticals.
	33.	Report lost, stolen, destroyed, or spilled drug to the Central Database using the Risk Management Report.
	34.	Monitor for all instances of patient and prescriber behavior that give rise to a reasonable suspicion of abuse, misuse, and diversion, including all requests for early refills, and all reports of lost, stolen, destroyed, or spilled drug. Report to Jazz Pharmaceuticals by documenting into the Central Database using the Risk Management Report.
	35.	Not distribute, transfer, loan, or sell XYWAV or XYREM.
	36.	Not stock XYWAV or XYREM in retail pharmacies.
	37.	Maintain records documenting staff's completion of the Pharmacy Training Program.
	38.	Comply with audits carried out by Jazz Pharmaceuticals or a third party acting on behalf of Jazz Pharmaceuticals to ensure that all processes and procedures are in place and are being followed.

Jazz Pharmaceuticals must provide training to healthcare providers who prescribe XYWAV and XYREM.
The training includes the following educational material: Prescriber Brochure. The training must be available on a website or delivered by Jazz Pharmaceuticals.

Jazz Pharmaceuticals must provide training to the pharmacy that dispenses XYWAV and XYREM.
The training includes the following educational materials: Certified Pharmacy Training Program-Module A and B, Module A Knowledge Assessment, and Module B Knowledge Assessment. The training must be available on a website or delivered by Jazz Pharmaceuticals.

To support REMS Program operations, Jazz Pharmaceuticals must:

1. Certify a pharmacy through a contract and distribute XYWAV and XYREM only to the certified pharmacy for dispensing.

2. Not stock XYWAV or XYREM in retail pharmacies.

3. Establish and maintain a REMS Program website, www.XYWAVXYREMREMS.com. The REMS Program website must include the capability to complete prescriber certification and patient enrollment, and the option to print the Prescribing Information and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS Program website must not link back to the promotional product website(s).

4. Make the REMS Program website fully operational and all REMS materials available through the website or call center within 180 calendar days of REMS modification (07/21/2020).

5. Establish and maintain a REMS Program call center for REMS participants at 1-866-997-3688.

6. Establish and maintain a validated, secure database, called the Central Database, of all REMS participants who have been or are enrolled and/or certified in the XYWAV and XYREM REMS Program. The database must include the following information: prescriber and patient enrollment status, all completed forms, prescription and shipment data as well as dosing, concomitant medications, behavior that raises suspicion of abuse, misuse, or diversion including all alerts and risk management reports.

7. Ensure prescribers are able to submit the Prescriber Enrollment Form by facsimile, mail, email, and online.

8. Ensure prescribers are able to submit the Patient Enrollment Form by facsimile, mail, and online.

9. Ensure prescribers are able to submit the Prescription Form by facsimile and mail.

10. Ensure prescribers are able to add refills and renew prescriptions by phone, facsimile, mail, and electronically

11. Ensure pediatric patients are able to change caregivers provided that the new caregiver has been counseled by the pharmacy on the serious risks and safe use of XYWAV and XYREM and acknowledges that he/she had any questions about XYWAV and XYREM answered before drug product is dispensed and shipped.

12. Ensure patients are able to change prescribers.

13. Ensure that the pharmacy is able to report lost, stolen, destroyed or spilled drug by completing a Risk Management Report in the Central Database.

14. Ensure that the pharmacy is able to report repeated incidents of lost, stolen, destroyed, or spilled drug by creating an alert on the patient's profile in the Central Database.

15. Ensure that the pharmacy is able to disenroll patients, in consultation with the prescriber and/or Jazz Pharmaceuticals, after review of incidents suggestive of abuse, misuse, or diversion by changing the patient's enrollment status in the Central Database.

16. Notify Prescribers within 2 business days after they become certified in the REMS Program.

17. Provide the certified pharmacy access to the database of certified prescribers and enrolled patients.

To ensure REMS participants' compliance with the REMS Program, Jazz Pharmaceuticals must:

18. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: XYREM distribution and dispensing; XYWAV distribution and dispensing, certification of prescribers, and the certified pharmacy; enrolled patients; and audits of REMS participants. These records must be readily available for FDA inspections.
19. Ensure that a prescriber is enrolled in the REMS Program only after verification that the Prescriber Enrollment Form is complete and all enrollment requirements are met.
20. Establish a plan for addressing noncompliance with REMS Program requirements.
21. Monitor prescribers and the certified pharmacy on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including de-certification.
22. Monitor the certified pharmacy for timely reporting to Jazz Pharmaceuticals of all potential adverse events and any behavior by patients or prescribers enrolled in the REMS Program that raises suspicion of abuse, misuse or diversion.
23. Monitor the Central Database on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified.
24. Audit the certified pharmacy at least annually.
25. Take reasonable steps to improve implementation of and compliance with the requirements in the XYWAV and XYREM REMS Program based on monitoring and evaluation of the XYWAV and XYREM REMS Program.

IV. REMS Assessment Timetable

Jazz Pharmaceuticals must submit REMS Assessments every 6 months from the date of the REMS approval (02/2015) for the first year, and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Jazz Pharmaceuticals must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the XYWAV and XYREM REMS:

Enrollment Forms

Prescriber:

1. Prescriber Enrollment Form

Patient:

2. Patient Enrollment Form

Training and Educational Materials

Prescriber:

3. Prescriber Brochure

Patient:

4. XYREM Patient Quick Start Guide
5. XYREM Brochure for Pediatric Patients and their Caregivers
6. XYWAV Patient Quick Start Guide
7. XYWAV Brochure for Pediatric Patients and their Caregivers

Pharmacy

8. Certified Pharmacy Training Program
9. Module A Knowledge Assessment
10. Module B Knowledge Assessment

Patient Care Forms

11. XYREM Prescription Form
12. XYWAV Prescription Form
13. Patient Counseling Checklist

Other Materials

14. Risk Management Report
15. REMS Program website

XYWAV and XYREM REMS

XYWAV and XYREM REMS PRESCRIBER ENROLLMENT FORM

XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL
XYREM® (sodium oxybate) oral solution 0.5 g/mL

Complete and submit form online at www.XYWAVXYREMREMS.com, OR scan and e-mail to ESSDSPrescribers@express-scripts.com, OR fax to XYWAV and XYREM REMS at 1-866-470-1744 (toll free), OR mail to XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589.

For more information, please call the XYWAV and XYREM REMS at 1-866-997-3688 (toll free).

Note: Completion of this form and enrollment in the REMS allows you to prescribe both XYWAV and XYREM.

Step 1: ALL BOXES BELOW MUST BE CHECKED (☑) IN ORDER FOR THE ENROLLMENT PROCESS TO BE COMPLETE AND BEFORE YOU CAN ENROLL PATIENTS AND PRESCRIBE XYWAV or XYREM.

☐ I understand that XYWAV and XYREM are indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

☐ I have read the Prescribing Information (PI) and the XYWAV and XYREM REMS Prescriber Brochure and understand that:
- XYWAV and XYREM are Schedule III CNS depressants and can cause obtundation and clinically significant respiratory depression at recommended doses
- The use of XYWAV or XYREM in combination with alcohol or sedative hypnotics is contraindicated.
- Concurrent use of XYWAV or XYREM with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptics, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with XYWAV or XYREM use

☐ I agree to:
- Enroll each patient in the XYWAV and XYREM REMS
- Screen each patient for history of alcohol or substance abuse, sleep-related breathing disorders, compromised respiratory function, depression, suicidality, and concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
- Counsel each patient and/or caregiver prior to initiating therapy on the serious risks and safe use, handling, and storage of XYWAV or XYREM
- Evaluate patients within the first 3 months of starting XYWAV or XYREM. It is recommended that patients be re-evaluated every 3 months thereafter while taking XYWAV or XYREM
- Report all potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, and death, and any cases of suspected abuse, misuse, or diversion to Jazz Pharmaceuticals

Step 2: To help expedite the enrollment process, please **PRINT** clearly (*denotes required field).

Prescriber Information

*First Name: _____ M.I.: _____ *Last Name: _____ Prof. Designation (MD, DO, PA, NP): _____

*DEA No.: _____ *State License No.: _____ *NPI no.: _____

Facility/Practice Name: _____

*Street Address: _____

*City: _____ *State: _____ *Zip Code: _____

*Phone: _____ *Fax: _____ E-mail: _____

Office Contact: _____ Office Contact Phone: _____

Additional office locations and contacts can be entered online at XYWAVXYREMREMS.com.

Step 3: Prescriber signature is required below for enrollment in the XYWAV and XYREM REMS.

By signing below, I acknowledge the above attestations, and I understand that my personally identifiable information provided above will be shared with Jazz Pharmaceuticals, Inc., its agents, contractors, and affiliates and entered into a prescriber database for the XYWAV and XYREM REMS. I agree that I may be contacted in the future by mail, e-mail, fax, and/or telephone concerning XYWAV, XYREM, and the XYWAV and XYREM REMS.

*Prescriber Signature: _____ *Date: _____

Report SERIOUS ADVERSE EVENTS by contacting Jazz Pharmaceuticals at 1-800-520-5568 or jazzsafety@jazzpharma.com.

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL III

XYREM® (sodium oxybate) oral solution III

Reference ID: 4644289

XYWAV and XYREM REMS

XYWAV and XYREM REMS PATIENT ENROLLMENT FORM

XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL
XYREM® (sodium oxybate) oral solution 0.5 g/mL

Complete and submit form online at www.XYWAVXYREMREMS.com, OR scan and e-mail to ESSDSPrescribers@express-scripts.com, OR fax to XYWAV and XYREM REMS at 1-866-470-1744 (toll free), OR mail to: XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589.
For more information, please call the XYWAV and XYREM REMS at 1-866-997-3688 (toll free).

Note: Use this form to enroll patients in the XYWAV and XYREM REMS for either product.

Please Print (*denotes required field)

Prescriber Information

*First Name: _____ M.I.: _____ *Last Name: _____ *DEA No.: _____

*Street Address: _____ *Phone: _____

*City: _____ *State: _____ *Zip Code: _____ *Fax: _____

Office Contact: _____ Office Contact Phone: _____ *NPI No: _____

Patient Information

*First Name: _____ M.I.: _____ *Last Name: _____ *Primary Phone: _____

*Date of Birth (MM/DD/YYYY): _____ *Gender: ☐ M ☐ F Cell Phone: _____

*Address: _____ Work Phone: _____

*City: _____ *State: _____ *Zip Code: _____ E-mail: _____

Caregiver Name: _____ Relationship to Patient: _____ Caregiver Phone (if different than above): _____

Insurance Information

Does Patient Have Prescription Coverage? ☐ Yes (provide photocopy of both sides of insurance identification card with this form) ☐ No

Policy Holder's Name: _____ Policy Holder's Date of Birth (MM/DD/YYYY): _____

Insurance Company Name: _____ Relationship to Patient: _____

Insurance Phone: _____ RxID No.: _____ RxGrp No.: _____

RxBIN No.: _____ RxPCN No.: _____

Patient/Caregiver: Form must be signed before enrollment can be processed.

By signing below, I acknowledge that:

- My doctor/prescriber has counseled me on the serious risks and safe use of XYWAV and XYREM
- I have asked my doctor/prescriber any questions I have about XYWAV and XYREM

***Patient/Caregiver Signature:** _____ ***Date:** _____

***Printed Caregiver Name (if applicable):** _____

Prescriber: Form must be signed before enrollment can be processed.

By signing below, I acknowledge that:

- I have counseled the patient and/or caregiver about the serious risks associated with the use of XYWAV and XYREM and the safe use conditions as descr bed in the XYWAV or XYREM Patient Quick Start Guide (for adult patients) or the XYWAV or XYREM Brochure for Pediatric Patients and their Caregivers (for pediatric patients)

☐ I have provided the patient and/or caregiver with the appropriate educational material [XYWAV or XYREM Patient Quick Start Guide (for adult patients) and XYWAV or XYREM Brochure for Pediatric Patients and their Caregivers (for pediatric patients) (optional)]

***Prescriber Signature:** _____ ***Date:** _____

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

XYREM® (sodium oxybate) oral solution

Reference ID: 4644289

XYWAV and XYREM REMS

PRESCRIBER BROCHURE

Includes important prescribing information
for adult and pediatric patients

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL C III

XYREM® (sodium oxybate) oral solution C III

Reference ID: 4644289

XYWAV and XYREM REMS

Dear Prescriber,

Welcome to the XYWAV and XYREM REMS, which was developed in collaboration with the Food and Drug Administration (FDA) as a Risk Evaluation and Mitigation Strategy (REMS). A REMS is a strategy to manage known or potential serious risks associated with a drug product and is required by the FDA to ensure that the benefits of the drug outweigh its risks.

This brochure provides information about the XYWAV and XYREM REMS that includes important prescribing information, educational and counseling requirements, and materials necessary for program enrollment and prescribing XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, and XYREM® (sodium oxybate) oral solution, including:

- **Prescriber Enrollment Form—**a one-time enrollment is required for all prescribers of XYWAV and XYREM.
- **Patient Enrollment Form—**a one-time patient enrollment in the XYWAV and XYREM REMS is required for each new patient for whom XYWAV or XYREM will be prescribed.
- **XYWAV and XYREM Prescription Forms—**required for prescribing XYWAV and XYREM. These forms must be used for initial prescriptions and may also be used for refills and renewals of XYWAV and XYREM prescriptions.
- **XYWAV and XYREM Patient Quick Start Guides—**these guides answer important questions for adult patients about how to get XYWAV and XYREM, how to use XYWAV and XYREM properly, and how to store them safely. It also gives important information about the risks associated with XYWAV and XYREM.
- **XYWAV and XYREM Brochures for Pediatric Patients and their Caregivers—**these guides answer important questions for caregivers of pediatric patients and pediatric patients about how to use XYWAV and XYREM properly, how to store them safely, and how to get XYWAV and XYREM. It also gives important information about the risks associated with XYWAV and XYREM.

The REMS Prescriber Enrollment Form, Patient Enrollment Form, and **XYWAV Prescription Form** or **XYREM Prescription Form** must be completed in full and sent to the XYWAV and XYREM REMS. For your convenience, all these forms are available online at **www.XYWAVXYREMREMS.com**, and can be requested by calling the XYWAV and XYREM REMS toll-free at 1-866-997-3688. The Certified Pharmacy with the XYWAV and XYREM REMS is responsible for processing all prescriptions for XYWAV and XYREM. Continue reading this brochure to learn more about the XYWAV and XYREM REMS and your responsibilities as a prescriber of XYWAV and XYREM.

Please review the Prescribing Information for XYWAV and XYREM.

XYWAV and XYREM may be dispensed only to patients enrolled in the XYWAV and XYREM REMS.

XYWAV and XYREM are indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy

If you require any additional assistance or information, please call the XYWAV and XYREM REMS at **1-866-997-3688** or visit **www.XYWAVXYREMREMS.com**.

Sincerely,

Jazz Pharmaceuticals

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- The use of XYWAV or XYREM in combination with sedative hypnotics is contraindicated.
- The use of XYWAV or XYREM in combination with alcohol is contraindicated.
- XYWAV and XYREM are contraindicated in patients with succinic semialdehyde dehydrogenase deficiency.

WARNINGS AND PRECAUTIONS

CNS Depression

- XYWAV and XYREM are CNS depressants. Concurrent use of XYWAV or XYREM with other CNS depressants, including but not limited to opioid analgesics; benzodiazepines; sedating antidepressants, antipsychotics, or anti-epileptics; general anesthetics; muscle relaxants; and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death.
  - If use of these CNS depressants in combination with XYWAV or XYREM is required, dose reduction or discontinuation of one or more CNS depressants (including XYWAV or XYREM) should be considered.
  - If short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with XYWAV or XYREM should be considered.
- Patients who have sleep apnea or compromised respiratory function may be at a higher risk of developing respiratory depression, loss of consciousness, coma, and death with XYWAV or XYREM use.

Healthcare providers should caution patients/caregivers against hazardous activities requiring complete mental alertness or motor coordination (e.g., driving) within the first 6 hours of dosing or after first initiating treatment until certain that XYWAV or XYREM do not affect the patient adversely.

Abuse and Misuse

- XYWAV and XYREM are Schedule III controlled substances.
- The active moiety of XYWAV and XYREM is oxybate, also known as gamma-hydroxybutyrate (GHB), a Schedule I controlled substance. Abuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse events, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. Illicit GHB has also been associated with drug-facilitated sexual assault.
- The rapid onset of sedation, coupled with the amnestic features of XYWAV and XYREM, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (e.g., assault victim).
- You should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of XYWAV or XYREM (e.g., increase in size or frequency of dosing; reports of lost, stolen, or spilled medication; drug-seeking behavior; feigned cataplexy).

XYWAV and XYREM REMS

- XYWAV and XYREM are to be prescribed only to patients enrolled in the XYWAV and XYREM REMS. XYWAV and XYREM are available only through a restricted distribution program called the XYWAV and XYREM REMS. Required components of the XYWAV and XYREM REMS are:
  - Healthcare providers who prescribe XYWAV or XYREM must be specially certified. To be certified, prescribers must complete the REMS Enrollment Forms and comply with the REMS requirements.
  - XYWAV and XYREM will be dispensed only by the central pharmacy that is specially certified.
  - XYWAV and XYREM will be shipped only to enrolled patients with documentation of safe use conditions. For a patient to be enrolled, patients or caregivers must sign the REMS Patient Enrollment Form and acknowledge that they have been counseled on the serious risks and safe use of XYWAV and XYREM.

Further information is available at **www.XYWAVXYREMREMS.com** or 1-866-997-3688.

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL III

XYREM® (sodium oxybate) oral solution III

Depression, Suicidality, and Other Behavioral/Neuropsychiatric Adverse Events

- Depression and suicidal ideation and behavior can occur in patients treated with XYWAV or XYREM
- The emergence of depression in patients treated with XYWAV and XYREM was seen in clinical trials and requires careful and immediate attention. Patients with a previous history of a depressive illness and/or suicide attempt should be monitored especially carefully for the emergence of depressive symptoms while taking XYWAV or XYREM. XYWAV and XYREM can cause the emergence of neuropsychiatric adverse events (psychosis, paranoia, hallucination, aggression, and agitation), confusion, and sleepwalking. Patients should be instructed to call their healthcare provider if they experience any of these events.
- Anxiety can also occur in patients treated with XYWAV and XYREM.

Use in Patients Sensitive to High Sodium Intake

- XYREM has a high sodium content. Administration of the maximum recommended dose of XYREM (9g/night) delivers 1,640mg of sodium, corresponding to 71% of the recommended maximum daily intake of sodium (2,300 mg/day).
- Daily sodium intake should be considered in patients, particularly those on salt-restricted diets or with heart failure, hypertension, or compromised renal function.

Most Common Adverse Events

- In three controlled clinical trials with adult patients, the most common adverse reactions (incidence ≥5% and twice the rate seen with placebo) in XYREM-treated patients were nausea (20%), dizziness (15%), vomiting (11%), somnolence (8%), enuresis (7%), and tremor (5%).
- Of the 398 XYREM-treated adult patients with narcolepsy, 10.3% of patients discontinued because of adverse reactions compared with 2.8% of patients receiving placebo. The most common adverse reaction leading to discontinuation was nausea (2.8%). The majority of adverse reactions leading to discontinuation began during the first few weeks of treatment.
- The overall adverse reaction profile of XYREM (same active moiety as XYWAV) in pediatric patients (7 years of age and older) is similar to that in adult patients. The most common adverse reactions (>5%) were enuresis (18%), nausea (17%), headache (16%), vomiting (16%), weight decreased (12%), decreased appetite (8%), and dizziness (6%).
- In a 16 week double-blind placebo-controlled randomized withdrawal study in 201 patients with narcolepsy with cataplexy the most common adverse reactions (incidence ≥ 5% of XYWAV-treated patients) were headache (20%), nausea (13%), dizziness (10%), decreased appetite (8%), parasomnia (6%), diarrhea (6%), hyperhidrosis (6%), anxiety (5%), and vomiting (5%). 9 out of 201 patients (4%) reported adverse reactions that led to withdrawal from the study (anxiety, decreased appetite, depressed mood, depression, fatigue, headache, irritability, nausea, pain in extremity, parasomnia, somnolence, and vomiting). The most common adverse reaction leading to discontinuation was nausea (1.5%). The majority of adverse reactions leading to discontinuation began during the first few weeks of treatment.

Please see Prescribing Information for XYWAV and XYREM.

TABLE OF CONTENTS

Prescribing Information is also included

Prescribing XYWAV and XYREM—A Brief Guide

The XYWAV and XYREM REMS applies to XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL, and XYREM® (sodium oxybate) oral solution, 0.5 g/mL. XYWAV and XYREM are both aqueous solutions with the active moiety of oxybate. These products are subject to a REMS because they both contain oxybate, or gamma-hydroxybutyrate (GHB), a CNS depressant and a known drug of abuse. In order to prescribe either of these products, you will need to comply with the prescribing requirements outlined in the XYWAV and XYREM REMS, which are the same for both drugs.
The procedures for writing and dispensing prescriptions for XYWAV and XYREM are outlined below.

PRESCRIBERS OF XYWAV AND XYREM

PRESCRIBER ENROLLMENT

Prescribing XYWAV and XYREM requires a one-time enrollment.

- **If you are prescribing XYWAV or XYREM for the first time**, complete the **REMS Prescriber Enrollment Form**, found either accompanying this Prescriber Brochure or online at **www.XYWAVXYREMREMS.com**. Please:
  - Submit the form online at **www.XYWAVXYREMREMS.com** *or*
  - Scan and send via e-mail to ESSDSPrescribers@express-scripts.com *or*
  - Mail to **XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589** *or*
  - Fax to **1-866-470-1744** (toll free).
- On the **REMS Prescriber Enrollment Form**, please confirm that:
  - You understand that XYWAV and **XYREM** are indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy
  - You have read and understand the Prescribing Information and this Prescriber Brochure

SCREEN

- You agree to screen each patient for:
  - History of alcohol or substance abuse
  - History of sleep-related breathing disorders
  - History of compromised respiratory function
  - Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
  - History of depression or suicidality

COUNSEL

- You agree to counsel your patients and/or caregivers (for pediatric patients) on:
  - The serious risks associated with XYWAV and XYREM
  - Contraindications (alcohol and sedative hypnotics)
  - Risks of concomitant use of XYWAV or XYREM with alcohol and/or other CNS depressants, including sedating antidepressants, antipsychotics, or anti-epileptics; opioids; benzodiazepines; muscle relaxants; and general anesthetics
  - Risk of engaging in hazardous activities requiring complete mental alertness or motor coordination (e.g., driving) within the first 6 hours of dosing or after first initiating treatment until certain that XYWAV or XYREM does not affect the patient adversely
  - Preparation and dosing instructions for XYWAV and XYREM
  - The risk of abuse and misuse associated with use of XYWAV and XYREM
  - Safe use, handling, and storage of XYWAV and XYREM

ENROLL

- You will enroll each patient in the XYWAV and XYREM REMS by completing the one-time **REMS Patient**

Enrollment Form and submitting the form to the XYWAV and XYREM REMS. A pediatric patient must have a caregiver

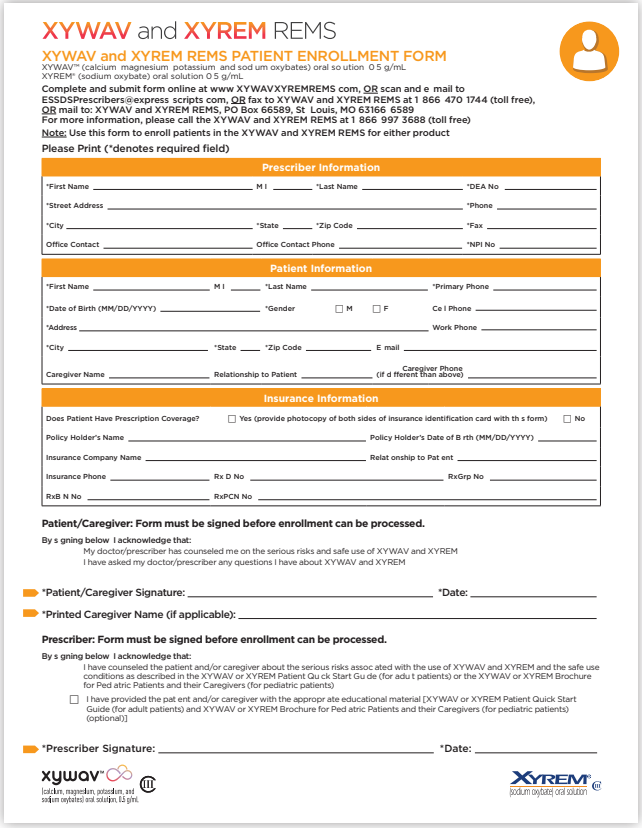
- You will evaluate each patient within the first 3 months of starting XYWAV or XYREM, including an evaluation of the following. It is recommended that patients be re-evaluated every 3 months thereafter while on XYWAV or XYREM therapy:
  - Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
  - Serious adverse events
  - Signs of abuse and misuse such as an increase in dose or frequency of dosing; reports of lost, stolen, or spilled medication; and/or drug-seeking behavior

REPORT

- You will report all potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, and death, and any cases of suspected abuse, misuse, or diversion to Jazz Pharmaceuticals

PATIENT ENROLLMENT

- All patients must be enrolled one time in the XYWAV and XYREM REMS, using the **REMS Patient Enrollment Form**. A pediatric patient must have a caregiver.
- On the **REMS Patient Enrollment Form**:
  - For adult patients, verify that you have provided counseling to the patient about the serious risks associated with the use of the medication and its safe use as described in the XYWAV or XYREM Patient Quick Start Guides
  - For pediatric patients, verify that you have provided counseling to the caregiver about the serious risks associated with the use of the medication and its safe use as described in the XYWAV or XYREM Brochures for Pediatric Patients and their Caregivers
  - Obtain mandatory patient or caregiver signature acknowledging that he/she has been counseled on the serious risks and safe use conditions of XYWAV or XYREM and has had the opportunity to ask you any questions he/she may have about XYWAV or XYREM
  - Fax the completed **REMS Patient Enrollment Form** to the XYWAV and XYREM REMS at **1-866-470-1744** (toll free) or mail to **XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589**. The form can also be completed online at **www.XYWAVXYREMREMS.com**.



XYWAV and XYREM REMS

XYWAV and XYREM REMS PATIENT ENROLLMENT FORM

XYWAV™ (calcium magnesium potassium and sod um oxybates) oral so ution 0 5 g/mL
XYREM® (sodium oxybate) oral solution 0 5 g/mL

Complete and submit form online at www XYWAVXYREMREMS com, OR scan and e mail to ESSDSPrescribers@express scripts com, OR fax to XYWAV and XYREM REMS at 1 866 470 1744 (toll free), OR mail to: XYWAV and XYREM REMS, PO Box 66589, St Louis, MO 63166 6589
For more information, please call the XYWAV and XYREM REMS at 1 866 997 3688 (toll free)

Note: Use this form to enroll patients in the XYWAV and XYREM REMS for either product

Please Print (*denotes required field)

Prescriber Information

*First Name ____ M I ____ *Last Name ____ *DEA No ____
*Street Address ____ *Phone ____
*City ____ *State ____ *Zip Code ____ *Fax ____
Office Contact ____ Office Contact Phone ____ *NPI No ____

Patient Information

*First Name ____ M I ____ *Last Name ____ *Primary Phone ____
*Date of Birth (MM/DD/YYYY) ____ *Gender ☐ M ☐ F Ce l Phone ____
*Address ____ Work Phone ____
*City ____ *State ____ *Zip Code ____ E mail ____
Caregiver Name ____ Relationship to Patient ____ Caregiver Phone (if d fferent than above) ____

Insurance Information

Does Patient Have Prescription Coverage? ☐ Yes (provide photocopy of both sides of insurance identification card with th s form) ☐ No
Policy Holder's Name ____ Policy Holder's Date of B rth (MM/DD/YYYY) ____
Insurance Company Name ____ Relat onship to Pat ent ____
Insurance Phone ____ Rx D No ____ RxGrp No ____
RxB N No ____ RxPCN No ____

Patient/Caregiver: Form must be signed before enrollment can be processed.

By s gning below I acknowledge that:
My doctor/prescriber has counseled me on the serious risks and safe use of XYWAV and XYREM
I have asked my doctor/prescriber any questions I have about XYWAV and XYREM

*Patient/Caregiver Signature: ____ *Date: ____
*Printed Caregiver Name (if applicable): ____

Prescriber: Form must be signed before enrollment can be processed.

By s gning below I acknowledge that:
I have counseled the patient and/or caregiver about the serious risks assoc ated with the use of XYWAV and XYREM and the safe use conditions as described in the XYWAV or XYREM Patient Qu ck Start Gu de (for adu t patients) or the XYWAV or XYREM Brochure for Ped atric Patients and their Caregivers (for pediatric patients)
☐ I have provided the pat ent and/or caregiver with the approp ate educational material [XYWAV or XYREM Patient Quick Start Guide (for adult patients) and XYWAV or XYREM Brochure for Ped atric Patients and their Caregivers (for pediatric patients) (optional)]

*Prescriber Signature: ____ *Date: ____

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL
XYREM® (sodium oxybate) oral solution

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

XYREM® (sodium oxybate) oral solution

XYWAV and XYREM REMS

PRESCRIBING REQUIREMENTS

- Write prescriptions using either the **XYREM Prescription Form** or the **XYWAV Prescription Form** (general prescription forms will not be accepted) for the initial prescription of either product, and for patients who are reinitiating XYWAV or XYREM after a lapse in therapy of either XYWAV or XYREM for 6 months or longer. The prescription form may also be used for refills and renewals.
  - Fill out the form completely and clearly to ensure timely fulfillment of your patient's prescription
  - Verify that you have screened your patient for:
    - History of alcohol or substance abuse
    - History of sleep-related breathing disorders
    - History of compromised respiratory function
    - Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
    - History of depression or suicidality
  - Verify that you have counseled the adult patient or caregiver (for pediatric patients) regarding the information below. Refer to pages 14 and 15 of this brochure for patient counseling information.
    - The serious risks associated with XYWAV or XYREM
    - Contraindications (alcohol and sedative hypnotics)
    - The risks of concomitant use of alcohol or other CNS depressants, including sedating antidepressants, antipsychotics, or anti-epileptics; opioids; benzodiazepines; muscle relaxants; and general anesthetics
    - The risks of engaging in hazardous activities requiring complete mental alertness or motor coordination (e.g. driving) within the first 6 hours of dosing or after first initiating treatment until certain that XYWAV or XYREM does not affect the patient adversely
    - Preparation and dosing instructions for XYWAV or XYREM
    - The risk of abuse and misuse associated with use of XYWAV or XYREM
    - Safe use, handling, and storage of XYWAV or XYREM (refer to pages 14 & 15 of this brochure for Patient Counseling Information)
  - Provide a list of all current prescription and non-prescription medications and dosages that the patient is currently taking, to the best of your knowledge. Additionally, indicate the presence of relevant comorbid medical conditions. This can be done by completing the appropriate fields on the **XYWAV** or **XYREM Prescription Form** or by faxing a separate page.
  - **NOTE:** Prior to dispensing each XYWAV or XYREM prescription (including refills), the Certified Pharmacy will complete an online Drug Utilization Review (DUR) and, during the patient counseling process, will ask the patient about the use of other medicines. If the pharmacist learns that the patient is taking a previously undisclosed contraindicated medication (sedative hypnotics), an opioid, or more than one CNS depressant, and the prescriber has not indicated awareness of the concomitant medication, the Certified Pharmacy will contact and inform the prescriber of the concomitant medication use prior to dispensing XYWAV or XYREM. The pharmacist may also contact the prescriber about other concomitant medications of concern. Verify that you have informed the patient and/or caregiver that the REMS will send him/her a copy of the appropriate educational material (the XYWAV or XYREM Patient Quick Start Guide for adult patients and the XYWAV or XYREM Brochure for Pediatric Patients and their Caregivers for caregivers of pediatric patients) prior to his/her first prescription fill, if you haven't provided one previously. These materials are available through Jazz Pharmaceuticals or may be downloaded at **www.XYWAVXYREMREMS.com**
  - Both the **XYWAV Prescription Form** and the **XYREM Prescription Form** are available online at **www.XYWAVXYREMREMS.com**. You can submit the prescription forms online directly to the XYWAV and XYREM REMS, or download the forms. Downloaded forms must be printed, signed, and either faxed to the XYWAV and XYREM REMS at **1-866-470-1744** (toll free), or mailed to the **XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589**.

Please see Pediatric Patient Supplement for information on dosing for pediatric patients.

PATIENT EVALUATION

- Evaluate each patient within the first 3 months of starting XYWAV or XYREM therapy, including an evaluation of the following. It is recommended that patients be re-evaluated every 3 months thereafter while they are taking XYWAV or XYREM for:
  - Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
  - Serious adverse events
  - Signs of abuse and misuse, such as an increase in dose or frequency of dosing; reports of lost, stolen, or spilled medication; and/or drug-seeking behavior

Follow up frequently during titration to review symptom response and adverse reactions. A follow up of every three months is recommended.

REFILL PRESCRIPTIONS

- Prescription refills and renewals may be conveyed by phone, fax, mail, or through online submission at **www.XYWAVXYREMREMS.com**. In addition, the Certified Pharmacy with the XYWAV and XYREM REMS will send you the **XYWAV Prescription Form** or the **XYREM Prescription Form** upon your request. Prescription refills and renewals must be documented in the XYWAV and XYREM REMS Central Database.
- Complete refills or renewals by submitting the **XYWAV** or **XYREM Prescription Form** online at **www.XYWAVXYREMSREMS.com**
- To phone in refills or renewals for XYWAV or XYREM, call 1-866-997-3688
- To fax or mail refills or renewals for XYWAV or XYREM:
  - Fill out the **XYWAV Prescription Form** or the **XYREM Prescription Form** completely and clearly to ensure timely fulfillment of your patient's prescription
    - If downloading the **XYWAV Prescription Form** or **XYREM Prescription Form** online through **www.XYWAVXYREMREMS.com**, you must print and sign the form prior to submitting it to the XYWAV and XYREM REMS.
  - Fax the completed **XYWAV** or **XYREM Prescription Form** and all subsequent prescriptions to the XYWAV and XYREM REMS at **1-866-470-1744** (toll free) or mail to **XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589**

XYWAV and XYREM REMS

Responsibilities of the XYWAV and XYREM REMS Certified Pharmacy

FOLLOWING RECEIPT OF A PATIENT'S PRESCRIPTION, THE CERTIFIED PHARMACY WILL:

- **Provide you with confirmation** of each new XYWAV or **XYREM Prescription Form** received from your office
- **Contact the patient's insurance provider** to verify XYWAV or XYREM prescription benefits
- **Prior to the first shipment, contact the patient or caregiver and complete the counseling checklist to:**
  - Confirm whether he/she has received a copy of the appropriate educational material (XYWAV or XYREM Patient Quick Start Guide for adult patients and XYWAV or XYREM Brochure for Pediatric Patients and their Caregivers for caregivers of pediatric patients). The Certified Pharmacy will send a copy of the appropriate educational material
  - Counsel the adult patient and/or caregiver on expectations from XYWAV or XYREM therapy and how to prepare and take XYWAV or XYREM doses safely and effectively
  - Review important XYWAV and XYREM safety information and precautions for XYWAV or XYREM use
  - Review XYWAV and XYREM safe handling and storage procedures
  - Review the adverse events associated with XYWAV and XYREM use
  - Review the patient's use of concomitant medications
    - Prior to dispensing each XYWAV or XYREM prescription (including refills), the Certified Pharmacy will complete an online Drug Utilization Review (DUR) and, during the patient counseling process, will ask the patient about the use of other medicines.
    - If the pharmacist learns that the patient is taking a previously undisclosed contraindicated medication (sedative hypnotics), an opioid, or more than one CNS depressant, and the prescriber has not indicated awareness of the concomitant medication, the Certified Pharmacy will contact and inform the prescriber of the concomitant medication use prior to dispensing XYWAV or XYREM.
    - The pharmacist may also contact the prescriber about other concomitant medications of concern.
  - Review the patient's comorbid medical conditions
  - You will be notified of any potential for drug interactions or relevant comorbid medical conditions based on patient counseling
  - Ask if the patient or caregiver has any questions about XYWAV or XYREM and answer the questions and/or refer the patient or caregiver back to the prescriber, as appropriate
- **Provide 24/7 toll-free telephone access to pharmacist support** for prescribers, office staff, patients, and caregivers by answering questions about safety, dosing, and patient care
- **Dispense and ship** XYWAV or XYREM by overnight service to the patient or his/her authorized adult designee
- **Remind** patients about monthly refills
- **Contact** the prescriber if a prescription refill or renewal is required

For your convenience, materials and information regarding the XYWAV and XYREM REMS are available online at www.XYWAVXYREMREMS.com.

Please be sure to review the Prescribing Information prior to prescribing XYWAV or XYREM for your patients.

Guidelines for Dosing and Titrating XYWAV and XYREM

DOSING XYWAV AND XYREM

The information presented on this page is for adult patients. Please see pages 16—18 for additional important information on dosing for pediatric patients (7 years of age and older).

XYWAV and XYREM are liquid medications taken orally at bedtime. Due to their short half-life, XYWAV and XYREM are taken in divided doses at night, with the first dose taken at bedtime and the second dose taken 2.5 to 4 hours later.

- The recommended starting dosage is 4.5 grams (g) per night administered orally divided into two doses: 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later
- The recommended dosage range is 6 g to 9 g/night orally
- Doses higher than 9 g/night have not been studied and should not ordinarily be administered
- The dose of XYWAV and XYREM should be titrated to effect
  - Increase the dosage by 1.5 g per night at weekly intervals (additional 0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later) to the effective dosage range, based on efficacy and tolerability.
- An initial XYWAV or XYREM dose reduction of at least 20% is recommended if divalproex sodium is prescribed to patients already taking XYWAV or XYREM. For patients already taking divalproex sodium, it is recommended that prescribers use a lower starting XYWAV or XYREM dose when introducing XYWAV or XYREM. Prescribers are advised to monitor patient response closely and adjust dose accordingly if concomitant use of XYWAV or XYREM with divalproex sodium is warranted.
- Improvement may occur during the first weeks of therapy; however, titration to an optimal dose may take longer
- Once a stable dose is established, patients should be evaluated periodically

The patient's first shipment of any oxybate-containing product within the XYWAV and XYREM REMS will be limited to a 1-month (30-day) supply, and future shipments cannot exceed a 3-month (90-day) supply.

RECOMMENDED ADULT XYWAV and XYREM DOSE REGIMEN				
	1st Dose	2nd Dose	Total Nightly Dose	
Recommended starting dose	2.25 g	2.25 g	4.5 g	
	3 g	3 g	6 g	Effective Dosing Range
	3.75 g	3.75 g	7.5 g	
Maximum dose	4.5 g	4.5 g	9 g	

IMPORTANT ADMINISTRATION INSTRUCTIONS

- Inform patients that all bottles contain concentrated medication ONLY and that water for dilution is not contained in the box. Advise patients to keep XYWAV and XYREM in the provided bottle(s)
- Patients should prepare both nighttime doses at bedtime
  - Instruct patients to make sure that pharmacy vials are empty prior to preparing each dose
  - Each dose of XYWAV and XYREM should be diluted with about ¼ cup of water
  - Patients should be instructed to store XYWAV and XYREM bottles and prepared nightly doses in a secure place out of the reach of children and pets
- Doses should be taken at least 2 hours after eating.
- Both doses should be taken while in bed and the patient should lie down immediately after dosing
- The first dose should be taken at bedtime and the second dose 2.5 to 4 hours later

CHANGING BETWEEN XYWAV AND XYREM

A gram of XYWAV and a gram of XYREM both contain the same amount of the active drug, oxybate. Patients changing between XYWAV and XYREM should be started on the same dose as the previously administered product. For example, if a patient on a stable dose of 4.5g of XYREM twice nightly changes to XYWAV, they should be prescribed 4.5g of XYWAV twice nightly. Patients should then be evaluated and dosing adjustments made if necessary.

When changing a patient's therapy:

- Inform patients that the safe use and administration instructions are the same for both products
- Advise patients to never take XYWAV and XYREM at the same time.
- For patients changing to XYREM therapy: Instruct patients and/or caregivers that XYREM contains a significant amount of sodium and XYREM-treated patients, particularly those who are sensitive to sodium intake (e.g., those with heart failure, hypertension, or renal impairment) should limit their sodium intake.

Additional Information About XYWAV and XYREM

XYWAV and XYREM have been placed in a bifurcated federal schedule. XYWAV and XYREM are Schedule III controlled substances when used for legitimate medical purposes, as prescribed. XYWAV and XYREM are both aqueous solutions with the active moiety of oxybate, or gamma-hydroxybutyrate (GHB), which is classified as a Schedule I controlled substance when used for any other reason or by anyone other than for whom it was prescribed. Your patients should be informed that federal law prohibits the transfer of XYWAV and XYREM to any persons other than the patient for whom it was prescribed. If you have any questions regarding this, please call the XYWAV and XYREM REMS toll free at **1-866-997-3688**.

Illicit use and abuse of GHB have been reported, including drug-facilitated sexual assault. Prescribers should carefully evaluate patients for a history of drug abuse and follow patients closely, observing them for signs of misuse or abuse of GHB (e.g., increase in dose or frequency of dosing, reports of lost, stolen, or spilled medication, drug-seeking behavior).

WHEN PRESCRIBING A CONTROLLED SUBSTANCE:

- Be judicious when deciding to increase a dose. Make sure the appropriate medical indicators for increasing or altering a dose are present
- Be suspicious of a pattern of excuses for additional refills or repeated requests for additional refills on an emergency basis
- Be vigilant. Recognize that there is potential to abuse XYWAV and XYREM

It is important you know that the XYWAV and XYREM REMS maintains records about who is prescribing XYWAV and XYREM. These records will be made available to any state or federal agency that requests them.

DEPENDENCE AND TOLERANCE

Dependence

- Cases of severe dependence and cravings for GHB have been reported
- There have been case reports of dependence after illicit use of GHB at frequent repeated doses
  - Doses (18 g/day to 250 g/day) were in excess of therapeutic dose range

Tolerance

- Open-label, long-term (≥6 months) clinical trials did not demonstrate development of tolerance
- There have been some case reports of symptoms of tolerance developing after illicit use at doses far in excess of the recommended XYWAV and XYREM dosage regimen

Discontinuation effects and tolerance of XYWAV and XYREM have not been systematically evaluated in controlled clinical trials.

XYWAV AND XYREM TAKEBACK PROGRAM

XYWAV and XYREM patients have an option to return any unused, leftover or expired XYWAV and/or XYREM product through a reverse distribution drug takeback program, upon request. Patients interested in this option can call the XYWAV and XYREM REMS Program for more information. The REMS Certified Pharmacy will be provided shippers that can be sent to the patient. Patients will be instructed to black out or remove their personal information from the bottle(s) and to place the bottles in the shipper.

For your convenience, materials and information regarding the XYWAV and XYREM REMS are available online at www.XYWAVXYREMREMS.com.

Use in Specific Populations

PREGNANCY

There are no adequate data on the developmental risk associated with the use of XYWAV or sodium oxybate in pregnant women. Oral administration of sodium oxybate to pregnant rats (150, 350, or 1,000 mg/kg/day) or rabbits (300, 600, or 1,200 mg/kg/day) throughout organogenesis produced no clear evidence of developmental toxicity; however, oral administration to rats throughout pregnancy and lactation resulted in increased stillbirths and decreased offspring postnatal viability and growth, at a clinically relevant dose.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

LABOR AND DELIVERY

XYWAV and XYREM have not been studied in labor or delivery. In obstetric anesthesia using an injectable formulation of sodium oxybate, newborns had stable cardiovascular and respiratory measures but were very sleepy, causing a slight decrease in Apgar scores. There was a fall in the rate of uterine contractions 20 minutes after injection. Placental transfer is rapid and gamma-hydroxybutyrate (GHB) has been detected in newborns at delivery after intravenous administration of GHB to mothers. Subsequent effects of sodium oxybate on later growth, development, and maturation in humans are unknown.

NURSING MOTHERS

GHB is excreted in human milk after oral administration of sodium oxybate. There is insufficient information on the risk to a breastfed infant, and there is insufficient information on milk production in nursing mothers. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XYWAV or XYREM and any potential adverse effects on the breastfed infant from XYWAV or XYREM or from the underlying maternal condition.

PEDIATRIC USE

The safety and effectiveness of XYWAV for the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy have been established. XYWAV has not been studied in a pediatric clinical trial. Use of XYWAV in pediatric patients 7 years of age and older with narcolepsy is supported by evidence from an adequate and well-controlled study of sodium oxybate in pediatric patients 7 to 17 years of age, a study in adults showing a treatment effect of XYWAV similar to that observed with sodium oxybate, pharmacokinetic data of sodium oxybate from adult and pediatric patients, and pharmacokinetic data of XYWAV from healthy adult volunteers.

In the pediatric clinical trial with sodium oxybate administration in patients with narcolepsy, serious adverse reactions of central sleep apnea and oxygen desaturation documented by polysomnography evaluation; suicidal ideation in one patient; neuropsychiatric reactions including acute psychosis, confusion, and anxiety; and parasomnias, including sleepwalking, have been reported. The safety and effectiveness of XYREM in the treatment of cataplexy or excessive daytime sleepiness in pediatric patients (7 years of age and older) with narcolepsy have been established and pharmacokinetics characterized in a double-blind, placebo-controlled, randomized-withdrawal study. Safety and effectiveness of XYWAV or XYREM in pediatric patients below the age of 7 years have not been established.

GERIATRIC USE

There is limited experience with oxybate in subjects 65 years and older. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease and other drug therapy.

RACE AND GENDER EFFECTS

There were too few non-Caucasian patients in the narcolepsy clinical trials to permit evaluation of racial effects on safety or efficacy. More than 90% of the subjects in the clinical trials were Caucasian. In the narcolepsy clinical trials, with a database that was 58% female, no important differences in safety or efficacy of sodium oxybate were noted between men and women.

Please read accompanying Prescribing Information.
The XYWAV and XYREM REMS is here to support you, your staff, and your patients.
For assistance, call 1-866-997-3688 (toll free).

Patient Counseling Information

Prior to initiating therapy, counsel each adult patient, caregiver (for pediatric patients 7 years of age and older), and, as appropriate, pediatric patient regarding the serious risks and safe use, handling, and storage of XYWAV and XYREM using the appropriate educational material [XYWAV or XYREM Patient Quick Start Guide (for adults) and XYWAV or XYREM Brochure for Pediatric Patients and Their Caregivers (for pediatric patients)] and encourage him/her to read the XYWAV or XYREM Medication Guide. **Please see pages 16-18 for additional counseling information important for caregivers of pediatric patients and, as appropriate, pediatric patients.**

- Inform patients and/or caregivers that XYWAV and XYREM are available only through the central pharmacy certified under a restricted distribution program called the XYWAV and XYREM REMS and provide them with the telephone number and website for more information about XYWAV, XYREM, and the XYWAV and XYREM REMS
- Confirm that patients understand the serious risks and safe use conditions of XYWAV and XYREM and that you have answered any questions the patient and/or caregiver has about XYWAV or XYREM by having the patient and/or caregiver sign and date the REMS Patient Enrollment Form. Inform the patient and/or caregiver that regular follow-up is recommended

To ensure safe and effective use of XYWAV and XYREM, you should provide the adult patient, caregiver (for pediatric patients), and, as appropriate, pediatric patient with the following guidance:

ALCOHOL OR SEDATIVE HYPNOTICS

Advise patients and/or caregivers that alcohol and other sedative hypnotics should not be taken with XYWAV or XYREM. Advise patients to never take XYWAV and XYREM at the same time.

SEDATION

Inform patients and/or caregivers that the patient is likely to fall asleep quickly after taking XYWAV or XYREM (often within 5 minutes and usually within 15 minutes), but the time it takes to fall asleep can vary from night to night. The sudden onset of sleep, including in a standing position or while rising from bed, has led to falls resulting in injuries, in some cases requiring hospitalization. Instruct patients and/or caregivers that patients should remain in bed following ingestion of their first and second doses, and patients should not take their second dose until 2.5 to 4 hours after the first dose.

FOOD EFFECTS ON XYWAV/XYREM

Inform patients and/or caregivers that the first nightly dose should be taken at least 2 hours after eating.

RESPIRATORY DEPRESSION

Inform patients and/or caregivers that XYWAV and XYREM can be associated with respiratory depression even at recommended doses and with concurrent use of XYWAV or XYREM with other CNS depressants.

PARTICIPATING IN HAZARDOUS ACTIVITIES

Inform patients and/or caregivers that patients should not participate in hazardous activities requiring complete mental alertness or motor coordination (e.g., driving) within the first 6 hours of dosing or after first initiating treatment until certain that XYWAV or XYREM does not affect the patient adversely.

SUICIDALITY

Instruct patients and/or caregivers to contact a healthcare provider immediately if the patient develops depressed mood, markedly diminished interest or pleasure in usual activities, significant change in weight and/or appetite, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, or suicidal ideation.

SLEEPWALKING

Instruct patients and/or caregivers and their families that XYWAV and XYREM have been associated with sleepwalking and to contact their healthcare provider if this occurs.

SODIUM INTAKE (FOR PATIENTS TAKING XYREM)

Instruct patients and/or caregivers that XYREM contains a significant amount of sodium and XYREM-treated patients, particularly those who are sensitive to sodium intake (e.g., those with heart failure, hypertension, or renal impairment) should limit their sodium intake.

SAFE HANDLING, STORAGE, AND DISPOSAL

- Discuss safe and proper use of XYWAV and XYREM and dosing information with patients and/or caregivers prior to the initiation of treatment
- Instruct patients and/or caregivers to store XYWAV and XYREM bottles and XYWAV and XYREM doses in a secure place, out of reach of children and pets
- Patients and/or caregivers should be instructed to divide the **total nightly dose** into 2 separate doses. They should not further divide each of the 2 separate doses
- Patients and/or caregivers should be informed that patients should be seen by their healthcare provider frequently to review dose titration, symptom response, and adverse reactions
- Instruct patients and/or caregivers to store XYWAV and XYREM at room temperature, between 59°F and 86°F
- Inform patients and/or caregivers that they may safely dispose of XYWAV and XYREM down the sink or toilet drain
- Inform patients and/or caregivers that they must report all instances of lost or stolen XYWAV and XYREM to the local police and to the XYWAV and XYREM REMS

Pediatric Patient Supplement

This pediatric patient supplement provides information specifically for pediatric patients and their caregivers about the XYWAV and XYREM REMS, including important prescribing information, educational and counseling requirements, and materials necessary for program enrollment and prescribing XYWAV and XYREM. **If you are prescribing XYWAV or XYREM for a pediatric patient, please read the Prescriber Brochure in its entirety, including this Pediatric Patient Supplement.**

PRESCRIBING XYWAV AND XYREM FOR PEDIATRIC PATIENTS

In addition to the procedure for writing and dispensing prescriptions for XYWAV and XYREM described above, prescribing XYWAV or XYREM to pediatric patients requires the following:

- Verify that you have counseled the caregiver on the serious risks and safe use conditions as described in the XYWAV or XYREM Brochure for Pediatric Patients and Their Caregivers and encourage him/her to read the XYWAV or XYREM Medication Guide.

RESPONSIBILITIES OF THE XYWAV AND XYREM REMS CERTIFIED PHARMACY FOR PEDIATRIC PATIENTS

In addition to the responsibilities described above, for pediatric patients the Certified Pharmacy will:

- Ensure that each enrolled pediatric patient has a caregiver
- Counsel the caregiver of each pediatric patient on the serious risks and safe use of XYWAV and XYREM

Each pediatric patient receiving XYWAV or XYREM must have a caregiver

GUIDELINES FOR DOSING AND TITRATING XYWAV AND XYREM FOR PEDIATRIC PATIENTS

- The safety and effectiveness of XYWAV in the treatment of cataplexy or excessive daytime sleepiness in pediatric patients (7 years of age and older) with narcolepsy were established in a pediatric clinical trial with XYREM (sodium oxybate). XYWAV has not been studied in a pediatric clinical trial.
- The recommended starting pediatric dosage, titration regimen, and maximum total nightly dosage are based on patient weight, as specified in table below. The dose might be gradually titrated based on efficacy and tolerability

- The nightly XYWAV or XYREM dose is divided into two doses; one dose at bedtime and a second dose 2.5 to 4 hours after the first dose. For patients who sleep more than 8 hours per night, the first dose of XYWAV or XYREM may be given at bedtime or after an initial period of sleep
- Titrate the dose of XYWAV or XYREM to effect and tolerability by increasing the total nightly dose by no more than the titration regimens specified in the table below
- Total nightly doses higher than 9 g/night have not been studied
- Follow up frequently during titration to review symptom response and adverse reactions. A follow up of every three months is recommended
- Improvement may occur during the first weeks of therapy; however, titration to an optimal dose may take longer
- Once a stable dose is established, it is recommended that patients be re-evaluated every 3 months

Recommended Pediatric XYWAV and XYREM Dosage for Patients 7 Years of Age and Older*						
Patient Weight	Initial Dosage		Maximum Weekly Dosage Increase		Maximum Recommended Dosage	
	Take at Bedtime:	Take 2.5 to 4 Hours Later:	Take at Bedtime:	Take 2.5 to 4 Hours Later:	Take at Bedtime:	Take 2.5 to 4 Hours Later:
<20 kg**	There is insufficient information to provide specific dosing recommendations for patients who weigh less than 20 kg.					
20 kg to <30 kg	≤1 g	≤1 g	0.5 g	0.5 g	3 g	3 g
30 kg to <45 kg	≤1.5 g	≤1.5 g	0.5 g	0.5 g	3.75 g	3.75 g
≥45 kg	≤2.25 g	≤2.25 g	0.75 g	0.75 g	4.5 g	4.5 g

*For patients who sleep more than 8 hours per night, the first dose of XYWAV or XYREM may be given at bedtime or after an initial period of sleep.

**If XYWAV or XYREM is used in patients 7 years of age and older who weigh less than 20 kg, a lower starting dosage, lower maximum weekly dosage increases and lower total maximum nightly dosage should be considered.

Note: Some patients may achieve better responses with unequal doses at bedtime and 2.5 to 4 hours later.

IMPORTANT ADMINISTRATION INSTRUCTIONS FOR PEDIATRIC PATIENTS

- Inform caregivers that they should ensure that all XYWAV and XYREM doses are kept in a safe place until given
- Inform caregivers and patients that all bottles contain concentrated medication ONLY and that water for dilution is not contained in the box. Advise caregivers to keep XYWAV and XYREM in the provided bottle(s)
- Inform caregivers and patients that it is important to follow a consistent nightly routine for taking XYWAV or XYREM
  - Caregivers should prepare both nighttime doses at bedtime
    - Instruct caregivers to make sure that pharmacy containers are empty prior to preparing each dose
    - Each dose of XYWAV or XYREM should be diluted with about ¼ cup of water
    - Caregivers should be instructed to store XYWAV and XYREM bottles and prepared nightly doses in a secure place out of the reach of children and pets
  - Doses should be taken at least 2 hours after eating
  - Both doses should be taken while in bed and the patient should lie down immediately after dosing
    - Encourage the child to urinate prior to taking the first nightly dose
  - Caution against hazardous activities requiring complete mental alertness or motor coordination (e.g., driving) within the first 6 hours of dosing or after first initiating treatment until certain that XYWAV or XYREM does not affect the patient adversely

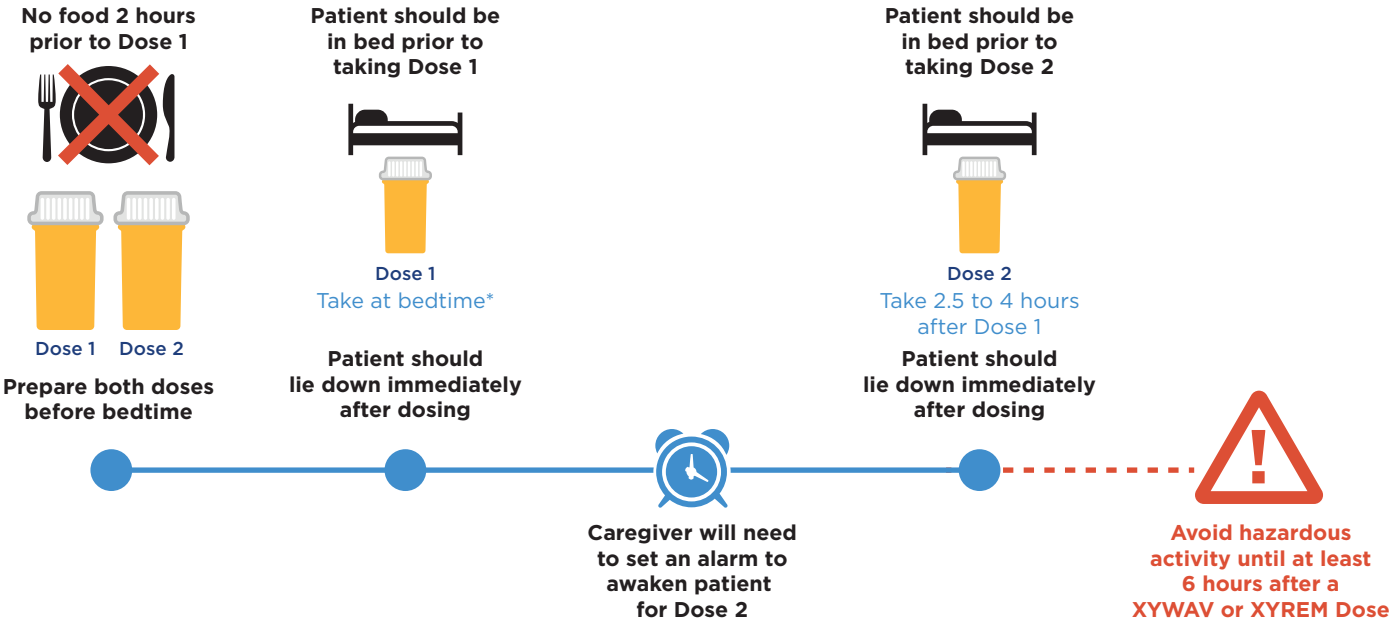
CHANGING BETWEEN XYWAV AND XYREM

A gram of XYWAV and a gram of XYREM both contain the same amount of the active drug, oxybate. Patients changing between XYWAV and XYREM should be started on the same dose as the previously administered product. For example, if a patient on a stable dose of 4.5g of XYREM twice nightly changes to XYWAV, they should be prescribed 4.5g of XYWAV twice nightly. Patients should then be evaluated and dosing adjustments made if necessary.

When changing a patient's therapy:

- Inform patients that the safe use and administration instructions are the same for both products
- Advise patients to never take XYWAV and XYREM at the same time.
- For patients changing to XYREM therapy: Instruct patients and/or caregivers that XYREM contains a significant amount of sodium and XYREM-treated patients, particularly those who are sensitive to sodium intake (e.g., those with heart failure, hypertension, or renal impairment) should limit their sodium intake.

Caregivers should be advised that the pediatric patient in their care is to take XYWAV or XYREM exactly as prescribed



*For patients who sleep more than 8 hours per night, the first dose of XYWAV or XYREM may be given at bedtime or after an initial period of sleep.

CONSIDERATIONS FOR INCLUDING PEDIATRIC PATIENTS IN THEIR OWN CARE

- Work with the caregiver to determine the child's readiness to participate in his or her own care
- Ensure that the pediatric patient is counseled on the serious risks and safe use of XYWAV and XYREM either by the prescriber or the Certified Pharmacy
  - Ensure that the patient also reads the XYWAV or XYREM Brochure for Pediatric Patients and Their Caregivers and asks any questions he or she may have

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xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL C III

XYREM® (sodium oxybate) oral solution C III

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XYWAV and XYREM REMS

PATIENT QUICK START GUIDE

Important information about the safe use and handling of XYREM

XYREM® (sodium oxybate) oral solution

C III

Reference ID: 4644289

XYWAV and XYREM REMS

Dear Patient,

Welcome to the XYWAV and XYREM REMS. You are receiving these materials because your healthcare provider has prescribed XYREM® (sodium oxybate) oral solution, 0.5 g/mL, for you. XYREM is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. *If you are the caregiver of a pediatric patient receiving XYREM, please refer to the XYREM Brochure for Pediatric Patients and Their Caregivers instead of this guide for important information about helping your child get started with XYREM.*

Because of the serious risks associated with XYREM, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS). The purpose of this REMS is to make sure the benefits of XYREM outweigh the risks. All patients must be enrolled in the REMS to receive XYREM. This Quick Start Guide contains information you need to know about XYREM and will help you to use XYREM correctly. Read this Quick Start Guide before you start taking XYREM.

After your healthcare provider sends in your enrollment form and first prescription for XYREM, you will receive a call from the Certified Pharmacy of the REMS to tell you how the REMS helps you get started with taking XYREM and to answer any questions you may have about XYREM.

You will also speak with appropriate staff at the Certified Pharmacy, who will go over your insurance information with you. Before you can receive your first shipment of XYREM, a pharmacist at the Certified Pharmacy will ask if your healthcare provider reviewed the XYREM Patient Quick Start Guide with you and explain that you will receive this guide with your first shipment, and that all drug shipments will include the XYREM Medication Guide. The pharmacist will also ask you about your medical history and other medications you may be taking, and give you advice on how to prepare and take your XYREM and how to store it safely. **You must take this call before you can get your XYREM.**

Please call your healthcare provider if you have questions about XYREM, or you can contact the REMS toll free at 1-866-997-3688. You can reach a pharmacist at this number 24 hours a day, 7 days a week with any questions.

We hope you find this information and the REMS services helpful.

Sincerely,

Jazz Pharmaceuticals

XYREM® (sodium oxybate) oral solution C III

XYWAV and XYREM REMS

WARNING: XYREM can cause serious side effects.
Do not drink alcohol or take other medicines that make you sleepy

XYREM is a prescription medicine used to treat patients 7 years of age and older with narcolepsy to reduce too much daytime sleepiness and to reduce cataplexy (suddenly weak or paralyzed muscles).

IMPORTANT INFORMATION ABOUT XYREM INCLUDES THE FOLLOWING:

- When taking XYREM, do not drink alcohol or take other medicines that slow your breathing or mental activity or make you sleepy. You could have serious side effects
- XYREM can cause serious side effects, including trouble breathing while asleep, confusion, unusual or disturbing thoughts, depression, and passing out, even at recommended doses. Tell your healthcare provider if you have any of these problems while taking XYREM
- Abuse of XYREM can lead to dependence (a physical need to take the drug), craving for the medicine, and severe withdrawal symptoms (symptoms that start when the drug is stopped, especially when it is stopped suddenly)
- Patients usually fall asleep in about 5 to 15 minutes, although some patients have reported falling asleep more quickly (without first feeling drowsy) and others take more time. The time that it takes to fall asleep might be different from night to night. You should take each dose of XYREM while in bed. Take the first dose at bedtime and the second 2½ to 4 hours later. You may need to set an alarm to awaken for the second dose

- Do not drive a car, use heavy machinery, fly an airplane, or do anything that is dangerous or that requires you to be alert for the first 6 hours after taking XYREM. When you first start taking XYREM, be careful until you know how XYREM affects you
- Keep XYREM out of the reach of children and pets. Get emergency medical help right away if a child drinks your XYREM
- Report all side effects to your healthcare provider

WHAT WILL YOU FIND IN THIS BOOKLET?

This booklet answers important questions about how to get your XYREM, how to use XYREM properly, and how to store it safely. It also gives you important information about XYREM.

WHAT IS THE XYWAV AND XYREM REMS PROGRAM?

Because of the serious risks associated with XYREM, the FDA has required a special program called REMS for XYWAV and XYREM. Enrollment in the REMS by prescribers and patients is required by the FDA to ensure the benefits of XYREM outweigh the risks associated with XYREM. You are enrolled in the program when your healthcare provider sends in the enrollment form you signed. At that time, your healthcare provider also sent your prescription for XYREM to the Certified Pharmacy.

The Certified Pharmacy staff will review important information about XYREM with you. They will also answer any questions you may have about XYREM.

XYREM® (sodium oxybate) oral solution C III

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XYREM® (sodium oxybate) oral solution C-III

ENROLLING IN THE XYWAV AND XYREM REMS

WHAT AM I REQUIRED TO DO IN THE XYWAV AND XYREM PROGRAM?

As a patient, your responsibility is to discuss the safe use of XYREM with your healthcare provider and to read this XYREM Patient Quick Start Guide before you begin taking XYREM. Be sure to let your healthcare provider know if you are taking other medications or if you have any conditions that might affect your breathing.

DO I HAVE TO ENROLL IN THIS PROGRAM?

Yes. In order for you to receive XYREM, your healthcare provider will have you sign an enrollment form and will send the form to the REMS. You must verify that you have been counseled by your healthcare provider on the serious risks and safe use of XYREM and that you were able to ask your healthcare provider any questions you have about XYREM.

FILLING YOUR XYREM PRESCRIPTION

HOW IS MY PRESCRIPTION FILLED?

All XYREM prescriptions are filled only by the REMS Certified Pharmacy.

WHAT DOES THE CERTIFIED PHARMACY DO?

Your healthcare provider sends your XYREM prescription directly to the Certified Pharmacy.

After your healthcare provider sends in your first prescription of XYREM, you will receive a call from the Certified Pharmacy to tell you how the REMS helps you get started with taking XYREM and to answer any questions you may have about XYREM. A staff member from the Certified Pharmacy will call you to complete a Patient Counseling Checklist. The Patient Counseling Checklist will include information about other medications that you are taking and other medical conditions which might increase your risk of serious side effects. The Certified Pharmacy will go over the information about how to use XYREM safely and provide a copy of the Medication Guide with each XYREM shipment.

The Certified Pharmacy will always ask you where and when you would like your XYREM delivered and who will sign for the shipment. XYREM will be shipped by an overnight service. When the courier arrives, you or an adult you name must sign for your XYREM.

XYREM® (sodium oxybate) oral solution C III

WHAT WILL I GET WITH MY XYREM PRESCRIPTION?

With each prescription, you will get 1 or more bottles of XYREM (each bottle, whether full or partial, has the concentrated medicine), a dosing syringe for drawing up your XYREM dose, 2 **empty** pharmacy containers with child-resistant caps, and a printed Medication Guide.

HOW DO I GET MY XYREM REFILLS?

The Certified Pharmacy will contact you when it is close to your refill time. You may opt-in to receive text, e-mail, or automated voice reminders. You may also call the Certified Pharmacy at 1-866-997-3688 to schedule your refills.

CAN MY LOCAL PHARMACY PROVIDE XYREM?

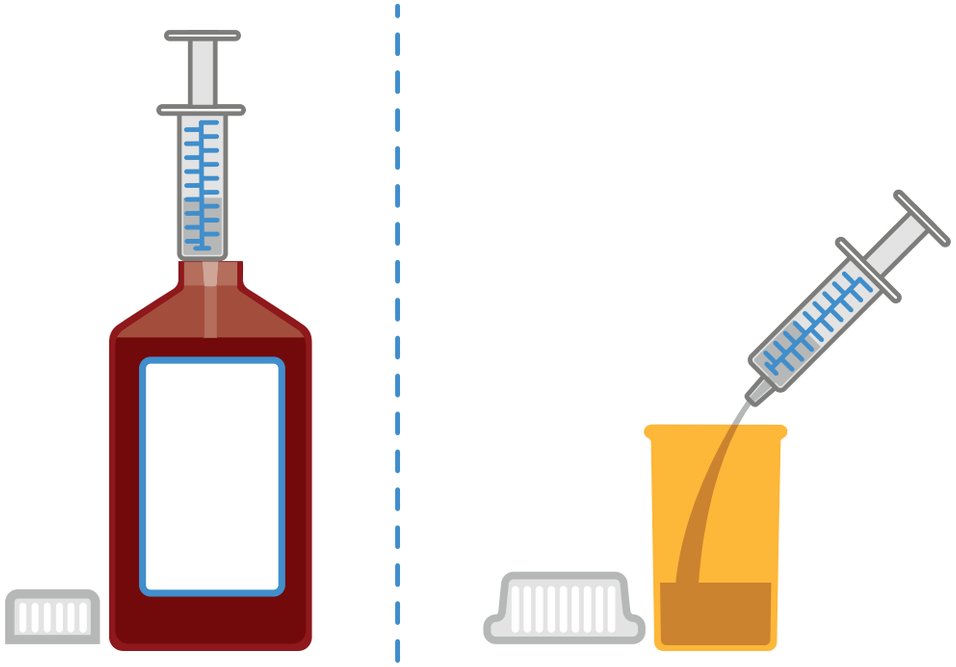
No. You can get your XYREM only from the REMS central Certified Pharmacy. You may be able to have your XYREM shipped to your place of work or to a local overnight carrier hub for pickup. Saturday deliveries may also be an option for you. The Certified Pharmacy will work with you on the best options available.

HOW DO I TAKE MY XYREM?

Take XYREM only as your healthcare provider tells you to take it.

HOW DO I PREPARE MY DOSES?

Place the bottle on a hard, flat surface and grip the bottle with one hand and firmly press the syringe into the center opening of the bottle with the other. Pull back on the plunger until the medication flows into the syringe and the liquid level is aligned with the corresponding tick mark for your dose. After you draw up the first XYREM dose, remove the syringe from the opening of the XYREM bottle. Empty all of the medicine from the syringe into one of the provided **empty** pharmacy containers by pushing down on the plunger until it stops.

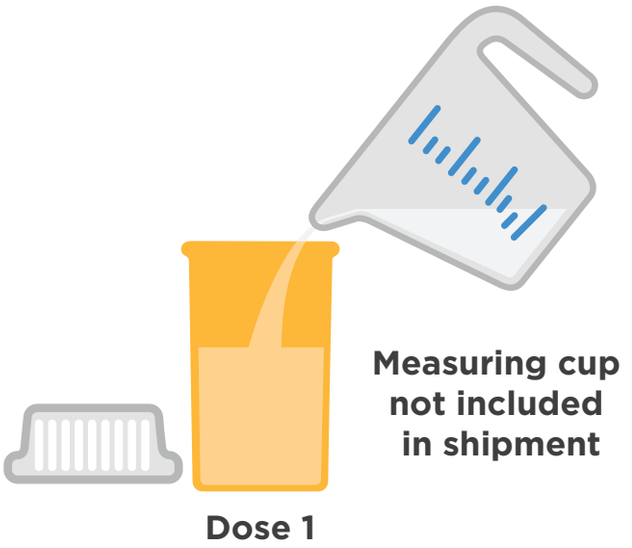


Dose 1

XYREM® (sodium oxybate) oral solution C-III

Using a measuring cup, pour about ¼ cup of water into the pharmacy container. **Be careful to add only water to the pharmacy container and not more XYREM.** Place the child-resistant cap provided on the filled pharmacy container and turn the cap clockwise (to the right) until it clicks and locks in its child-resistant position.

Repeat the steps described above by drawing up the amount of medicine prescribed for your second dose; emptying the syringe into the second pharmacy container, adding about ¼ cup of water, and closing the pharmacy container.



Put the cap back on the XYREM bottle and store the XYREM bottle and both prepared doses in a safe and secure place. Store in a locked place if needed. Keep the XYREM bottle and both prepared XYREM doses out of the reach of children and pets.

Rinse out the syringe and pharmacy containers with water after each use. Please refer to the Instructions for Use within the Medication Guide for additional details.

HOW DO I TAKE MY DOSES?

Wait at least 2 hours after eating before taking XYREM.

XYREM is a medicine that can make you sleepy quickly; therefore, take your doses while you are in bed. Take the first dose at bedtime and the second dose 2½ to 4 hours later. If you continue evening activities after taking your dose, such as watching television or walking around, you may experience light-headedness, dizziness, nausea, confusion, or other unpleasant feelings.

WHAT SHOULD I DO IF I MISS A XYREM DOSE?

- It is very important to take both doses of XYREM each night, as prescribed. If you miss the second dose, skip that dose
  - Do not take XYREM again until the next night
  - Never take both XYREM doses at once
- Any unused XYREM doses that you prepared but didn't take must be thrown away within 24 hours from the time you first prepared your doses

XYREM® (sodium oxybate) oral solution C III

HOW SOON WILL I SEE A CHANGE IN MY SYMPTOMS?

After starting XYREM, it may take a few weeks or longer to see your symptoms improve. It may also take time to find the right dose that works for you. It is important that you talk with your healthcare provider often when you first start taking XYREM.

Tell your healthcare provider if you don't feel any improvements while taking XYREM. XYREM may not be right for you.

WHAT ARE THE SIDE EFFECTS OF XYREM?

XYREM can cause serious side effects, including breathing problems (slower breathing, trouble breathing, and short periods of no breathing while asleep), mental health problems (confusion, seeing or hearing things that are not real, unusual or disturbing thoughts, feeling anxious or upset, depression, thoughts of suicide), and sleepwalking. If you have any of these side effects, call your healthcare provider right away.

The most common side effects with XYREM are nausea, dizziness, throwing up, bedwetting, and diarrhea. Side effects may increase with higher doses.

These are not the only possible side effects with XYREM. If you are worried about any possible side effects with XYREM, talk with your healthcare provider or the pharmacist at the REMS.

You should report all side effects by contacting your healthcare provider,

Jazz Pharmaceuticals at 1-800-520-5568, or the FDA at 1-800-FDA-1088.

ARE THERE ANY PRECAUTIONS I SHOULD TAKE WHILE ON XYREM?

- While taking XYREM, do not drink alcohol or take medicines that cause sleepiness
- Do not drive a car, use heavy machinery, or do anything that is dangerous or requires you to be alert, for the first 6 hours after taking XYREM. When you first start taking XYREM, be careful until you know how it will affect you
- Before starting XYREM, tell your healthcare provider if you are pregnant, or plan to become pregnant, or if you are breastfeeding. XYREM passes into breast milk. You and your doctor should decide if you will take XYREM or breastfeed.
- Keep your XYREM in a safe place, out of the reach of children
- Take XYREM while in bed

Tell your healthcare provider and pharmacist about any other medicines you are taking, including prescription and non-prescription medicines, vitamins, and supplements.

It is also important to tell other healthcare providers, including pharmacists, that you are taking XYREM before you start or change any medications.

XYREM® (sodium oxybate) oral solution C III

HOW OFTEN SHOULD MY HEALTHCARE PROVIDER CHECK MY PROGRESS WITH XYREM?

When you first start taking XYREM, you may need to talk to your healthcare provider often until he or she has determined the best dose for you. You can expect that your dose may need to be adjusted. After your dose has been established, your healthcare provider should check on you every 3 months while you are taking XYREM.

WHAT DO I NEED TO DO IF I AM TAKING XYWAV AND MY DOCTOR PRESCRIBES XYREM FOR ME?

- **Never take both XYREM and XYWAV at the same time, it can lead to serious side effects**
- XYREM contains the same medicine as XYWAV, which is called oxybate, but with more sodium
- Take your XYREM exactly as instructed by your doctor
- Prepare your XYREM the same way you prepared XYWAV
- Do not mix XYREM and XYWAV together. If you have unused XYWAV, dispose of it before starting XYREM. Refer to “HOW DO I PROPERLY DISPOSE OF XYREM?” for further instructions
- The Certified Pharmacy will contact you to talk to you about how to make this change
- XYREM contains a high amount of sodium (salt) and may not be right for you, especially if you are on a salt-restricted diet or have had heart failure, high blood pressure (hypertension), or kidney problems. Make sure to tell your doctor if you have any of these conditions before you start XYREM.

STORAGE AND SAFETY TIPS AT HOME

HOW DO I STORE XYREM?

- Always store XYREM in its original bottle
- Store XYREM at room temperature. Do not refrigerate XYREM
- Keep XYREM in a safe place, out of the reach of children and pets. Get emergency medical help (call 911) right away if a child drinks your XYREM

HOW DO I PROPERLY DISPOSE OF XYREM?

To properly dispose of XYREM, pour any unused XYREM down the sink or toilet drain. Mark out all personal information on the prescription label, including the XYREM name, to make it unreadable before putting the empty bottle in the trash.

XYREM patients have the option to return unused or expired drug. Please ask the Certified Pharmacy for more details.

If you misplace, lose, or damage your XYREM dosing syringe, contact the Certified Pharmacy to have it replaced. Do not use a different syringe or try to guess the correct dose.

XYREM® (sodium oxybate) oral solution C-III

XYWAV AND XYREM TAKEBACK PROGRAM

XYWAV or XYREM patients have an option to return any unused, leftover or expired XYWAV or XYREM product through a drug takeback program, upon request. Patients can request a shipper from the Certified Pharmacy. Once you receive the shipper, remember to mark out or remove your personal information from the bottle(s) and place the bottles in the shipper. For more information, please ask the Certified Pharmacy for more details.

WHAT IF I HAVE CONCERNS ABOUT HAVING XYREM IN MY HOME?

- If your XYREM is lost or stolen, report the incident right away to the local police and to the Certified Pharmacy
- Use XYREM only as your healthcare provider tells you. Remember that use of your XYREM by others is illegal
- If you have any questions or concerns, or if you need advice about XYREM, call your healthcare provider or the Certified Pharmacy

INSURANCE COVERAGE

WILL INSURANCE PAY FOR MY XYREM?

In most cases, YES. A staff member from the Certified Pharmacy will call and work with your insurance company to help you get coverage for XYREM. In the unlikely event your insurance does not cover XYREM or you can't afford the out-of-pocket costs, ask the Certified Pharmacy about available financial assistance programs.

WHAT IS THE PHARMACY'S ROLE WITH MY INSURANCE?

An experienced staff member will:

- Call you to go over your prescription benefits and coverage
- Tell you what your co-pay is, if applicable
- Tell you about any XYREM prescription savings plans for which you may qualify
- Work with your healthcare provider on prior authorizations, if required by your insurance company
- Provide information about any financial help that may be available to you

The Certified Pharmacy's attempt to get coverage from a third-party payer does not guarantee that you will get coverage.

XYREM® (sodium oxybate) oral solution C-III

GETTING MORE INFORMATION

WHERE CAN I GET MORE INFORMATION ABOUT XYREM?

For more information about XYREM, contact the REMS:

- **Phone:** 1-866-997-3688
- **Fax:** 1-866-470-1744 (toll free)
- **Outside the US:** +314-475-6000, ext 361 587
- **Website:** www.XYWAVXYREMREMS.com

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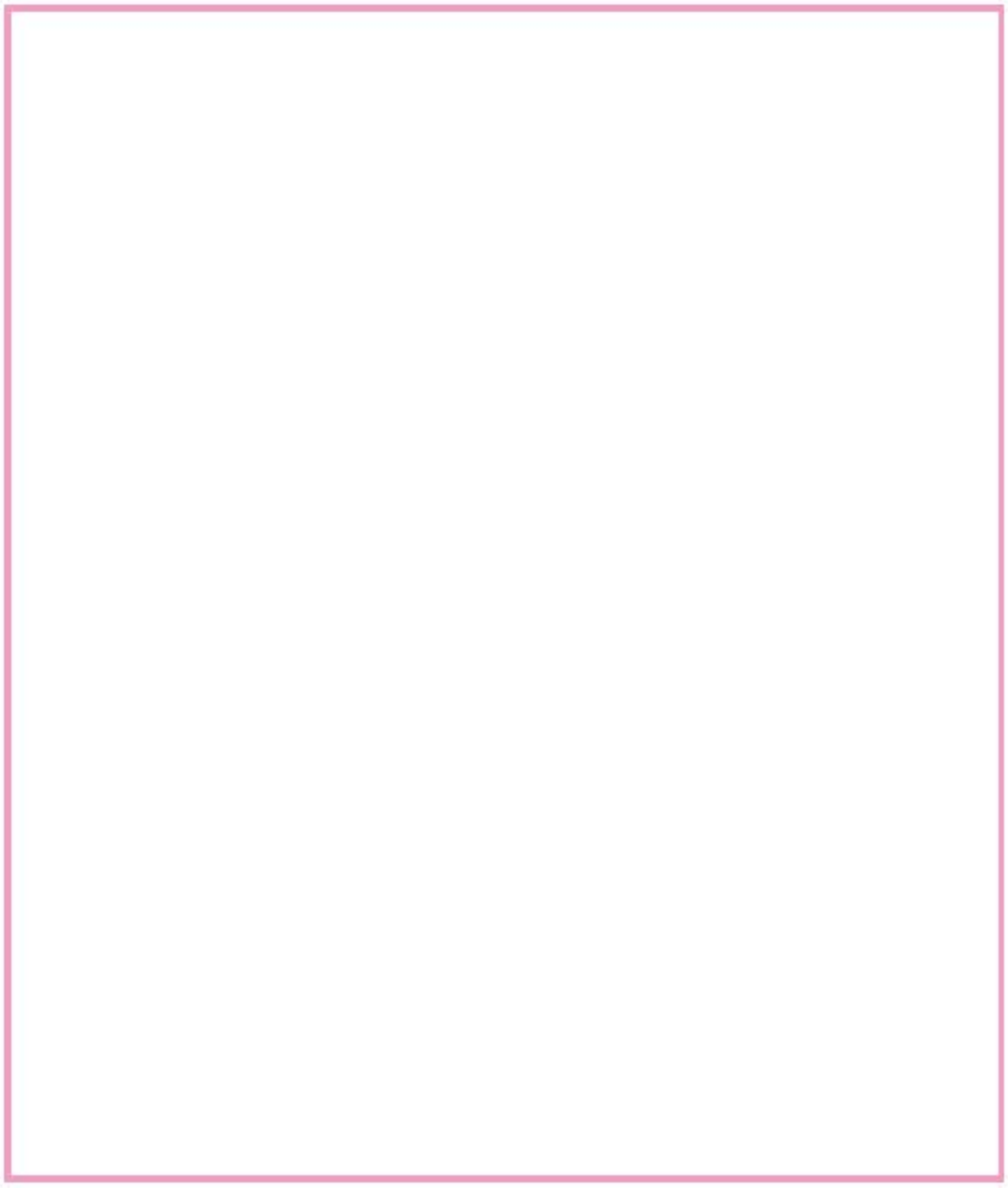

XYREM® (sodium oxybate) oral solution

KEEP THIS BOOKLET AS A HELPFUL REMINDER

If you have questions or need information,
contact the XYWAV and XYREM REMS Program.

Please see the Medication Guide for more detailed information about XYREM.

Jazz Pharmaceuticals®

XYREM® (sodium oxybate) oral solution CIII

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The pharmacy may ask you to measure how much XYREM is left in your bottle. Please use this ruler to give them this information.

XYWAV and XYREM REMS

BROCHURE FOR PEDIATRIC PATIENTS AND THEIR CAREGIVERS

Important information about the safe use and handling of XYREM

Reference ID: 4644289

XYREM® (sodium oxybate) oral solution

XYWAV and XYREM REMS

Dear Caregiver,

Welcome to the XYWAV and XYREM REMS You are receiving these materials because your child's healthcare provider has prescribed **XYREM**® (sodium oxybate) oral solution, 0.5 g/mL, for your child. XYREM is a medicine used to treat cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. XYREM may only be given to patients enrolled in the REMS.

Because of the serious risks associated with XYREM, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS). The purpose of this REMS is to make sure the benefits of XYREM outweigh the risks. All patients must be enrolled in the REMS to receive XYREM. Each pediatric patient must have a caregiver who is counseled on the serious risks and safe use of XYREM. This brochure contains information you need to know about XYREM and will help you give XYREM to your child correctly. Read this brochure before you start giving your child XYREM.

After your child's healthcare provider sends in your child's enrollment form and first prescription for XYREM, you will receive a call from the Certified Pharmacy from the XYWAV and XYREM REMS to counsel you on the serious risks and safe use of Xyrem, to tell you about the XYWAV and XYREM REMS requirements, and to answer any questions you or your child may have about XYREM.

A few things must happen before you receive your child's first shipment of XYREM:

- The Certified Pharmacy will call to:
  - Ask if your child's healthcare provider reviewed the XYREM Brochure for Pediatric Patients and Their Caregivers with you
  - Explain that you will receive this brochure with your child's first shipment, and that all drug shipments will include the XYREM Medication Guide
  - Ask you about your child's medical history and other medications he or she may be taking
  - Give you advice on how to prepare and give XYREM to your child and how to store it safely
  - Go over your child's insurance information
- **You must take this call before you can get your child's XYREM**

XYREM® (sodium oxybate) oral solution CIII

If you have any additional questions about XYREM, please call your child's healthcare provider, or you can contact the XYWAV and XYREM REMS toll free at 1-866-997-3688. You can reach a pharmacist at this number 24 hours a day, 7 days a week with any questions. We hope you find this information and the XYWAV and XYREM REMS helpful.

Sincerely,

Jazz Pharmaceuticals

WARNING: XYREM can cause serious side effects.
Your child should not drink alcohol or take other medicines that cause sleepiness

XYREM is a prescription medicine used to treat patients 7 years of age and older with narcolepsy to reduce too much daytime sleepiness and to reduce cataplexy (suddenly weak or paralyzed muscles).

IMPORTANT INFORMATION ABOUT XYREM INCLUDES THE FOLLOWING:

- When taking XYREM, your child should not drink alcohol or take other medicines that may slow his or her breathing or mental activity or make him or her sleepy. Your child could have serious side effects
- XYREM can cause serious side effects, including slow breathing or changes in alertness. Call your child's doctor right away if your child has any of these serious side effects
- Abuse of XYREM can lead to dependence (a physical need to take the drug), craving for the medicine, and severe withdrawal symptoms (symptoms that start when the drug is stopped, especially when it is stopped suddenly)

XYREM® (sodium oxybate) oral solution CIII

- Patients usually fall asleep in about 5 to 15 minutes, although some patients have reported falling asleep more quickly (without first feeling drowsy) and others take more time. The time that it takes to fall asleep might be different from night to night. You should give each dose of XYREM while your child is sitting up in bed and have your child lie down immediately after. Give the first dose at the time prescribed by your child's healthcare provider, and the second dose 2 ½ to 4 hours later. You may need to set an alarm to awaken to give the second dose
- Your child should not do anything that requires him or her to be fully alert for the first 6 hours after taking XYREM. When your child first starts taking XYREM, you and your child will need to be careful until you know how XYREM affects him or her.
- Keep XYREM out of the reach of children and pets. Get emergency medical help right away if a child who has not been prescribed XYREM drinks XYREM
- Report all side effects to your child's healthcare provider

WHAT WILL YOU FIND IN THIS BROCHURE?

This brochure provides information on the serious risks and safe use of XYREM, answers important questions about how to use XYREM properly, how to store it safely, and how to get your child's XYREM.

WHAT IS THE XYWAV AND XYREM REMS PROGRAM?

Because of the serious risks associated with XYREM, the FDA has required a special program called REMS for XYWAV and XYREM. Enrollment in the REMS by prescribers and patients is required by the FDA to ensure the benefits of XYREM outweigh the risks associated with XYREM. Your child is enrolled when your child's healthcare provider sends in your signed enrollment form. At that time, your child's healthcare provider also will send your child's prescription for XYREM to the Certified Pharmacy.

The Certified Pharmacy staff will review important information about XYREM with you. They will also answer any questions you and your child may have about XYREM.

XYREM® (sodium oxybate) oral solution CIII

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XYREM® (sodium oxybate) oral solution

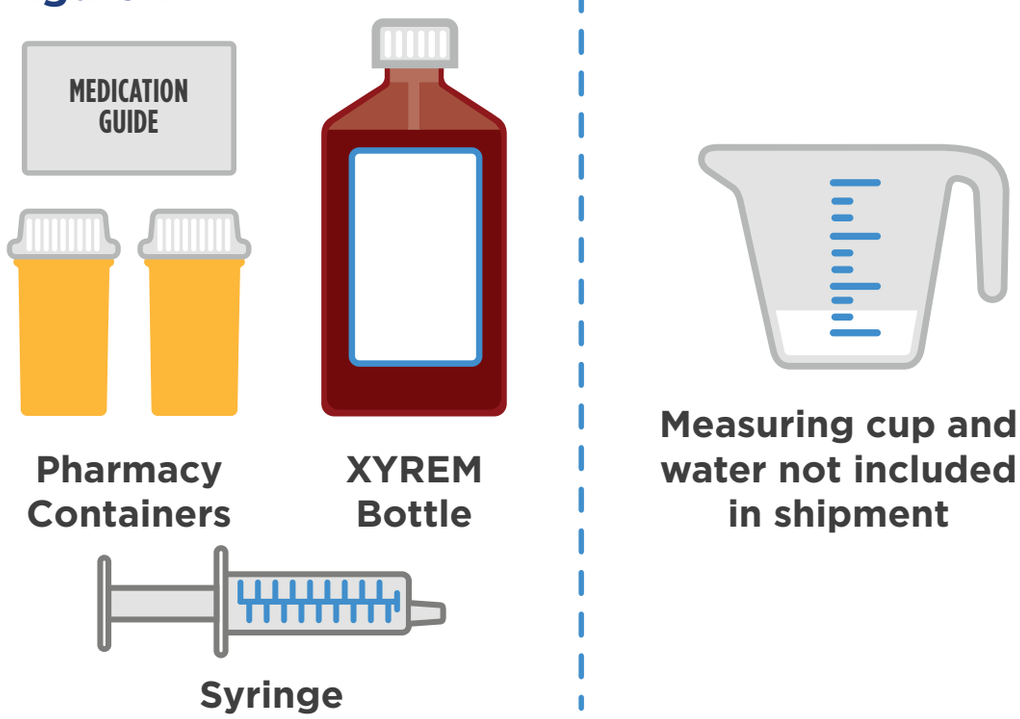
Preparation and Administration of XYREM

XYREM should be prepared and taken only as prescribed by your child's healthcare provider.

WHAT WILL I GET WITH MY CHILD'S XYREM PRESCRIPTION?

With each prescription, you will get 1 or more bottles of XYREM (each bottle, whether full or partial, contains the concentrated medicine), a dosing syringe for drawing up your child's XYREM dose, 2 **empty** pharmacy containers with child-resistant caps, and a printed Medication Guide (Figure 1).

Figure 1

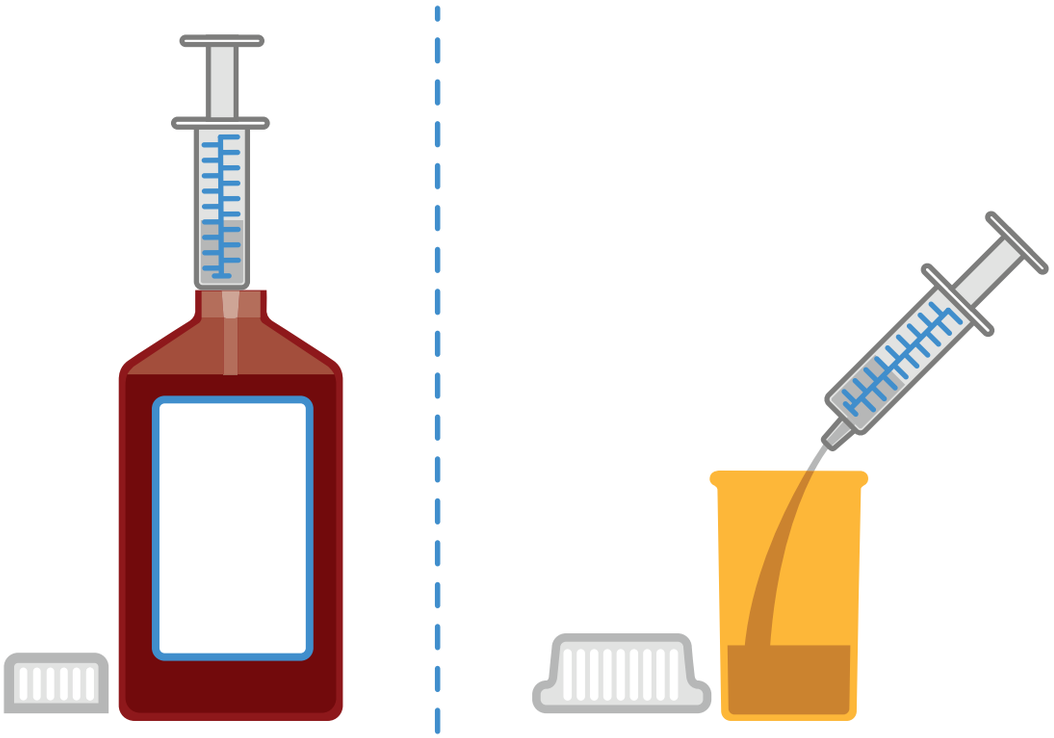


XYREM® (sodium oxybate) oral solution

HOW DO I PREPARE MY CHILD'S DOSES?

Place the bottle on a hard, flat surface and grip the bottle with one hand and firmly press the syringe into the center opening of the bottle with the other. Pull back on the plunger until the medication flows into the syringe and the liquid level is aligned with the corresponding tick mark for your child's dose. After you draw up the first XYREM dose, remove the syringe from the opening of the XYREM bottle. Empty all of the medicine from the syringe into one of the provided **empty** pharmacy containers by pushing down on the plunger until it stops (Figure 2).

Figure 2

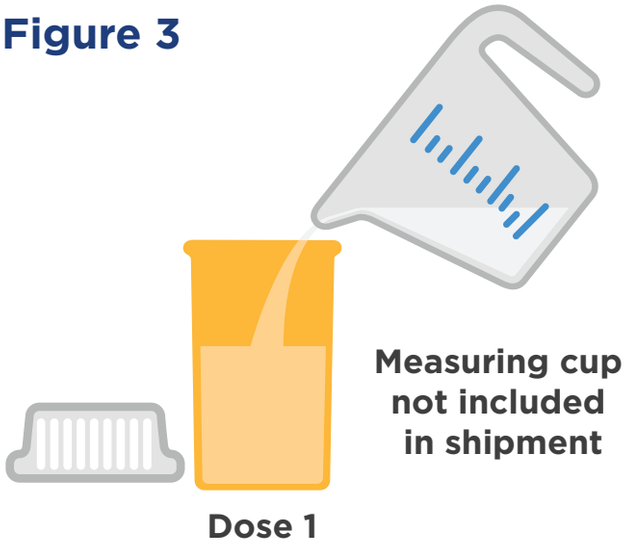


Dose 1

Using a measuring cup, pour about ¼ cup of water into the pharmacy container. **Be careful to add only water to the pharmacy container and not more XYREM.** Place the child-resistant cap provided on the filled pharmacy container and turn the cap clockwise (to the right) until it clicks and locks in its child-resistant position.

Repeat the steps described above by drawing up the amount of medicine prescribed for your child's second dose; emptying the syringe into the second pharmacy container, adding about ¼ cup of water, and closing the pharmacy container.

Figure 3



Put the cap back on the XYREM bottle and store the XYREM bottle and both prepared doses in a safe and secure place. Store in a locked place if needed. Keep the XYREM bottle and both prepared XYREM doses out of the reach of children and pets.

Rinse out the syringe and pharmacy containers with water after each use. Please refer to the Instructions for Use within the Medication Guide for additional details.

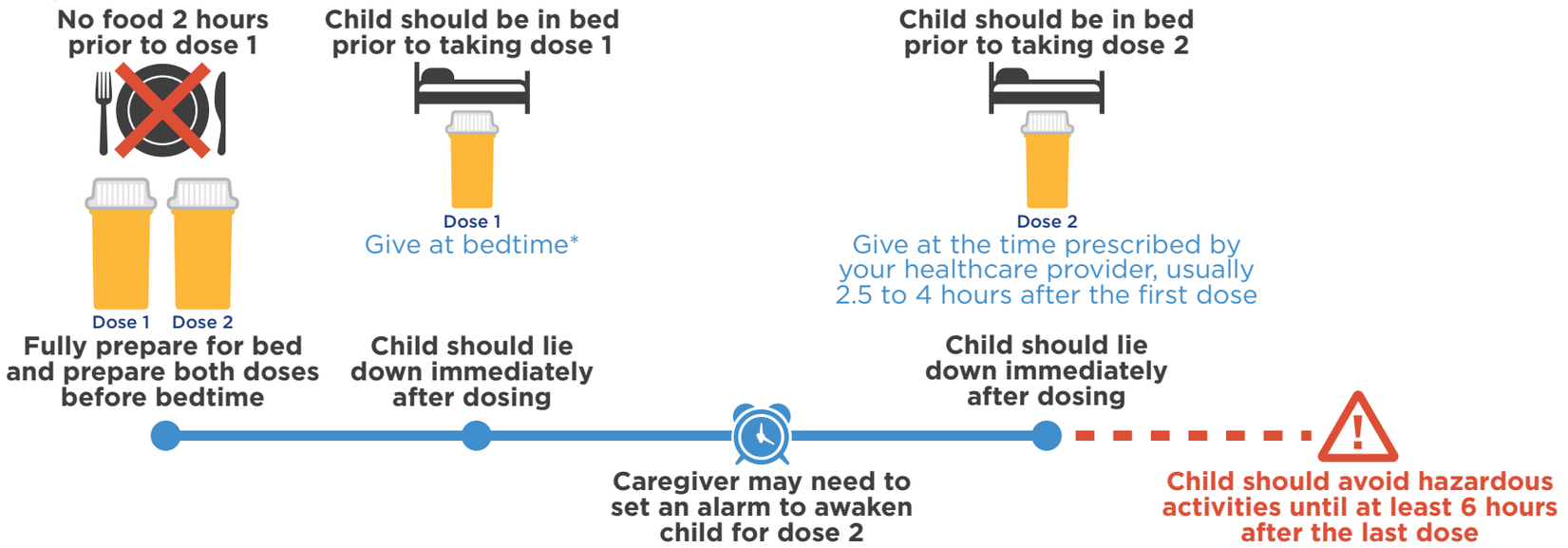
XYREM® (sodium oxybate) oral solution CIII

HOW DO I GIVE MY CHILD'S DOSES?

Wait at least 2 hours after your child eats before giving XYREM.

XYREM is a medicine that can make your child sleepy quickly; therefore, give your child's doses while he or she is sitting up in bed and have your child lie down immediately after dosing and remain in bed. Ensure your child is fully prepared for bed prior to taking the first nightly dose of XYREM (for example, has brushed teeth, gone to the bathroom). Give the first dose at the time prescribed by your child's healthcare provider, and the second dose 2 ½ to 4 hours later. Ensure that all XYREM doses are kept in a safe place until given. If your child continues evening activities after taking his or her dose, such as watching television or walking around, your child may experience light-headedness, dizziness, nausea, confusion, or other unpleasant feelings. Have the child lie down immediately after dosing and remain in bed (Figure 4).

Figure 4



*For children who sleep more than 8 hours per night, the first dose of XYREM may be given at bedtime or after an initial period of sleep.

WHAT DO I DO IF MY CHILD MISSES A DOSE?

- It is very important to give both doses of XYREM each night as prescribed. If the second dose is missed, skip that dose
  - Do not give your child XYREM again until the next night
  - Never give your child both XYREM doses at once
- Any unused XYREM doses that you prepared but didn't give to your child must be thrown away within 24 hours from the time you first prepared your child's doses

HOW SOON WILL WE SEE A CHANGE IN SYMPTOMS?

After starting XYREM, it may take a few weeks or longer to see your child's symptoms improve. It may also take time to find the right dose that works for your child. It is important that you talk with your child's healthcare provider often when your child first starts taking XYREM.

Tell your child's healthcare provider if you or your child do not see any improvements.

WHAT ARE THE SIDE EFFECTS OF XYREM?

XYREM can cause serious side effects, including breathing problems (slower breathing, trouble breathing, and short periods of no breathing while asleep), mental health problems (confusion, seeing or hearing things that are not real, unusual or disturbing thoughts, feeling anxious or upset, depression, thoughts of suicide), and sleepwalking. If your child has any of these side effects, call your child's healthcare provider right away.

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The most common side effects with XYREM in pediatric patients are bedwetting, nausea, headache, throwing up, and weight loss. Side effects may increase with higher doses.

These are not the only possible side effects with XYREM. If you or your child are worried about any possible side effects with XYREM, talk with your child's healthcare provider or the pharmacist at the XYWAV and XYREM REMS.

You should report all side effects by contacting your child's healthcare provider, Jazz Pharmaceuticals at 1-800-520-5568, or the FDA at 1-800-FDA-1088.

ARE THERE ANY PRECAUTIONS THAT SHOULD BE TAKEN WHILE MY CHILD IS ON XYREM?

- While taking XYREM, your child should not drink alcohol or take medicines that cause sleepiness
- Your child should not do anything that requires him or her to be fully alert for the first 6 hours after taking XYREM. When your child first starts taking XYREM, you and your child will need to be careful until you know how XYREM affects him or her.
- Before starting XYREM, tell your child's healthcare provider if your child is pregnant, or plans to become pregnant, or is breastfeeding. XYREM passes into breast milk. You and your child's healthcare provider should decide if your child will take XYREM or breastfeed.
- Keep XYREM in a safe place, out of the reach of children
- Give XYREM to your child while he or she is sitting up in bed and have your child lie down immediately and remain in bed after dosing

Tell your child's healthcare provider and pharmacist about any other medicines he or she is taking, including if your child begins a new medicine while taking XYREM. This would include prescription and non-prescription medicines, vitamins, and supplements.

It is also important to tell other healthcare providers, including pharmacists, that your child is taking XYREM before your child starts or changes any medications.

How Often Should My Child's Healthcare Provider Check on My Child's Progress On XYREM?

When your child first starts taking XYREM, you may need to talk to his or her healthcare provider often until he or she has determined the best dose for your child. You can expect that your child's dose may need to be adjusted. After your child's dose has been established, his or her healthcare provider should check on your child every 3 months while taking XYREM.

What do I need to do if my child is taking XYWAV and their doctor prescribes XYREM for them?

- **Your child should never take both XYREM and XYWAV at the same time, it can lead to serious side effects**
- XYREM contains the same medicine as XYWAV, which is called oxybate, but with more sodium
- Your child should take their XYREM exactly as instructed by their doctor
- Prepare your child's XYREM the same way you prepared XYWAV

XYREM® (sodium oxybate) oral solution

- Do not mix XYREM and XYWAV together. If you have unused XYWAV, dispose of it before your child starts XYREM. Refer to "HOW DO I PROPERLY DISPOSE OF XYREM?" for further instructions
- The Certified Pharmacy will contact you to talk to you about how to make this change
- XYREM contains a large amount of sodium (salt) and may not be right for your child, especially if they are on a salt-restricted diet or have had heart failure, high blood pressure (hypertension), or kidney problems. Make sure to tell your child's doctor if your child has any of these conditions before they start XYREM.

Storage and Safety Tips at Home

HOW DO I STORE XYREM?

- Always store XYREM in its original bottle
- Store XYREM at room temperature. Do not refrigerate XYREM
- Keep XYREM in a safe place, out of the reach of children and pets. Get emergency medical help (call 911) right away if a child not prescribed XYREM drinks XYREM

HOW DO I PROPERLY DISPOSE OF XYREM?

To properly dispose of XYREM, pour any unused XYREM down the sink or toilet drain. Mark out all personal information on the prescription label, including the XYREM name, to make it unreadable before putting the empty bottle in the trash.

XYREM patients have the option to return unused or expired drug. Please ask the Certified Pharmacy for more details.

If you misplace, lose, or damage your child's XYREM dosing syringe, contact the Certified Pharmacy to have it replaced. Do not use a different syringe or try to guess the correct dose.

XYWAV AND XYREM TAKEBACK PROGRAM

XYWAV or XYREM patients have an option to return any unused, leftover or expired XYWAV or XYREM product through a drug takeback program, upon request. Patients can request a shipper from the Certified Pharmacy. Once you receive the shipper, remember to mark out or remove your personal information from the bottle(s) and place the bottles in the shipper. For more information, please ask the Certified Pharmacy for more details.

WHAT IF I HAVE CONCERNS ABOUT HAVING XYREM IN MY HOME?

- If your child's XYREM is lost or stolen, report the incident right away to the local police and to the Certified Pharmacy
- Give XYREM only as your child's healthcare provider tells you. Remember that use of your child's XYREM by others is illegal
- If you have any questions or concerns, or if you need advice about XYREM, call your child's healthcare provider or the Certified Pharmacy

XYREM® (sodium oxybate) oral solution CIII

XYWAV and **XYREM** REMS

Important Information Your Child Must Know About Taking XYREM

You can use these pages to help teach your young child what they need to know about taking their XYREM.

WHAT SHOULD MY CHILD KNOW ABOUT TAKING XYREM?

Get Ready

- Get ready for bed before you drink your XYREM
- Finish your bedtime routine before you get in bed and drink your XYREM

Any questions? Please call the XYWAV and XYREM REMS at 1-866-997-3688.
Please see the Medication Guide for more-detailed information about XYREM.

Reference ID: 4644289

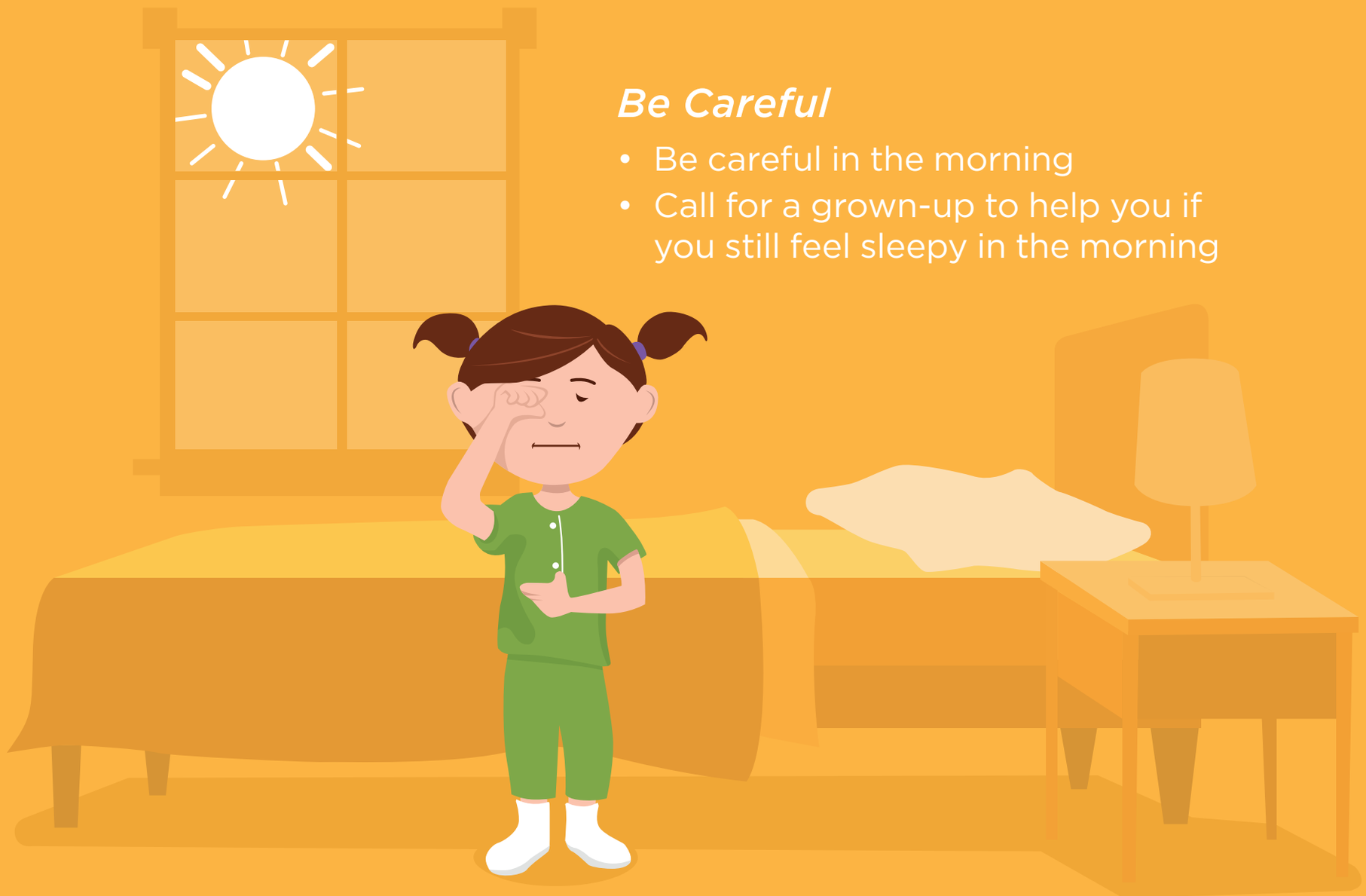
Stay In Bed

- Drink your XYREM while sitting up in bed. Lie down right away after you drink it and stay in bed
- Call for a grown-up if you want to get out of bed after taking XYREM
- It may take a while, or you may fall asleep quickly after taking XYREM

XYREM® (sodium oxybate) oral solution C-III

Reference ID: 4644289

XYWAV and **XYREM** REMS



Be Careful

- Be careful in the morning
- Call for a grown-up to help you if you still feel sleepy in the morning

Any questions? Please call the XYWAV and XYREM REMS at 1-866-997-3688.
Please see the Medication Guide for more-detailed information about XYREM.

Reference ID: 4644289

Always Remember!

- Don’t share your XYREM with anyone else
  - This medicine is only for you!
- Don’t drink too much XYREM
  - Never drink more than one of your XYREM cups at a time
  - Only drink XYREM from your XYREM cup
- Tell a grown-up how you are feeling and about any changes in how you are feeling

XYREM®
(sodium oxybate) oral solution
CIII

Reference ID: 4644289

Including Your Child in His or Her Care

HOW CAN I PREPARE MY CHILD TO BE ABLE TO CARRY OUT ONE OR MORE SAFE USE ACTIVITIES?

It is important for your child to take an active part in the safe use of his or her XYREM. This is especially true for teenagers and those going to college. This brochure can help you talk with your child about taking XYREM.

Before your child moves away from your home (for example, going away to college), talk with your healthcare provider and the Certified Pharmacy about additional ways to ensure safe use, handling, and storage. To help prepare your child for this transition, make sure that he or she is counseled about the serious risks and safe use of XYREM by a member of your child's XYREM healthcare team (for example, your child's healthcare provider or the Certified Pharmacy). Your child should also read this brochure and ask his or her healthcare provider any questions he or she may have.

Enrolling Your Child in the XYWAV and XYREM REMS

DOES MY CHILD HAVE TO ENROLL IN THE XYWAV AND XYREM REMS?

Yes. In order for your child to receive XYREM, your healthcare provider will have you sign an enrollment form and will send the form to the REMS. You must verify that you have been counseled by your child's healthcare provider on the serious risks and safe use of XYREM and that you were able to ask your child's healthcare provider any questions you have about XYREM. You may choose to have your child also receive counseling from your healthcare provider on the serious risks and safe use of XYREM.

WHAT IS MY ROLE AS A CAREGIVER?

As a caregiver of a pediatric patient who is in the REMS, you are required to:

- Read this brochure and ask your child's healthcare provider any questions you have about XYREM.
- Ensure that XYREM is prepared and given only as prescribed
- Ensure that XYREM is kept in a safe place, away from children and pets, and protected from theft

XYREM® (sodium oxybate) oral solution

- Notify your child's healthcare provider right away if you notice any serious side effects while your child is taking XYREM

Also be sure to let your child's healthcare provider know if your child is taking other medicines or if your child has any medical conditions that might affect his or her breathing.

If you need to give your responsibilities as your child's caregiver to someone else, please notify your child's healthcare provider. You also can contact the REMS toll free at 1-866-997-3688 to make sure that the new caregiver is counseled on the risks and safe use of XYREM.

Filling Your Child's XYREM Prescription

HOW IS MY CHILD'S PRESCRIPTION FILLED?

All XYREM prescriptions are filled and shipped directly to your home only by the REMS Certified Pharmacy.

WHAT ELSE DOES THE CERTIFIED PHARMACY DO?

Your child's healthcare provider sends your child's XYREM prescription directly to the Certified Pharmacy.

You will then receive a call from the Certified Pharmacy to counsel you on the serious risks and safe use of XYREM, to tell you how to get your child started on XYREM and to answer any questions about XYREM. A staff member from the Certified Pharmacy will call you to complete a counseling checklist. The counseling checklist will include information about other medicines that your child is taking and other medical conditions that might increase your child's risk of serious side effects. The Certified Pharmacy will go over the information about how to use XYREM safely and provide a copy of the Medication Guide with each XYREM shipment.

XYREM® (sodium oxybate) oral solution C-III

The Certified Pharmacy will always ask you where and when you would like your child's XYREM delivered and who will sign for the shipment. XYREM will be shipped by an overnight service. You may be able to have your child's XYREM shipped to your place of work or to a local overnight carrier hub for pickup. Saturday deliveries may also be an option for you. The Certified Pharmacy will work with you to find the best options available. When the courier arrives, you or another adult you previously named must sign for your child's XYREM.

Finally, the Certified Pharmacy will call you soon after you receive your child's first XYREM shipment to confirm receipt and answer any questions you may have about your child's first few days taking XYREM.

HOW DO I GET XYREM REFILLS FOR MY CHILD?

The Certified Pharmacy will contact you when it is close to your child's refill time. You may opt-in to receive text, e-mail, or automated voice reminders for refills. You may also call the Certified Pharmacy at 1-866-997-3688 to schedule your child's refills.

CAN MY LOCAL PHARMACY PROVIDE XYREM FOR MY CHILD?

No. You can get your child's XYREM only from the XYWAV and XYREM REMS Certified Pharmacy.

Insurance Coverage

WILL INSURANCE PAY FOR MY CHILD'S XYREM?

In most cases, YES. A staff member from the Certified Pharmacy will call and work with your child's insurance company to help you get coverage for your child's XYREM. In the unlikely event your child's insurance does not cover XYREM or you can't afford the out-of-pocket costs, ask the Certified Pharmacy about available financial assistance programs.

WHAT IS THE PHARMACY'S ROLE WITH MY CHILD'S INSURANCE?

An experienced staff member will:

- Call you to go over your child's prescription benefits and coverage
- Tell you what your co-pay is, if applicable
- Tell you about any XYREM prescription savings plans for which you may qualify
- Work with your child's healthcare provider on prior authorizations, if required by the insurance company
- Provide information about any financial help that may be available to you

The Certified Pharmacy's attempt to get coverage from a third-party payer does not guarantee that you will get coverage.

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Contact Information

WHOM SHOULD I CONTACT WITH CONCERNS OR FOR MORE INFORMATION ABOUT XYREM?

FOR QUESTIONS ABOUT SIDE EFFECTS OR FOR MORE INFORMATION ABOUT XYREM, CONTACT YOUR CHILD'S HEALTHCARE PROVIDER:

Name: _____

Phone: _____

Email: _____

FOR MORE INFORMATION ABOUT XYREM, CONTACT THE CERTIFIED PHARMACY:

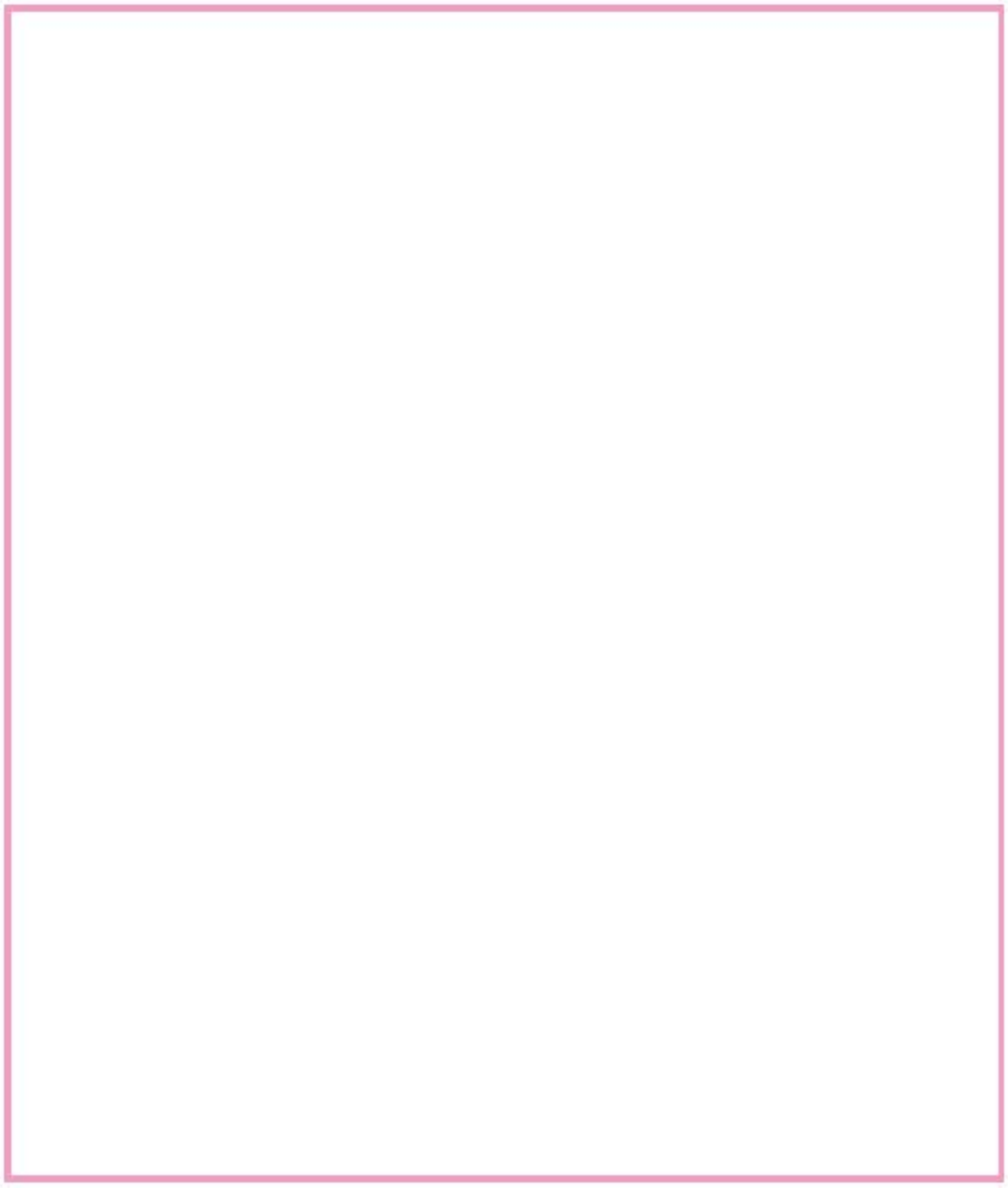
- **Phone:** 1-866-997-3688
- **Fax:** 1-866-470-1744 (toll free)
- **Outside the US:** +314-475-6000, ext. 361 587
- **Website:** www.XYWAVXYREMREMS.com

TO REPORT ALL SIDE EFFECTS, YOU CAN CONTACT:

- Jazz Pharmaceuticals at 1-800-520-5568
- The FDA at 1-800-FDA-1088

FOR EMERGENCIES:

- Call 911



XYREM® (sodium oxybate) oral solution

KEEP THIS BOOKLET AS A HELPFUL REMINDER

If you have questions or need information,
contact the XYWAV and XYREM REMS

Please see the Medication Guide for more detailed information about XYREM.

Jazz Pharmaceuticals®

XYREM® (sodium oxybate) oral solution C III

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The pharmacy may ask you to measure how much XYREM is left in your bottle. Please use this ruler to give them this information.

XYWAV and XYREM REMS

PATIENT QUICK START GUIDE

Important information about the safe use and handling of XYWAV

xywav™
(calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL
CIII

Reference ID: 4644289

Dear Patient,

Welcome to the XYWAV and XYREM REMS. You are receiving these materials because your healthcare provider has prescribed XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL, for you. XYWAV is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. *If you are the caregiver of a pediatric patient receiving XYWAV, please refer to the XYWAV Brochure for Pediatric Patients and Their Caregivers instead of this guide for important information about helping your child get started with XYWAV.*

Because of the serious risks associated with XYWAV, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS) for XYWAV. The purpose of this REMS is to make sure the benefits of XYWAV outweigh the risks. All patients must be enrolled in the REMS to receive XYWAV. This Quick Start Guide contains information you need to know about XYWAV and will help you to use XYWAV correctly. Read this Quick Start Guide before you start taking XYWAV.

After your healthcare provider sends in your enrollment form and first prescription for XYWAV, you will receive a call from the Certified Pharmacy of the REMS to tell you how the REMS helps you get started with taking XYWAV and to answer any questions you may have about XYWAV.

You will also speak with appropriate staff at the Certified Pharmacy, who will go over your insurance information with you. Before you can receive your first shipment of XYWAV, a pharmacist at the Certified Pharmacy will ask if your healthcare provider reviewed the XYWAV Patient Quick Start Guide with you and explain that you will receive this guide with your first shipment, and that all drug shipments will include the XYWAV Medication Guide. The pharmacist will also ask you about your medical history and other medications you may be taking, and give you advice on how to prepare and take your XYWAV and how to store it safely. **You must take this call before you can get your XYWAV.**

Please call your healthcare provider if you have questions about XYWAV, or you can contact the REMS toll free at 1-866-997-3688. You can reach a pharmacist at this number 24 hours a day, 7 days a week with any questions.

We hope you find this information and the REMS services helpful.

Sincerely,

Jazz Pharmaceuticals

XYWAV and XYREM REMS

WARNING: XYWAV can cause serious side effects.
Do not drink alcohol or take other medicines that make you sleepy

XYWAV is a prescription medicine used to treat patients 7 years of age and older with narcolepsy to reduce too much daytime sleepiness and to reduce cataplexy (suddenly weak or paralyzed muscles).

IMPORTANT INFORMATION ABOUT XYWAV INCLUDES THE FOLLOWING:

- When taking XYWAV, do not drink alcohol or take other medicines that slow your breathing or mental activity or make you sleepy. You could have serious side effects
- XYWAV can cause serious side effects, including trouble breathing while asleep, confusion, unusual or disturbing thoughts, depression, and passing out, even at recommended doses. Tell your healthcare provider if you have any of these problems while taking XYWAV
- Abuse of XYWAV can lead to dependence (a physical need to take the drug), craving for the medicine, and severe withdrawal symptoms (symptoms that start when the drug is stopped, especially when it is stopped suddenly)
- Patients usually fall asleep in about 5 to 15 minutes, although some patients have reported falling asleep more quickly (without first feeling drowsy) and others take more time. The time that it takes to fall asleep might be different from night to night. You should take each dose of XYWAV while in bed. Take the first dose at bedtime and the second 2½ to 4 hours later. You may need to set an alarm to awaken for the second dose

- Do not drive a car, use heavy machinery, fly an airplane, or do anything that is dangerous or that requires you to be alert for the first 6 hours after taking XYWAV. When you first start taking XYWAV, be careful until you know how XYWAV affects you
- Keep XYWAV out of the reach of children and pets. Get emergency medical help right away if a child drinks your XYWAV
- Report all side effects to your healthcare provider

WHAT WILL YOU FIND IN THIS BOOKLET?

This booklet answers important questions about how to get your XYWAV, how to use XYWAV properly, and how to store it safely. It also gives you important information about XYWAV.

WHAT IS THE XYWAV AND XYREM REMS PROGRAM?

Because of the serious risks associated with XYWAV, the FDA has required a special program called REMS for XYWAV and XYREM. Enrollment in the REMS by prescribers and patients is required by the FDA to ensure the benefits of XYWAV outweigh the risks associated with XYWAV. You are enrolled in the program when your healthcare provider sends in the enrollment form you signed. At that time, your healthcare provider also sent your prescription for XYWAV to the Certified Pharmacy.

The Certified Pharmacy staff will review important information about XYWAV with you. They will also answer any questions you may have about XYWAV.

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ENROLLING IN THE XYWAV AND XYREM REMS

WHAT AM I REQUIRED TO DO IN THE XYWAV AND XYREM REMS PROGRAM?

As a patient, your responsibility is to discuss the safe use of XYWAV with your healthcare provider and to read this XYWAV Patient Quick Start Guide before you begin taking XYWAV. Be sure to let your healthcare provider know if you are taking other medications or if you have any conditions that might affect your breathing.

DO I HAVE TO ENROLL IN THIS PROGRAM?

Yes. In order for you to receive XYWAV, your healthcare provider will have you sign an enrollment form and will send the form to the REMS. You must verify that you have been counseled by your healthcare provider on the serious risks and safe use of XYWAV and that you were able to ask your healthcare provider any questions you have about XYWAV.

FILLING YOUR XYWAV PRESCRIPTION

HOW IS MY PRESCRIPTION FILLED?

All XYWAV prescriptions are filled only by the REMS Certified Pharmacy.

WHAT DOES THE CERTIFIED PHARMACY DO?

Your healthcare provider sends your XYWAV prescription directly to the Certified Pharmacy.

After your healthcare provider sends in your first prescription of XYWAV, you will receive a call from the Certified Pharmacy to tell you how the REMS helps you get started with taking XYWAV and to answer any questions you may have about XYWAV. A staff member from the Certified Pharmacy will call you to complete a Patient Counseling Checklist. The Patient Counseling Checklist will include information about other medications that you are taking and other medical conditions which might increase your risk of serious side effects. The Certified Pharmacy will go over the information about how to use XYWAV safely and provide a copy of the Medication Guide with each XYWAV shipment.

The Certified Pharmacy will always ask you where and when you would like your XYWAV delivered and who will sign for the shipment. XYWAV will be shipped by an overnight service. When the courier arrives, you or an adult you name must sign for your XYWAV.

WHAT WILL I GET WITH MY XYWAV PRESCRIPTION?

With each prescription, you will get 1 or more bottles of XYWAV (each bottle, whether full or partial, has the concentrated medicine), a dosing syringe for drawing up your XYWAV dose, 2 **empty** pharmacy containers with child-resistant caps, and a printed Medication Guide.

HOW DO I GET MY XYWAV REFILLS?

The Certified Pharmacy will contact you when it is close to your refill time. You may opt-in to receive text, e-mail, or automated voice reminders. You may also call the Certified Pharmacy at 1-866-997-3688 to schedule your refills.

CAN MY LOCAL PHARMACY PROVIDE XYWAV?

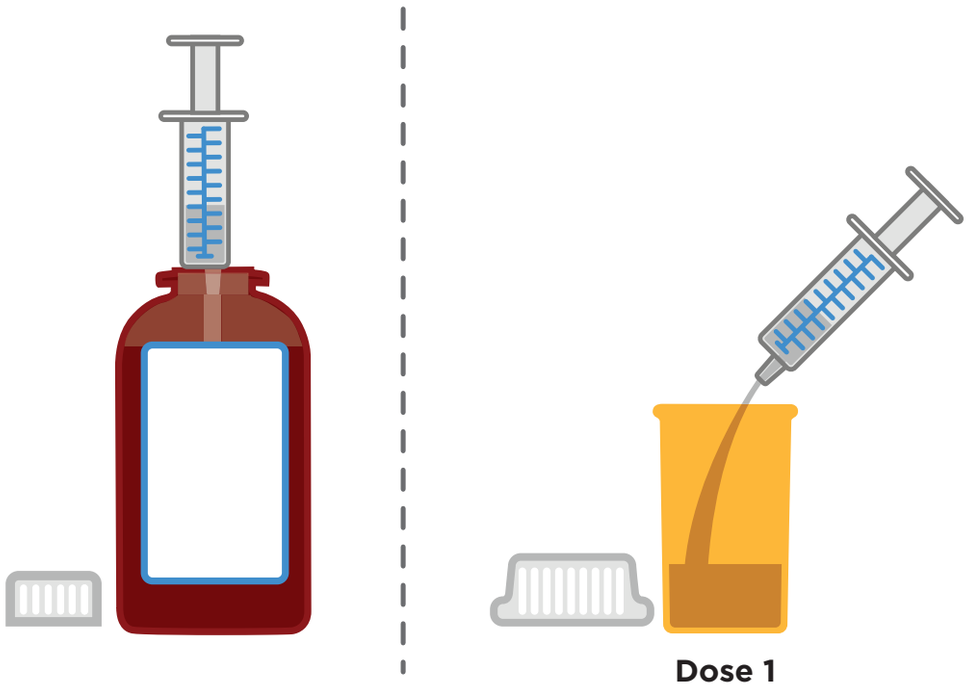
No. You can get your XYWAV only from the REMS central Certified Pharmacy. You may be able to have your XYWAV shipped to your place of work or to a local overnight carrier hub for pickup. Saturday deliveries may also be an option for you. The Certified Pharmacy will work with you on the best options available.

HOW DO I TAKE MY XYWAV?

Take XYWAV only as your healthcare provider tells you to take it.

HOW DO I PREPARE MY DOSES?

Place the bottle on a hard, flat surface and grip the bottle with one hand and firmly press the syringe into the center opening of the bottle with the other. Pull back on the plunger until the medication flows into the syringe and the liquid level is aligned with the corresponding tick mark for your dose. After you draw up the first XYWAV dose, remove the syringe from the opening of the XYWAV bottle. Empty all of the medicine from the syringe into one of the provided **empty** pharmacy containers by pushing down on the plunger until it stops.



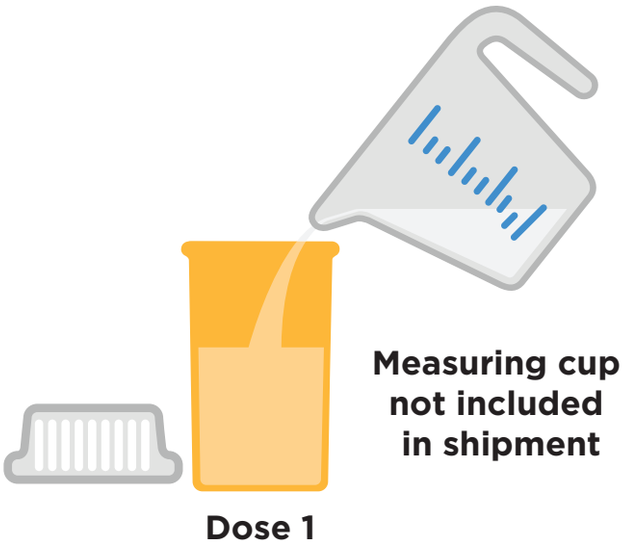
Dose 1

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

Reference ID: 4644289

Using a measuring cup, pour about ¼ cup of water into the pharmacy container. **Be careful to add only water to the pharmacy container and not more XYWAV.** Place the child-resistant cap provided on the filled pharmacy container and turn the cap clockwise (to the right) until it clicks and locks in its child-resistant position.

Repeat the steps described above by drawing up the amount of medicine prescribed for your second dose; emptying the syringe into the second pharmacy container, adding about ¼ cup of water, and closing the pharmacy container. Put the cap back on the XYWAV bottle and store the XYWAV bottle and both prepared doses in a safe and secure place. Store in a locked place if needed. Keep the XYWAV bottle and both prepared XYWAV doses out of the reach of children and pets.



Rinse out the syringe and pharmacy containers with water after each use. Please refer to the Instructions for Use within the Medication Guide for additional details.

HOW DO I TAKE MY DOSES?

Wait at least 2 hours after eating before taking XYWAV.

XYWAV is a medicine that can make you sleepy quickly; therefore, take your doses while you are in bed. Take the first dose at bedtime and the second dose 2½ to 4 hours later. If you continue evening activities after taking your dose, such as watching television or walking around, you may experience light-headedness, dizziness, nausea, confusion, or other unpleasant feelings.

WHAT SHOULD I DO IF I MISS A XYWAV DOSE?

- It is very important to take both doses of XYWAV each night, as prescribed. If you miss the second dose, skip that dose
  - Do not take XYWAV again until the next night
  - Never take both XYWAV doses at once
- Any unused XYWAV doses that you prepared but didn't take must be thrown away within 24 hours from the time you first prepared your doses

HOW SOON WILL I SEE A CHANGE IN MY SYMPTOMS?

After starting XYWAV, it may take a few weeks or longer to see your symptoms improve. It may also take time to find the right dose that works for you. It is important that you talk with your healthcare provider often when you first start taking XYWAV.

Tell your healthcare provider if you don't feel any improvements while taking XYWAV. XYWAV may not be right for you.

WHAT ARE THE SIDE EFFECTS OF XYWAV?

XYWAV can cause serious side effects, including breathing problems (slower breathing, trouble breathing, and short periods of no breathing while asleep), mental health problems (confusion, seeing or hearing things that are not real, unusual or disturbing thoughts, feeling anxious or upset, depression, thoughts of suicide), and sleepwalking. If you have any of these side effects, call your healthcare provider right away.

The most common side effects with XYWAV are headache, nausea, dizziness, decreased appetite, sleep walking, diarrhea, extensive sweating, anxiety, and throwing up. Side effects may increase with higher doses.

These are not the only possible side effects with XYWAV. If you are worried about any possible side effects with XYWAV, talk with your healthcare provider or the pharmacist at the REMS.

You should report all side effects by contacting your healthcare provider, Jazz Pharmaceuticals at 1-800-520-5568, or the FDA at 1-800-FDA-1088.

ARE THERE ANY PRECAUTIONS I SHOULD TAKE WHILE ON XYWAV?

- While taking XYWAV, do not drink alcohol or take medicines that cause sleepiness
- Do not drive a car, use heavy machinery, or do anything that is dangerous or requires you to be alert, for the first 6 hours after taking XYWAV. When you first start taking XYWAV, be careful until you know how it will affect you
- Before starting XYWAV, tell your healthcare provider if you are pregnant, or plan to become pregnant, or if you are breastfeeding. XYWAV passes into breast milk. You and your doctor should decide if you will take XYWAV or breastfeed.
- Keep your XYWAV in a safe place, out of the reach of children
- Take XYWAV while in bed

Tell your healthcare provider and pharmacist about any other medicines you are taking, including prescription and non-prescription medicines, vitamins, and supplements.

It is also important to tell other healthcare providers, including pharmacists, that you are taking XYWAV before you start or change any medications.

HOW OFTEN SHOULD MY HEALTHCARE PROVIDER CHECK MY PROGRESS WITH XYWAV?

When you first start taking XYWAV, you may need to talk to your healthcare provider often until he or she has determined the best dose for you. You can expect that your dose may need to be adjusted. After your dose has been established, your healthcare provider should check on you every 3 months while you are taking XYWAV.

WHAT DO I NEED TO DO IF I AM TAKING XYREM AND MY DOCTOR PRESCRIBES XYWAV FOR ME?

- **Never take both XYREM and XYWAV at the same time, it can lead to serious side effects**
- XYWAV contains the same medication as XYREM, which is called oxybate, but with less sodium
- Take XYWAV exactly as instructed by your doctor
- Prepare your XYWAV the same way you prepared XYREM
- Do not mix XYREM and XYWAV together. If you have unused XYREM, dispose of it before starting XYWAV. Refer to “HOW DO I PROPERLY DISPOSE OF XYWAV?” for further instructions
- The Certified Pharmacy will contact you to talk to you about how to make this change

STORAGE AND SAFETY TIPS AT HOME

HOW DO I STORE XYWAV?

- Always store XYWAV in its original bottle
- Store XYWAV at room temperature. Do not refrigerate XYWAV
- Keep XYWAV in a safe place, out of the reach of children and pets. Get emergency medical help (call 911) right away if a child drinks your XYWAV

HOW DO I PROPERLY DISPOSE OF XYWAV?

To properly dispose of XYWAV, pour any unused XYWAV down the sink or toilet drain. Mark out all personal information on the prescription label, including the XYWAV name, to make it unreadable before putting the empty bottle in the trash.

XYWAV patients have the option to return unused or expired drug. Please ask the Certified Pharmacy for more details.

If you misplace, lose, or damage your XYWAV dosing syringe, contact the Certified Pharmacy to have it replaced. Do not use a different syringe or try to guess the correct dose.

XYWAV AND XYREM TAKEBACK PROGRAM

XYWAV or XYREM patients have an option to return any unused, leftover or expired XYWAV or XYREM product through a drug takeback program, upon request. Patients can request a shipper from the Certified Pharmacy. Once you receive the shipper, remember to mark out or remove your personal information from the bottle(s) and place the bottles in the shipper. For more information, please ask the Certified Pharmacy for more details.

WHAT IF I HAVE CONCERNS ABOUT HAVING XYWAV IN MY HOME?

- If your XYWAV is lost or stolen, report the incident right away to the local police and to the Certified Pharmacy
- Use XYWAV only as your healthcare provider tells you. Remember that use of your XYWAV by others is illegal
- If you have any questions or concerns, or if you need advice about XYWAV, call your healthcare provider or the Certified Pharmacy

INSURANCE COVERAGE

WILL INSURANCE PAY FOR MY XYWAV?

In most cases, YES. A staff member from the Certified Pharmacy will call and work with your insurance company to help you get coverage for XYWAV. In the unlikely event your insurance does not cover XYWAV or you can't afford the out-of-pocket costs, ask the Certified Pharmacy about available financial assistance programs.

WHAT IS THE PHARMACY'S ROLE WITH MY INSURANCE?

An experienced staff member will:

- Call you to go over your prescription benefits and coverage
- Tell you what your co-pay is, if applicable
- Tell you about any XYWAV prescription savings plans for which you may qualify
- Work with your healthcare provider on prior authorizations, if required by your insurance company
- Provide information about any financial help that may be available to you

The Certified Pharmacy's attempt to get coverage from a third-party payer does not guarantee that you will get coverage.

GETTING MORE INFORMATION

WHERE CAN I GET MORE INFORMATION ABOUT XYWAV?

For more information about XYWAV, contact the REMS:

- **Phone:** 1-866-997-3688
- **Fax:** 1-866-470-1744 (toll free)
- **Outside the US:** +314-475-6000, ext 361 587
- **Website:** www.XYWAVXYREMREMS.com

NOTES

NOTES

KEEP THIS BOOKLET AS A HELPFUL REMINDER

If you have questions or need information,
contact the XYWAV and XYREM REMS Program.

Please see the Medication Guide for more detailed information about XYWAV.

Jazz Pharmaceuticals®

xywav™

(calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

C-III

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The pharmacy may ask you to measure how much XYWAV is left in your bottle. Please use this ruler to give them this information.

XYWAV and XYREM REMS

BROCHURE FOR PEDIATRIC PATIENTS AND THEIR CAREGIVERS

Important information about the safe use and handling of XYWAV

xywav™
(calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL
CIII

Reference ID: 4644289

XYWAV and XYREM REMS

Dear Caregiver,

Welcome to the XYWAV and XYREM REMS. You are receiving these materials because your child's healthcare provider has prescribed **XYWAV**™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL, for your child. XYWAV is a medicine used to treat cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. XYWAV may only be given to patients enrolled in the REMS.

Because of the serious risks associated with XYWAV, the Food and Drug Administration (FDA) has required a special program called a Risk Evaluation and Mitigation Strategy (REMS). The purpose of this REMS is to make sure the benefits of XYWAV outweigh the risks. All patients must be enrolled in the REMS to receive XYWAV. Each pediatric patient must have a caregiver who is counseled on the serious risks and safe use of XYWAV. This brochure contains information you need to know about XYWAV and will help you give XYWAV to your child correctly. Read this brochure before you start giving your child XYWAV.

After your child's healthcare provider sends in your child's enrollment form and first prescription for XYWAV, you will receive a call from the Certified Pharmacy of the XYWAV and XYREM REMS to counsel you on the serious risks and safe use of XYWAV, to tell you about the REMS requirements, and to answer any questions you or your child may have about XYWAV.

A few things must happen before you receive your child's first shipment of XYWAV:

- The Certified Pharmacy will call to:
  - Ask if your child's healthcare provider reviewed the XYWAV Brochure for Pediatric Patients and Their Caregivers with you
  - Explain that you will receive this brochure with your child's first shipment, and that all drug shipments will include the XYWAV Medication Guide
  - Ask you about your child's medical history and other medications he or she may be taking
  - Give you advice on how to prepare and give XYWAV to your child and how to store it safely
  - Go over your child's insurance information
- **You must take this call before you can get your child's XYWAV**

If you have any additional questions about XYWAV, please call your child's healthcare provider, or you can contact the REMS toll free at 1-866-997-3688. You can reach a pharmacist at this number 24 hours a day, 7 days a week with any questions. We hope you find this information and the REMS helpful.

Sincerely,

Jazz Pharmaceuticals

WARNING: XYWAV can cause serious side effects.
Your child should not drink alcohol or take other medicines that cause sleepiness

XYWAV is a prescription medicine used to treat patients 7 years of age and older with narcolepsy to reduce too much daytime sleepiness and to reduce cataplexy (suddenly weak or paralyzed muscles).

IMPORTANT INFORMATION ABOUT XYWAV INCLUDES THE FOLLOWING:

- When taking XYWAV, your child should not drink alcohol or take other medicines that may slow his or her breathing or mental activity or make him or her sleepy. Your child could have serious side effects
- XYWAV can cause serious side effects, including slow breathing or changes in alertness. Call your child's doctor right away if your child has any of these serious side effects
- Abuse of XYWAV can lead to dependence (a physical need to take the drug), craving for the medicine, and severe withdrawal symptoms (symptoms that start when the drug is stopped, especially when it is stopped suddenly)

- Patients usually fall asleep in about 5 to 15 minutes, although some patients have reported falling asleep more quickly (without first feeling drowsy) and others take more time. The time that it takes to fall asleep might be different from night to night. You should give each dose of XYWAV while your child is sitting up in bed and have your child lie down immediately after. Give the first dose at the time prescribed by your child's healthcare provider, and the second dose 2 ½ to 4 hours later. You may need to set an alarm to awaken to give the second dose
- Your child should not do anything that requires him or her to be fully alert for the first 6 hours after taking XYWAV. When your child first starts taking XYWAV, you and your child will need to be careful until you know how XYWAV affects him or her.
- Keep XYWAV out of the reach of children and pets. Get emergency medical help right away if a child who has not been prescribed XYWAV drinks XYWAV
- Report all side effects to your child's healthcare provider

WHAT WILL YOU FIND IN THIS BROCHURE?

This brochure provides information on the serious risks and safe use of XYWAV, answers important questions about how to use XYWAV properly, how to store it safely, and how to get your child's XYWAV.

WHAT IS THE XYWAV AND XYREM REMS PROGRAM?

Because of the serious risks associated with XYWAV, the FDA has required a special program called REMS for XYWAV and XYREM. Enrollment in the REMS by prescribers and patients is required by the FDA to ensure the benefits of XYWAV outweigh the risks associated with XYWAV. Your child is enrolled in the program when your child's healthcare provider sends in your signed enrollment form. At that time, your child's healthcare provider also will send your child's prescription for XYWAV to the Certified Pharmacy.

The Certified Pharmacy staff will review important information about XYWAV with you. They will also answer any questions you and your child may have about XYWAV.

Table of Contents

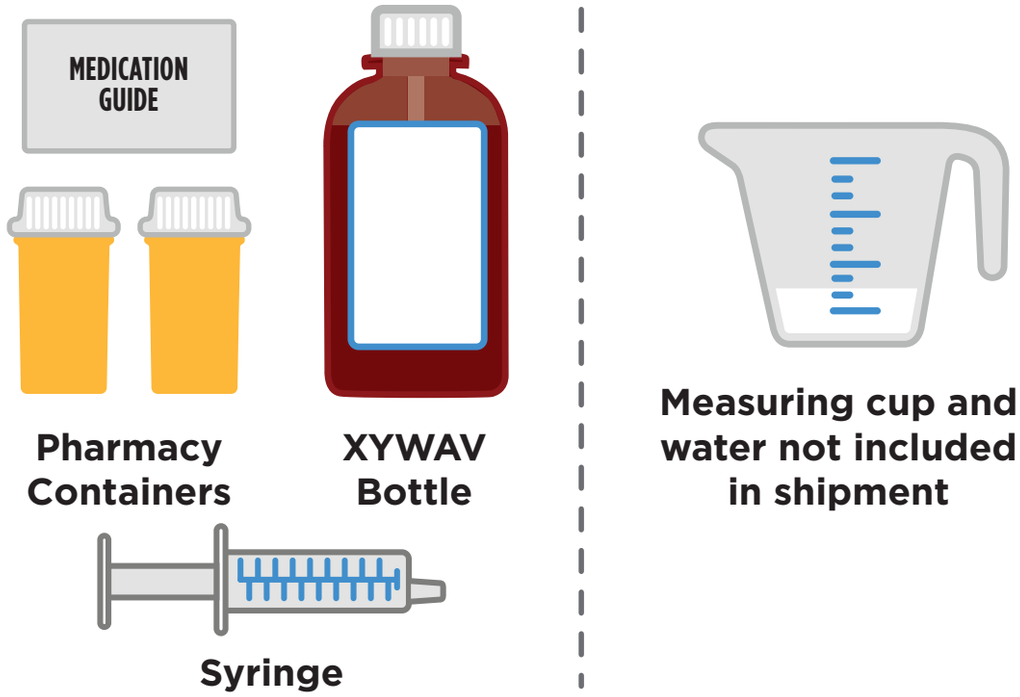
Preparation and Administration of XYWAV

XYWAV should be prepared and taken only as prescribed by your child's healthcare provider.

WHAT WILL I GET WITH MY CHILD'S XYWAV PRESCRIPTION?

With each prescription, you will get 1 or more bottles of XYWAV (each bottle, whether full or partial, contains the concentrated medicine), a dosing syringe for drawing up your child's XYWAV dose, 2 **empty** pharmacy containers with child-resistant caps, and a printed Medication Guide (Figure 1).

Figure 1



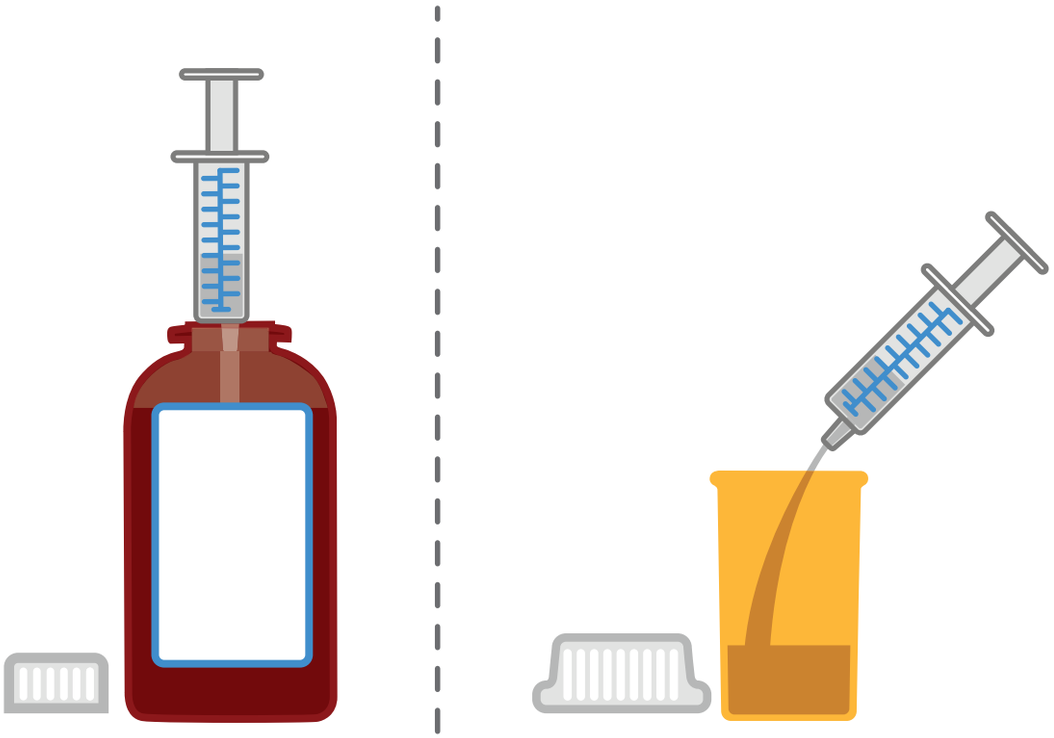
xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

C III

HOW DO I PREPARE MY CHILD'S DOSES?

Place the bottle on a hard, flat surface and grip the bottle with one hand and firmly press the syringe into the center opening of the bottle with the other. Pull back on the plunger until the medication flows into the syringe and the liquid level is aligned with the corresponding tick mark for your child's dose. After you draw up the first XYWAV dose, remove the syringe from the opening of the XYWAV bottle. Empty all of the medicine from the syringe into one of the provided **empty** pharmacy containers by pushing down on the plunger until it stops (Figure 2).

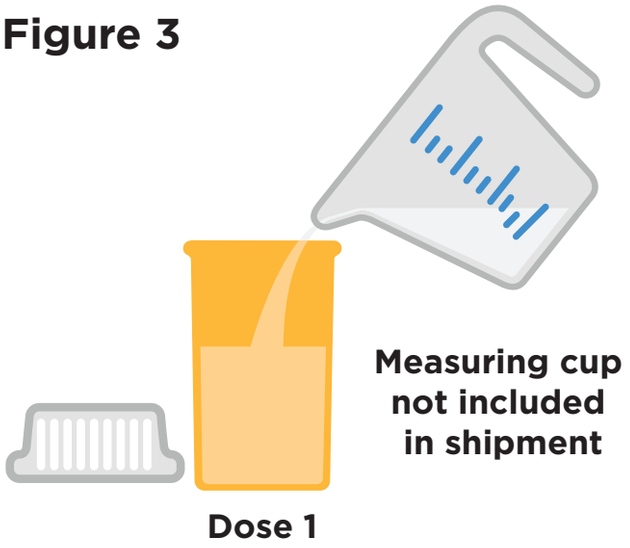
Figure 2



Using a measuring cup, pour about ¼ cup of water into the pharmacy container. **Be careful to add only water to the pharmacy container and not more XYWAV.** Place the child-resistant cap provided on the filled pharmacy container and turn the cap clockwise (to the right) until it clicks and locks in its child-resistant position.

Repeat the steps described above by drawing up the amount of medicine prescribed for your child's second dose; emptying the syringe into the second pharmacy container, adding about ¼ cup of water, and closing the pharmacy container.

Figure 3



Put the cap back on the XYWAV bottle and store the XYWAV bottle and both prepared doses in a safe and secure place. Store in a locked place if needed. Keep the XYWAV bottle and both prepared XYWAV doses out of the reach of children and pets.

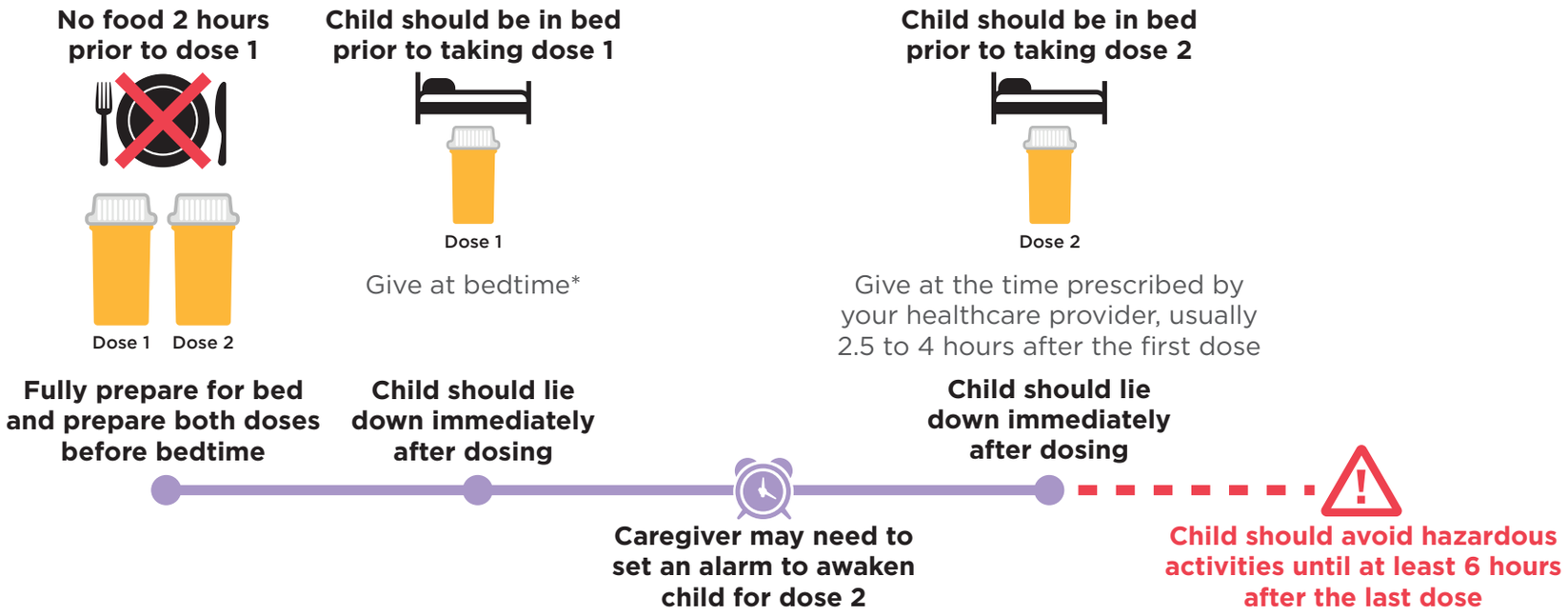
Rinse out the syringe and pharmacy containers with water after each use. Please refer to the Instructions for Use within the Medication Guide for additional details.

HOW DO I GIVE MY CHILD'S DOSES?

Wait at least 2 hours after your child eats before giving XYWAV.

XYWAV is a medicine that can make your child sleepy quickly; therefore, give your child's doses while he or she is sitting up in bed and have your child lie down immediately after dosing and remain in bed. Ensure your child is fully prepared for bed prior to taking the first nightly dose of XYWAV (for example, has brushed teeth, gone to the bathroom). Give the first dose at the time prescribed by your child's healthcare provider, and the second dose 2 ½ to 4 hours later. Ensure that all XYWAV doses are kept in a safe place until given. If your child continues evening activities after taking his or her dose, such as watching television or walking around, your child may experience light-headedness, dizziness, nausea, confusion, or other unpleasant feelings. Have the child lie down immediately after dosing and remain in bed (Figure 4).

Figure 4



*For children who sleep more than 8 hours per night, the first dose of XYWAV may be given at bedtime or after an initial period of sleep.

WHAT DO I DO IF MY CHILD MISSES A DOSE?

- It is very important to give both doses of XYWAV each night as prescribed. If the second dose is missed, skip that dose
  - Do not give your child XYWAV again until the next night
  - Never give your child both XYWAV doses at once
- Any unused XYWAV doses that you prepared but didn't give to your child must be thrown away within 24 hours from the time you first prepared your child's doses

HOW SOON WILL WE SEE A CHANGE IN SYMPTOMS?

After starting XYWAV, it may take a few weeks or longer to see your child's symptoms improve. It may also take time to find the right dose that works for your child. It is important that you talk with your child's healthcare provider often when your child first starts taking XYWAV.

Tell your child's healthcare provider if you or your child do not see any improvements.

WHAT ARE THE SIDE EFFECTS OF XYWAV?

XYWAV can cause serious side effects, including breathing problems (slower breathing, trouble breathing, and short periods of no breathing while asleep), mental health problems (confusion, seeing or hearing things that are not real, unusual or disturbing thoughts, feeling anxious or upset, depression, thoughts of suicide), and sleepwalking. If your child has any of these side effects, call your child's healthcare provider right away.

The most common side effects with XYWAV in pediatric patients are bedwetting, nausea, headache, throwing up, weight loss, decreased appetite, and dizziness. Side effects may increase with higher doses.

These are not the only possible side effects with XYWAV. If you or your child are worried about any possible side effects with XYWAV, talk with your child's healthcare provider or the pharmacist at the REMS.

You should report all side effects by contacting your child's healthcare provider, Jazz Pharmaceuticals at 1-800-520-5568, or the FDA at 1-800-FDA-1088.

ARE THERE ANY PRECAUTIONS THAT SHOULD BE TAKEN WHILE MY CHILD IS ON XYWAV?

- While taking XYWAV, your child should not drink alcohol or take medicines that cause sleepiness

- Your child should not do anything that requires him or her to be fully alert for the first 6 hours after taking XYWAV. When your child first starts taking XYWAV, you and your child will need to be careful until you know how XYWAV affects him or her.
- Before starting XYWAV, tell your child's healthcare provider if your child is pregnant, or plans to become pregnant, or is breastfeeding. XYWAV passes into breast milk. You and your child's healthcare provider should decide if your child will take XYWAV or breastfeed.
- Keep XYWAV in a safe place, out of the reach of children
- Give XYWAV to your child while he or she is sitting up in bed and have your child lie down immediately and remain in bed after dosing

Tell your child's healthcare provider and pharmacist about any other medicines he or she is taking, including if your child begins a new medicine while taking XYWAV. This would include prescription and non-prescription medicines, vitamins, and supplements.

It is also important to tell other healthcare providers, including pharmacists, that your child is taking XYWAV before your child starts or changes any medications.

How Often Should My Child's Healthcare Provider Check on My Child's Progress On XYWAV?

When your child first starts taking XYWAV, you may need to talk to his or her healthcare provider often until he or she has determined the best dose for your child. You can expect that your child's dose may need to be adjusted. After your child's dose has been established, his or her healthcare provider should check on your child every 3 months while taking XYWAV.

What do I need to do if my child is taking XYREM and their doctor prescribes XYWAV FOR THEM?

- **Your child should never take both XYWAV and XYREM at the same time, it can lead to serious side effects**
- XYWAV contains the same medication as XYREM, which is called oxybate, but with less sodium
- Your child should take their XYWAV exactly as instructed by their doctor
- Prepare your child's XYWAV the same way you prepared XYREM
- Do not mix XYREM and XYWAV together. If you have unused XYREM, dispose of it before starting XYWAV. Refer to "HOW DO I PROPERLY DISPOSE OF XYWAV?" for further instructions
- The Certified Pharmacy will contact you to talk to you about how to make this change

Storage and Safety Tips at Home

HOW DO I STORE XYWAV?

- Always store XYWAV in its original bottle
- Store XYWAV at room temperature. Do not refrigerate XYWAV
- Keep XYWAV in a safe place, out of the reach of children and pets. Get emergency medical help (call 911) right away if a child not prescribed XYWAV drinks XYWAV

HOW DO I PROPERLY DISPOSE OF XYWAV?

To properly dispose of XYWAV, pour any unused XYWAV down the sink or toilet drain. Mark out all personal information on the prescription label, including the XYWAV name, to make it unreadable before putting the empty bottle in the trash.

XYWAV patients have the option to return unused or expired drug. Please ask the Certified Pharmacy for more details.

If you misplace, lose, or damage your child's XYWAV dosing syringe, contact the Certified Pharmacy to have it replaced. Do not use a different syringe or try to guess the correct dose.

XYWAV AND XYREM TAKEBACK PROGRAM

XYWAV or XYREM patients have an option to return any unused, leftover or expired XYWAV or XYREM product through a drug takeback program, upon request. Patients can request a shipper from the Certified Pharmacy. Once you receive the shipper, remember to mark out or remove your personal information from the bottle(s) and place the bottles in the shipper. For more information, please ask the Certified Pharmacy for more details.

WHAT IF I HAVE CONCERNS ABOUT HAVING XYWAV IN MY HOME?

- If your child's XYWAV is lost or stolen, report the incident right away to the local police and to the Certified Pharmacy
- Give XYWAV only as your child's healthcare provider tells you. Remember that use of your child's XYWAV by others is illegal
- If you have any questions or concerns, or if you need advice about XYWAV, call your child's healthcare provider or the Certified Pharmacy

xywav™
(calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL
CIII

XYWAV and **XYREM** REMS

Important Information Your Child Must Know About Taking XYWAV

You can use these pages to help teach your young child what he or she needs to know about taking his or her XYWAV.

WHAT SHOULD MY CHILD KNOW ABOUT TAKING XYWAV?

Get Ready

- Get ready for bed before you drink your XYWAV
- Finish your bedtime routine before you get in bed and drink your XYWAV

Any questions? Please call the XYWAV and XYREM REMS at 1-866-997-3688.
Please see the Medication Guide for more-detailed information about XYWAV.

Stay In Bed

- Drink your XYWAV while sitting up in bed. Lie down right away after you drink it and stay in bed
- Call for a grown-up if you want to get out of bed after taking XYWAV
- It may take a while, or you may fall asleep quickly after taking XYWAV

xywav™ III

(calcium, magnesium, potassium, and sodium oxybates) oral solution

Reference ID: 4644289

XYWAV and **XYREM** REMS

Be Careful

- Be careful in the morning
- Call for a grown-up to help you if you still feel sleepy in the morning

Any questions? Please call the XYWAV and XYREM REMS at 1-866-997-3688.
Please see the Medication Guide for more-detailed information about XYWAV.

Reference ID: 4644289

Always Remember!

- Don’t share your XYWAV with anyone else
  - This medicine is only for you!
- Don’t drink too much XYWAV
  - Never drink more than one of your XYWAV cups at a time
  - Only drink XYWAV from your XYWAV cup
- Tell a grown-up how you are feeling and about any changes in how you are feeling

xywav™

(calcium, magnesium, potassium, and sodium oxybates) oral solution

Reference ID: 4644289

Including Your Child in His or Her Care

HOW CAN I PREPARE MY CHILD TO BE ABLE TO CARRY OUT ONE OR MORE SAFE USE ACTIVITIES?

It is important for your child to take an active part in the safe use of his or her XYWAV. This is especially true for teenagers and those going to college. This brochure can help you talk with your child about taking XYWAV.

Before your child moves away from your home (for example, going away to college), talk with your healthcare provider and the Certified Pharmacy about additional ways to ensure safe use, handling, and storage. To help prepare your child for this transition, make sure that he or she is counseled about the serious risks and safe use of XYWAV by a member of your child's XYWAV healthcare team (for example, your child's healthcare provider or the Certified Pharmacy). Your child should also read this brochure and ask his or her healthcare provider any questions he or she may have.

Enrolling Your Child in the XYWAV and XYREM REMS

DOES MY CHILD HAVE TO ENROLL IN THE XYWAV AND XYREM PROGRAM?

Yes. In order for your child to receive XYWAV, your healthcare provider will have you sign an enrollment form and will send the form to the REMS. You must verify that you have been counseled by your child's healthcare provider on the serious risks and safe use of XYWAV and that you were able to ask your child's healthcare provider any questions you have about XYWAV. You may choose to have your child also receive counseling from your healthcare provider on the serious risks and safe use of XYWAV.

WHAT IS MY ROLE AS A CAREGIVER?

As a caregiver of a pediatric patient who is in the REMS, you are required to:

- Read this brochure and ask your child's healthcare provider any questions you have about XYWAV.
- Ensure that XYWAV is prepared and given only as prescribed
- Ensure that XYWAV is kept in a safe place, away from children and pets, and protected from theft
- Notify your child's healthcare provider right away if you notice any serious side effects while your child is taking XYWAV

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

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Also be sure to let your child's healthcare provider know if your child is taking other medicines or if your child has any medical conditions that might affect his or her breathing.

If you need to give your responsibilities as your child's caregiver to someone else, please notify your child's healthcare provider. You also can contact the REMS toll free at 1-866-997-3688 to make sure that the new caregiver is counseled on the risks and safe use of XYWAV.

Filling Your Child's XYWAV Prescription

HOW IS MY CHILD'S PRESCRIPTION FILLED?

All XYWAV prescriptions are filled and shipped directly to your home only by the REMS Certified Pharmacy.

WHAT ELSE DOES THE CERTIFIED PHARMACY DO?

Your child's healthcare provider sends your child's XYWAV prescription directly to the Certified Pharmacy.

You will then receive a call from the Certified Pharmacy to counsel you on the serious risks and safe use of XYWAV, to tell you how to get your child started on XYWAV and to answer any questions about XYWAV. A staff member from the Certified Pharmacy will call you to complete a counseling checklist. The counseling checklist will include information about other medicines that your child is taking and other medical conditions that might increase your child's risk of serious side effects. The Certified Pharmacy will go over the information about how to use XYWAV safely and provide a copy of the Medication Guide with each XYWAV shipment.

The Certified Pharmacy will always ask you where and when you would like your child's XYWAV delivered and who will sign for the shipment. XYWAV will be shipped by an overnight service. You may be able to have your child's XYWAV shipped to your place of work or to a local overnight carrier hub for pickup. Saturday deliveries may also be an option for you. The Certified Pharmacy will work with you to find the best options available. When the courier arrives, you or another adult you previously named must sign for your child's XYWAV.

Finally, the Certified Pharmacy will call you soon after you receive your child's first XYWAV shipment to confirm receipt and answer any questions you may have about your child's first few days taking XYWAV.

HOW DO I GET XYWAV REFILLS FOR MY CHILD?

The Certified Pharmacy will contact you when it is close to your child's refill time. You may opt-in to receive text, e-mail, or automated voice reminders for refills. You may also call the Certified Pharmacy at 1-866-997-3688 to schedule your child's refills.

CAN MY LOCAL PHARMACY PROVIDE XYWAV FOR MY CHILD?

No. You can get your child's XYWAV only from the REMS Certified Pharmacy.

Insurance Coverage

WILL INSURANCE PAY FOR MY CHILD'S XYWAV?

In most cases, YES. A staff member from the Certified Pharmacy will call and work with your child's insurance company to help you get coverage for your child's XYWAV. In the unlikely event your child's insurance does not cover XYWAV or you can't afford the out-of-pocket costs, ask the Certified Pharmacy about available financial assistance programs.

WHAT IS THE PHARMACY'S ROLE WITH MY CHILD'S INSURANCE?

An experienced staff member will:

- Call you to go over your child's prescription benefits and coverage
- Tell you what your co-pay is, if applicable
- Tell you about any XYWAV prescription savings plans for which you may qualify
- Work with your child's healthcare provider on prior authorizations, if required by the insurance company
- Provide information about any financial help that may be available to you

The Certified Pharmacy's attempt to get coverage from a third-party payer does not guarantee that you will get coverage.

Contact Information

WHOM SHOULD I CONTACT WITH CONCERNS OR FOR MORE INFORMATION ABOUT XYWAV?

FOR QUESTIONS ABOUT SIDE EFFECTS OR FOR MORE INFORMATION ABOUT XYWAV, CONTACT YOUR CHILD'S HEALTHCARE PROVIDER:

Name: _____

Phone: _____

Email: _____

FOR MORE INFORMATION ABOUT XYWAV, CONTACT THE CERTIFIED PHARMACY:

- **Phone:** 1-866-997-3688
- **Fax:** 1-866-470-1744 (toll free)
- **Outside the US:** +314 475-6000, ext. 361 587
- **Website:** www.XYWAVXYREMREMS.com

TO REPORT ALL SIDE EFFECTS, YOU CAN CONTACT:

- Jazz Pharmaceuticals at 1-800-520-5568
- The FDA at 1-800-FDA-1088

FOR EMERGENCIES:

- Call 911

KEEP THIS BOOKLET AS A HELPFUL REMINDER

If you have questions or need information,
contact the XYREM REMS Program.

Please see the Medication Guide for more detailed information about XYWAV.

Jazz Pharmaceuticals®

xywav™

(calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

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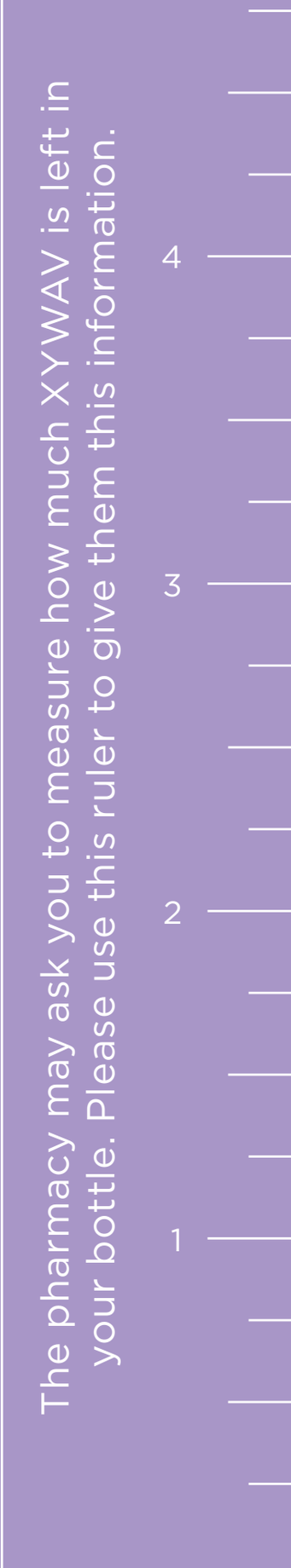
The pharmacy may ask you to measure how much XYWAV is left in your bottle. Please use this ruler to give them this information.



XYWAV and XYREM REMS

Certified Pharmacy Training

MODULES A AND B

All XYWAV and XYREM REMS Certified Pharmacy staff must complete Module A and the Module A Knowledge Assessment. Pharmacists must also complete Module B and the Module B Knowledge Assessment.

Dear XYWAV and XYREM REMS Certified Pharmacy Staff,

Welcome to the XYWAV and XYREM REMS, which has been approved by the Food and Drug Administration (FDA) as a Risk Evaluation and Mitigation Strategy (REMS).

THE XYWAV and XYREM REMS

The FDA has determined that a REMS is necessary to ensure that the benefits of XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution 0.5 g/mL and XYREM® (sodium oxybate) oral solution 0.5 g/mL outweigh the risks of serious adverse outcomes resulting from inappropriate prescribing, misuse, abuse, and diversion of XYWAV and XYREM by:

1. Informing prescribers, pharmacists, and patients of:
   - The risk of significant central nervous system (CNS) and respiratory depression associated with XYWAV and XYREM
   - The contraindication of use of XYWAV and XYREM with sedative hypnotics and alcohol
   - The potential for abuse, misuse, and overdose associated with XYWAV and XYREM
   - The safe use, handling, and storage of XYWAV and XYREM
2. Ensuring that pharmacy controls exist prior to filling prescriptions for XYWAV and XYREM that:
   - Screen for concomitant use of sedative hypnotics and other potentially interacting agents
   - Monitor for inappropriate prescribing, misuse, abuse, and diversion of XYWAV and XYREM
   - Notify prescribers when patients are receiving concomitant contraindicated medications or when there are signs of potential abuse, misuse, or diversion.

This training provides information about the XYWAV and XYREM REMS that includes important information about XYWAV and XYREM and the responsibilities of the Certified Pharmacy staff involved in the dispensing of XYWAV and XYREM.

XYWAV and XYREM are indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy

XYWAV and XYREM may be prescribed only by prescribers enrolled in the XYWAV and XYREM REMS and dispensed only to patients enrolled in the XYWAV and XYREM REMS.

Sincerely,

Jazz Pharmaceuticals

Table of Contents

XYWAV and XYREM REMS

Certified Pharmacy Training Module A

TRAINING FOR PHARMACY STAFF INVOLVED IN THE XYWAV AND XYREM REMS

All XYWAV and XYREM REMS Certified Pharmacy staff must complete training on Module A and successfully complete the associated Knowledge Assessment. Training must be completed annually.

Module A: XYWAV and XYREM REMS

IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

XYWAV and XYREM are indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

XYWAV and XYREM may be prescribed only by prescribers enrolled in the XYWAV and XYREM REMS and dispensed only to patients enrolled in the XYWAV and XYREM REMS.

HOW SUPPLIED

XYWAV and XYREM are shipped from the XYWAV and XYREM REMS Certified Pharmacy directly to patients. Each shipment to a patient will contain:

- The prescribed amount of medication, contained in one or more bottles of XYWAV or XYREM
- A press-in-bottle adaptor (PIBA) pre-inserted into the bottle
- A XYWAV and XYREM grams-based oral measuring device (plastic syringe) to measure out each nightly dose
- Two empty pharmacy containers with child-resistant caps for preparation of both nightly doses (XYWAV or XYREM dose mixed with water)
- A XYWAV or XYREM Medication Guide

CONTROLLED SUBSTANCE SCHEDULING

XYWAV and XYREM both contain oxybate, or gamma-hydroxybutyrate (GHB, a known drug of abuse). GHB has been used to facilitate sexual assaults. Because of its rapid sedative effects (particularly when mixed with alcohol) and its colorless and odorless appearance, GHB has been used to “spike” the drinks of unsuspecting victims. Because of its abuse potential, GHB is designated a controlled substance by the Drug Enforcement Administration (DEA) and has been placed in a bifurcated federal schedule:

- GHB products approved by the FDA, such as XYWAV and XYREM, and used as prescribed for therapeutic purposes are Schedule III drugs
- The active ingredients of XYWAV and XYREM are classified as Schedule I controlled substances when used for any other reason or by anyone other than for whom it was prescribed. Federal law prohibits the transfer of XYWAV and XYREM to any persons other than the patient for whom it was prescribed.

BOXED WARNINGS

WARNING: CENTRAL NERVOUS SYSTEM DEPRESSION
and ABUSE AND MISUSE.

- Central Nervous System Depression
  XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) is a CNS depressant. Clinically significant respiratory depression and obtundation may occur in patients treated with XYWAV at recommended doses [see Warnings and Precautions (5.1, 5.4)]. Many patients who received XYWAV during clinical trials in narcolepsy were receiving central nervous system stimulants [see Clinical Trials (14.1)].

- Abuse and Misuse
  The active moiety of XYWAV is oxybate or gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death [see Warnings and Precautions (5.2)].

  Because of the risks of CNS depression and abuse and misuse, XYWAV is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XYWAV and XYREM REMS [see Warnings and Precautions (5.3)].

WARNING: CENTRAL NERVOUS SYSTEM DEPRESSION
and ABUSE AND MISUSE.

- Central Nervous System Depression
  XYREM® (sodium oxybate) is a CNS depressant. In clinical trials at recommended doses, obtundation and clinically significant respiratory depression occurred in adult patients treated with Xyrem. Many patients who received XYREM during clinical trials in narcolepsy were receiving central nervous system stimulants.

- Abuse and Misuse
  XYREM (sodium oxybate) is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death.

  Because of the risks of CNS depression and abuse and misuse, XYREM is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the XYWAV and XYREM REMS.

CONTRAINDICATIONS

- XYWAV and XYREM are contraindicated in:
  - Patients who take sedative hypnotic agents
  - Patients who drink alcohol while using XYWAV or XYREM
  - Patients with succinic semialdehyde dehydrogenase deficiency, a rare disorder of inborn error of metabolism variably characterized by mental retardation, hypotonia, and ataxia.

WARNINGS AND PRECAUTIONS

CNS Depression

- XYWAV and XYREM are CNS depressants.
- Concurrent use of XYWAV or XYREM with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptic drugs, general anesthetics, muscle

relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death.
  - If use of these CNS depressants in combination with XYWAV or XYREM is required, dose reduction or discontinuation of one or more CNS depressants (including XYWAV or XYREM) should be considered.
  - If short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with XYWAV or XYREM should be considered.
- Patients who have sleep apnea or compromised respiratory function may be at a higher risk of developing respiratory depression, loss of consciousness, coma, and death with XYWAV and XYREM use.
- Healthcare providers should caution patients/caregivers against hazardous activities requiring complete mental alertness or motor coordination (e.g., driving) within the first 6 hours of dosing or after first initiating treatment with XYWAV or XYREM until certain that the drug does not affect the patient adversely.

Abuse, Misuse, and Diversion

- The active ingredients of XYWAV and XYREM contain oxybate, or GHB, a Schedule I controlled substance. Abuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse events, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death.
- The rapid onset of sedation, coupled with the amnestic features of XYWAV and XYREM, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (e.g., assault victim).
- Patients should be carefully evaluated for a history of substance abuse. Patients with a history of drug abuse should be closely monitored for signs of misuse or abuse of GHB (e.g., increase in dose or frequency of dosing, drug-seeking behavior, feigned cataplexy).

For complete safety information, please see the full Prescribing Information for XYWAV or XYREM.

XYWAV and XYREM REMS Requirements

XYWAV and XYREM may be prescribed only by prescribers enrolled in the XYWAV and XYREM REMS and dispensed only to patients enrolled in the XYWAV and XYREM REMS. Because of the risks of central nervous system depression, abuse, misuse, and diversion, XYWAV and XYREM are available only through a restricted distribution program called the XYWAV and XYREM REMS.

Required Components of this program include:

- Use of the central Certified Pharmacy.
- Healthcare Providers who prescribe XYWAV and XYREM must have completed the XYWAV and XYREM REMS Prescriber Enrollment Form and must comply with the requirements of the XYWAV and XYREM REMS.

- To receive XYWAV or XYREM, patients must be enrolled in the XYWAV and XYREM REMS and adult patients or caregivers (for pediatric patients) must be counseled on the serious risks and safe use of XYWAV and XYREM. Patients are enrolled by prescribers who must fill out and submit the XYWAV and XYREM REMS Patient Enrollment Form. Prescribers must also complete and submit either a XYWAV Prescription Form or a XYREM Prescription Form for all new XYWAV and XYREM prescriptions and for XYWAV and XYREM prescriptions for patients restarting treatment after not receiving either of the drug products for 6 months or more.
- Further information is available at www.XYWAVXYREMREMS.com.

Overview of Certified Pharmacy Responsibilities

DATABASE

The Certified Pharmacy will utilize the secure and validated XYWAV and XYREM REMS Central Database containing the following types of information:

- Patient and prescriber enrollment
- Patient medical history
- Prescription
- Risk management
- Shipment
- Interactions with patients, caregivers (for pediatric patients), and prescribers.

ENROLLMENT PROCESSING AND MAINTENANCE

- Prescriber and patient enrollment forms are submitted to the XYWAV and XYREM REMS by the prescriber.
- Information from the enrollment forms is maintained in the Central Database.
  - The Central Database will assign a unique identifier to each prescriber, patient or caregiver once their information is entered within the database by Certified Pharmacy staff.
- No duplicate patients may be enrolled:
  - When a new XYWAV and XYREM REMS Patient Enrollment Form is received, the Central Database must be searched to determine if the patient is already enrolled in the XYWAV and XYREM REMS.
  - If a match (duplicate patient) is found, the Certified Pharmacy will contact the patient and/or prescriber(s) to determine why a duplicate enrollment form was sent to the program.
  - If abuse, misuse, or diversion is suspected, the new enrollment will not be processed, the prescriber(s) will be notified, and a XYWAV and XYREM REMS Risk Management Report (RMR) will be completed and submitted to Jazz Pharmaceuticals.
- Patients or caregivers (for pediatric patients) attest that they have been counseled on the serious risks and safe use of XYWAV and XYREM; the Certified Pharmacy will also provide counseling for new patients and those restarting treatment, as required (after more than a 6 month lapse in treatment), as well as for new caregivers (for pediatric patients).
- The Certified Pharmacy will notify the prescriber of successful enrollment in the XYWAV and XYREM REMS, and that he or she is eligible to prescribe XYWAV and XYREM.
  - If there is a delay in shipping while a question about the prescriber's credentials could not be resolved, the patient/caregiver will be notified by the Certified Pharmacy.
  - If the prescription cannot be filled because a question about the prescriber's credentials could not be resolved, the patient/caregiver will be notified by a XYWAV and XYREM REMS pharmacist.
  - The prescriber will be notified that he or she cannot be enrolled in the event of credential verification failure.
- The Certified Pharmacy will notify the prescriber of successful patient enrollment in the XYWAV and XYREM REMS.
- Enrollment status is maintained in the Central Database.
  - The Certified Pharmacy will confirm that the prescriber's DEA, state license, and NPI numbers are active and that the prescriber has provided all REMS-required attestations.
  - A prescriber may be disenrolled from the program for expired DEA or NPI numbers, for expired state licensures, or for noncompliance with the XYWAV and XYREM REMS.

- Following enrollment, the patient remains in the XYWAV and XYREM REMS unless the Certified Pharmacy and/or the prescriber determines that the patient should be disenrolled.
- A patient may be disenrolled from the program for noncompliance with the XYWAV and XYREM REMS, including for multiple suspicious early refill requests, or other information that indicates abuse, misuse, or diversion.
- The Certified Pharmacy will contact a prescriber if an enrollment form is received for a patient previously disenrolled from the program at prescriber request, or for suspicions of abuse, misuse, or diversion, and will provide the prescriber with all relevant patient history.

PRESCRIPTION PROCESSING

- Upon receipt of a XYWAV or XYREM Prescription Form, the prescription information will be entered into the Central Database.
- The Certified Pharmacy will validate all prescriptions prior to dispensing XYWAV or XYREM. This includes verifying that:
  - The prescription form is complete and signed by the prescriber.
  - The prescriber is enrolled in the XYWAV and XYREM REMS and has active DEA, state license, and NPI numbers.
  - The patient is enrolled in the XYWAV and XYREM REMS and has no other active XYWAV or XYREM prescriptions.
    - If the Certified Pharmacy receives overlapping prescriptions for XYWAV or XYREM for a patient, the Certified Pharmacy will notify and consult each prescriber.
    - Prescriptions are considered overlapping when more than one prescription for XYWAV or XYREM is received for a patient from multiple prescribers within an overlapping timeframe.
    - If the Certified Pharmacy suspects abuse, misuse, or diversion, the prescription will not be filled, the prescriber will be notified, and an RMR will be completed.
    - There are valid reasons why a patient may have overlapping prescriptions, including if the patient moves or changes prescribers, or if the prescriber sends in a new prescription prior to the completion of all refills.
    - The Certified Pharmacy will ensure that under these situations a patient does not receive multiple overlapping shipments of XYWAV or XYREM.
  - The prescription form was received from the prescriber's office.
  - The prescription is dated within the last 6 months.
  - The prescription is for only a one-month supply on a patient's first shipment of any oxybate-containing product within the XYWAV and XYREM REMS, and no more than a 3-month supply on subsequent fills.
  - There are no discrepancies or concerns with the dosing and titration.
    - If there are discrepancies, or if the prescription form is incomplete, the Certified Pharmacy must contact the prescriber.

  Note: If a patient changes from XYREM to XYWAV, a XYWAV Prescription Form must be completed.
- Prior to dispensing XYWAV or XYREM to pediatric patients, the Certified Pharmacy will ensure each pediatric patient has a caregiver that has been counseled on the serious risks and safe use, handling and storage of XYWAV and XYREM.
- Once the prescription is validated, the Certified Pharmacy will contact the patient to schedule shipment and complete the required counseling
  - For a new patient, the Certified Pharmacy provides the XYWAV or XYREM Patient Quick Start Guide (for adult patients) or XYWAV or XYREM Brochure for Pediatric Patients and Their Caregivers (for pediatric patients).
  - A pharmacist must counsel the patient or caregiver (for pediatric patients) by completing the XYWAV and XYREM REMS Patient Counseling Checklist prior to the initial dispensing of XYWAV or XYREM.

SHIPPING

All XYWAV and XYREM is shipped to patients (or their adult designee) by an overnight service with receipt signature required.

- The patient or caregiver (for pediatric patients) may request an alternate shipping address, which is subject to approval by the Certified Pharmacy.

- See How Supplied for details of the contents of each XYWAV and XYREM shipment
- Daily tracking reports are generated to confirm the receipt of each order shipped
- Lost shipments are investigated.

MONITORING FOR INAPPROPRIATE PRESCRIBING, ABUSE, MISUSE, AND DIVERSION

The Certified Pharmacy must conduct detailed monitoring on an ongoing basis of patients and prescribers for signs of inappropriate prescribing, abuse, misuse, and diversion. The Certified Pharmacy will:

- Document early refill requests and instances of patient and prescriber behavior that suggest potential abuse, misuse, or diversion by completing an RMR. This information is maintained in the Central Database.
- Review the patient's RMR history and alerts in the Central Database prior to granting an early refill request or if abuse, misuse, or diversion is suspected.
- Discuss early refill requests or other patient incidents with the prescriber so that the prescriber can make a decision to allow or deny the early refill, or to take some other action based on the patient's behavior and history.
- Report all RMRs to Jazz Pharmaceuticals.
- Determine whether an alert should be placed in the patient's profile within the Central Database for repeated reports of lost, stolen, destroyed, or spilled drug for review prior to shipping XYWAV or XYREM.
- Inform a XYWAV and XYREM REMS pharmacist immediately if Certified Pharmacy staff suspect patients, or prescribers of abuse, misuse, or diversion.

ADVERSE EVENT REPORTING

- Everyone on the Certified Pharmacy staff has an essential role to play in the process of collecting information on potential adverse events for reporting to Jazz Pharmaceuticals. Potential adverse events must be reported to Jazz Pharmaceuticals within one business day. Jazz Pharmaceuticals reports adverse event information to the FDA.

ONGOING PATIENT AND CAREGIVER EDUCATION

Patients and caregivers in the XYWAV and XYREM REMS have access to ongoing education during XYWAV and XYREM treatment:

- 24-hour toll-free telephone help line staffed by a XYWAV and XYREM REMS pharmacist
- Continued contact with the Certified Pharmacy for every refill
- XYWAV and XYREM REMS website (www.XYWAVXYREMREMS.com).

XYWAV AND XYREM TAKEBACK PROGRAM

XYWAV and XYREM patients have an option to return any unused, leftover or expired XYWAV and/or XYREM product through a reverse distribution drug takeback program, upon request. Patients interested in this option can call the XYWAV and XYREM REMS for more information. The REMS Certified Pharmacy will be provided shippers that can be sent to the patient. Patients will be instructed to black out or remove their personal information from the bottle(s) and to place the bottles in the shipper.

XYWAV and XYREM REMS

Certified Pharmacy Training Module B

XYWAV AND XYREM REMS TRAINING FOR PHARMACISTS INVOLVED IN THE DISPENSING OF XYWAV AND XYREM

All XYWAV and XYREM REMS Certified Pharmacy pharmacists must complete training on Module B (in addition to Module A) and successfully complete the associated Knowledge Assessment. For all pharmacists who dispense XYWAV and XYREM, training must be completed annually.

Module B: XYWAV and XYREM REMS Training for Pharmacists

All pharmacists involved in dispensing XYWAV and XYREM must complete the following additional training at least annually. The XYWAV and XYREM REMS and functional training for pharmacists typically ranges from three to four weeks, depending upon job function and individual learning curve. Training may be extended as information retention of the trainee dictates. Training will be conducted by a pharmacist currently specializing in the XYWAV and XYREM REMS. Upon completion of formal training, a new pharmacist employee will perform assigned duties with a senior pharmacist employee as a resource and a mentor. The mentor will observe and monitor the performance of duties by the new employee to ensure competency. These duties will include:

- Execution of the XYWAV and XYREM REMS Patient Counseling Checklist
- Detailed monitoring including completion of a XYWAV and XYREM REMS Risk Management Report (RMR)
- Follow-up interactions with patients, caregivers (for pediatric patients), and prescribers
- System documentation

The mentoring senior pharmacist will release the trainee from observation upon confirmation that the new pharmacist employee has mastered the required skills.

XYWAV and XYREM REMS Requirements

XYWAV and XYREM may be prescribed and dispensed only to patients enrolled in the XYWAV and XYREM REMS. Because of the risks of central nervous system (CNS) depression, abuse, misuse, and diversion, XYWAV and XYREM are available only through a restricted distribution program called the XYWAV and XYREM REMS.

Required components of this program include:

- Use of a central Certified Pharmacy
- Healthcare providers who prescribe XYWAV and XYREM must complete and submit the following to the XYWAV and XYREM REMS:
  - The XYWAV and XYREM REMS Prescriber Enrollment Form
  - The XYWAV and XYREM REMS Patient Enrollment Form
  - Prescriptions for XYWAV on the XYWAV Prescription Form
    - Prescription refills and renewals may be conveyed by phone, by fax, or electronically and must be documented in the XYWAV and XYREM REMS Central Database.
  - Prescriptions for XYREM on the XYREM Prescription Form
    - Prescription refills and renewals may be conveyed by phone, by fax, or electronically and must be documented in the XYWAV and XYREM REMS Central Database.
- To receive XYWAV or XYREM, patients must be:
  - Enrolled in the XYWAV and XYREM REMS
  - Prescribed XYWAV or XYREM by a prescriber enrolled in the XYWAV and XYREM REMS
  - Counseled on the serious risks and safe use of XYWAV and XYREM
    - For pediatric patients, the caregiver must be counseled on the serious risks and safe use of XYWAV and XYREM
  - Have only one active XYWAV or XYREM prescription.

CERTIFIED PHARMACY RESPONSIBILITIES

The central Certified Pharmacy will:

- Limit the first prescription fill to a one-month supply of XYWAV or XYREM and limit subsequent prescription fills to no more than a 3-month supply
- Report potential adverse events to Jazz Pharmaceuticals within one business day.

- Notify prescribers when there are signs of potential abuse or misuse or when patients are taking sedative hypnotics, other CNS depressants, or other potentially interacting agents of which the prescriber is not already aware
- Utilize the Central Database containing the following:
  - Complete prescriber enrollment information
  - Complete patient information, including:
    - Name and two additional identifiers (date of birth, phone number, address, gender)
    - Current and previous prescribers
    - Comorbid conditions and concomitant medications reported by the patient
    - Prescription history
    - Caregiver(s) (for pediatric patients)
  - Prescription information, including:
    - XYWAV or XYREM
    - Date
    - Dose
    - Titration instructions
    - Number of refills
    - Directions
    - Total quantity (volume and number of days' supply)
    - Concomitant medications
  - Risk Management Reports (RMRs)
  - Shipment information, including:
    - Dates of shipments
    - Dates of shipment receipts
    - Patient addresses
    - Designee information
    - Number of shipments sent daily
    - Quantities of XYWAV and XYREM dispensed daily
  - Documentation of interactions with prescribers, patients, caregivers (for pediatric patients), and other parties.

These data must be available to the Certified Pharmacy for review on an ongoing basis to ensure that XYWAV and XYREM are dispensed to enrolled patients only after completion and documentation of safe use conditions. In certain cases, a pharmacist must access a patient's or prescriber's historical data in the Central Database and review it prior to dispensing XYWAV or XYREM.

PATIENT COUNSELING AND SCREENING

- Prior to dispensing XYWAV or XYREM, the Certified Pharmacy ensures the completion of the XYWAV and XYREM REMS Patient Counseling Checklist and its requirements and the documentation of the information received in the Central Database.
  - For new patients (first shipment of any oxybate-containing product within the XYWAV and XYREM REMS), and for patients who are restarting XYWAV or XYREM treatment after not receiving either of the drug products for 6 months or longer, the XYWAV and XYREM REMS Patient Counseling Checklist must be completed in its entirety.
  - For a new caregiver of an already enrolled pediatric patient, confirmation should be obtained, that he or she has been counseled on the serious risks and safe use of XYWAV and XYREM and that he or she has asked any questions he or she has about XYWAV or XYREM; the XYWAV and XYREM REMS Patient Counseling Checklist must be completed in its entirety.
  - For prescription renewals and refills, if the patient or caregiver has indicated a change in the patient's health or medications, the patient or caregiver will be transferred to the pharmacist to determine if further counseling and prescriber outreach is required. Steps 1, 3, 4 and 5 of the Counseling Checklist must be completed if the patient or caregiver indicates that the patient is taking a new medication or has a new comorbid medical condition that is listed in Step 4 of the Counseling Checklist.

- Each time a pharmacist completes the XYWAV and XYREM REMS Patient Counseling Checklist the pharmacist must:
  - Verify that early refill requests have been thoroughly questioned and approved through the RMR procedure (see below).
  - Screen for concomitant use of contraindicated medications (sedative hypnotics), alcohol, other CNS depressants, and other potentially interacting agents by the patient.
    - The pharmacist asks the patient or caregiver if the patient is taking any other medications and can consult external pharmacy databases to identify drug interactions or prescriptions for other drug products that might have been filled at different pharmacies before filling the prescription.
    - If patient use of a contraindicated medication or other potentially interacting agent is confirmed, and if the prescriber has not indicated prior knowledge, then the pharmacist will notify and consult the prescriber about the risks of concomitant medication use prior to shipping XYWAV or XYREM.
    - Instruct the patient/caregiver to alert the pharmacy to any new medication the patient begins as soon as possible.
  - Screen for other medical conditions.
    - The pharmacist asks the patient or caregiver what other medical conditions the patient has.
    - If the patient or caregiver indicates that the patient has a certain medical condition listed on the XYWAV and XYREM REMS Patient Counseling Checklist, the pharmacist counsels the patient or caregiver, and notifies the prescriber about the medical condition, if the prescriber has not indicated prior knowledge, prior to shipping XYWAV or XYREM.
    - Steps 4 and 5 of the counseling checklist may be completed after the patient/caregiver phone call.

- Document the results of the patient screening, all reported concomitant medications and comorbid medical conditions, the action(s) taken, and the date the checklist is completed in the Central Database.
- Document the completion of the XYWAV and XYREM REMS Patient Counseling Checklist in the Central Database.
- Include additional requirements (if any) per federal or state requirements that need to be collected as part of the patient counseling process.

- Patients or caregivers will also have access to a XYWAV and XYREM REMS pharmacist via the 24/7 toll-free telephone help line.

CLINICAL USAGE CLARIFICATIONS

The pharmacist must:

- Review the information on each XYWAV or XYREM Prescription Form
- Notify and consult the prescriber if there are any clinical usage clarifications required, such as:
  - Dose over maximum recommended dose (9 g/night)
  - Non-standard doses or instructions
  - Possible errors in dosing or titration amounts or directions
  - Weight has not been given for pediatric patients on initial and restart fills
- If the issue is not resolved with the prescriber, the pharmacist may consult with the Pharmacist in Charge at the Certified Pharmacy and with Jazz Pharmaceuticals.

PRESCRIPTION REFILLS

- Up to 5 refills are allowed on a XYWAV or XYREM prescription (per DEA regulations for CIII controlled substances).
- Refills and renewals may be conveyed by phone, by fax, or electronically from the prescriber and must be documented in the Central Database. Refill orders are opened at the Certified Pharmacy when the patient has approximately 10 days of XYWAV or XYREM therapy remaining from the previous shipment.
  - The Certified Pharmacy will contact the patient or caregiver and schedule a shipment if the patient or caregiver has not already contacted the Certified Pharmacy to request a refill.
  - The Certified Pharmacy will ask the patient or caregiver if there has been any change in the patient's medications or medical history. If the patient or caregiver indicates a change, the patient or caregiver will be transferred to a pharmacist, who determines if additional counseling and prescriber notification is required. Steps 1, 3, 4, and 5 of the XYWAV and XYREM REMS Patient Counseling Checklist must be completed if the patient or caregiver indicates that the patient is taking a new medication or has a new comorbid medical condition listed in Step 4 of the Counseling Checklist. Steps 4 and 5 should be completed post-call and should summarize the information learned on the call. The patient or caregiver should be counseled on:
    - Sedative hypnotics (e.g., diazepam, phenobarbital, zolpidem)
    - CNS depressants: including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptic drugs, general anesthetics, and muscle relaxants
    - Alcohol
    - Sleep apnea
    - Asthma, COPD, or other conditions affecting the patient's breathing
    - Other current medical conditions
  - The pharmacist must document refill counseling information and confirmation of prescriber consultation or notification in the Central Database.
- All patient requests for early refills are to be questioned and documented by the pharmacist.
  - An early refill request is a request for a XYWAV or XYREM shipment prior to the date of the next shipment.
  - Requests to accommodate shipment logistics (e.g., scheduled delivery date falls on a Sunday, holidays, and vacations) are not considered early refills.
  - If the early refill is required due to a dosage increase, a pharmacist must:

- Confirm the new dosage with the prescriber prior to processing the prescription.

– If an early refill is requested for any other reason, a pharmacist must:
  - Discuss the request with the patient or caregiver to evaluate the patient's compliance with therapy, assessing for misuse, abuse, and diversion
  - Evaluate the patient's record in the Central Database and review the patient's prior XYWAV and XYREM REMS RMR history to identify previous reports of early refills or other incidents suggestive of abuse, misuse, and diversion
  - Contact the prescriber to discuss the request and any prior early refill requests or incidents suggestive of abuse, misuse, and diversion
  - Send new shipments of XYWAV or XYREM to the patient only if approved by the prescriber
  - Send new shipments to replace XYWAV or XYREM reported stolen by a patient or caregiver only after obtaining a copy of the police report filed by the patient or caregiver
  - Document the discussion and outcome in the Central Database by completing a XYWAV and XYREM REMS RMR.

PATIENTS CHANGING BETWEEN XYWAV AND XYREM

Patients may change therapies while enrolled in the XYWAV and XYREM REMS provided that the following requirements have been met:

- The patient does not have overlapping active prescriptions of XYWAV and XYREM
- If a patient is changing between XYWAV and XYREM for the first time, or has not changed between them within the past 6 months, the Certified Pharmacy must contact the patient or caregiver and:
  – Inform the patient or caregiver that:
    - The safe use and administration instructions and REMS requirements for both products are the same
    - It is important that XYWAV or XYREM are taken as instructed by you or your child's doctor
    - Never take both XYWAV and XYREM at the same time
  – If the patient is changing from XYWAV to XYREM:
    - XYREM contains a high amount of sodium (salt) and may not be right for them, particularly if the patient is on a salt-restricted diet or has heart failure, hypertension, or compromised renal function.

Determine if the patient is on a salt-restricted diet, has high blood pressure, heart failure, or kidney problems. If the patient has any of these conditions, the patient and/or caregiver must complete Steps 1, 3, 4, and 5 of the XYWAV and XYREM REMS Patient Counseling Checklist (as described on page 15).

MONITORING AND ASSESSING FOR SIGNS OF ABUSE, MISUSE, AND DIVERSION

- Risk management events must be documented in the Central Database by completing a XYWAV and XYREM REMS RMR.
  – Risk management events are reported or discovered events outside the norm that give rise to a reasonable suspicion of abuse, misuse, or diversion
  – Examples of events that should generate an RMR include but are not limited to:
    - Requests for early refills
    - Patient's misuse or abuse of product
    - Lost, stolen, destroyed, or spilled drug
    - Delivery to incorrect address and not returned
    - Patient claims that product was not delivered while carrier shows receipt of delivery
    - Product tampering
    - Counterfeit product
    - Contaminated product

  - Inquiries and/or arrests by law or regulatory enforcement agencies associated with the misuse, abuse, or diversion of the product
  - Crimes related to the product
- RMRs must document:
  - Patient, caregiver (for pediatric patients), and prescriber identifying information (patient name to be concealed)
  - Reason for report
  - Certified Pharmacy actions
  - Prescriber contact
  - Supporting documentation if applicable (e.g., a police report, fire report, DEA Form 106, or shipper investigation report)
- If abuse, misuse, or diversion is suspected, the pharmacist must review the patient's RMR history and discuss the incident with the prescriber prior to shipping XYWAV or XYREM.
- Repeated reports of lost, stolen, destroyed, or spilled drug will be documented as an alert to the patient record stored in the Central Database and will be accessible to the dispensing pharmacist for review prior to shipping drug.
- The Certified Pharmacy and/or prescriber may disenroll a patient from the XYWAV and XYREM REMS after review and discussion of incidents suggestive of abuse and misuse.
- All RMRs must be reported to Jazz Pharmaceuticals.

SHIPPING PROCEDURES

- XYWAV and XYREM must be shipped via an overnight service with receipt signature required.
  - XYWAV and XYREM are shipped directly to the patient or adult designee (≥18 years, or ≥21 years if required by carrier) if the patient is not available to receive the order.
- The patient or caregiver (for pediatric patients) may request an alternate shipping address, which is then subject to approval by the Certified Pharmacy.
- If the patient or caregiver requests Saturday delivery, the Certified Pharmacy will verify with the overnight shipping service that it is available for the shipping address.

- Each XYWAV and XYREM shipment includes:
  - The prescribed amount of medication, contained in one or more bottles of XYWAV or XYREM
  - A press-in-bottle adaptor (PIBA) that is pre-inserted into the bottle
  - A XYWAV and XYREM grams-based oral measuring device (plastic syringe) to measure out each nightly dose
  - Two empty pharmacy vials with child-resistant caps for preparation of both nightly doses (XYWAV or XYREM dose mixed with water)
  - A XYWAV or XYREM Medication Guide.
- Daily tracking reports are generated to confirm the receipt of each order shipped during the previous 48 hours. Saturday deliveries are confirmed the following Monday.
  - A patient or caregiver (for pediatric patients) will be contacted if there is no proof of patient or designee signature, if the patient or designee on file did not sign for the shipment, or if there is a potential incomplete delivery.
  - If a shipment is reported lost, an investigation will be launched to find it.

INVENTORY CONTROL

The XYWAV and XYREM inventories must be reconciled at the start and end of each business day and recorded in the Central Database. A physical count must match the count in the Central Database. If not, no other patient orders can be processed until an investigation is completed and approved by the Pharmacist in Charge.

Pharmacy Staff Information

Name: _____

Job Title: _____

Knowledge Assessment: Module A

XYWAV and XYREM REMS Overview

1. XYWAV™ (calcium, magnesium potassium, and sodium oxybates) oral solution, 0.5 g/mL, and XYREM® (sodium oxybate) oral solution, 0.5 g/mL, are indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.
   - **A.** True
   - **B.** False

   (Answer: A)

2. Both XYWAV and XYREM contain GHB, and are controlled substances because:
   - **A.** It must be administered twice nightly
   - **B.** It has abuse potential
   - **C.** It requires dilution before dosing
   - **D.** It is a central nervous system (CNS) depressant

   (Answer: B)

3. XYWAV and XYREM are contraindicated in patients:
   - **A.** Who take sedative hypnotics
   - **B.** Who drink alcohol while using XYWAV or XYREM
   - **C.** Who have succinic semialdehyde dehydrogenase deficiency, a rare disorder of inborn error of metabolism variably characterized by mental retardation, hypotonia, and ataxia
   - **D.** A, B, and C

   (Answer: D)

4. XYWAV and XYREM are CNS depressants. Which of the following is NOT a warning related to CNS depression?
   - **A.** Concurrent use with other CNS depressants may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death
   - **B.** Patients who have sleep apnea or compromised respiratory function may be at a higher risk of developing respiratory depression, loss of consciousness, coma, and death with XYWAV or XYREM use
   - **C.** All surgeries and procedures must be reported as adverse events
   - **D.** Healthcare providers should caution patients/caregivers against hazardous activities requiring complete mental alertness or motor coordination (e.g., driving) within the first 6 hours of dosing or after first initiating treatment until certain that XYWAV or XYREM do not affect the patient adversely

   (Answer: C)

5. The XYWAV and XYREM REMS has which of the following requirements?
   - **A.** Use of the central Certified Pharmacy
   - **B.** Healthcare providers who prescribe XYWAV or XYREM must have completed the XYWAV and XYREM REMS Prescriber Enrollment Form and must comply with the requirements of the XYWAV and XYREM REMS
   - **C.** For adult patients to receive XYWAV or XYREM, they must be enrolled in the XYWAV and XYREM REMS and be counseled on the serious risks and safe use of XYWAV and XYREM treatment
   - **D.** For pediatric patients to receive XYWAV or XYREM, they must be enrolled in the XYWAV and XYREM REMS and their caregiver must be counseled on the serious risks and safe use of XYWAV and XYREM
   - **E.** All of the above

   (Answer: E)

6. In processing enrollment information, the XYWAV and XYREM REMS requires all of the following EXCEPT:
   - **A.** The Certified Pharmacy will confirm that the prescriber's DEA, state license, and NPI numbers are active and that the prescriber has provided all REMS-related attestations
   - **B.** Prescribers are notified when they are enrolled in the XYWAV and XYREM REMS and can prescribe XYWAV and XYREM
   - **C.** When a patient enrollment form is received, the Central Database is searched to determine if a patient is already enrolled (duplicate patient)
   - **D.** The Certified Pharmacy will ensure that refill orders are shipped when a patient has approximately 10 days of therapy remaining from the previous shipment
   - **E.** A patient or prescriber may be disenrolled for noncompliance with the XYWAV and XYREM REMS

   (Answer: D)

7. Which of the following is NOT true of caregivers of pediatric patients within the XYWAV and XYREM REMS?
   - **A.** A caregiver for a pediatric patient can be changed
   - **B.** They must complete a separate enrollment form
   - **C.** They must sign the patient enrollment form attesting that they have been counseled
   - **D.** They must be counseled on the serious risks and safe use of XYWAV and XYREM

   (Answer: B)

8. Which of the following is NOT entered in the Central Database in the XYWAV and XYREM REMS?
   - **A.** Patient and prescriber enrollment information
   - **B.** Patient medical history
   - **C.** Interactions with patients, caregivers and prescribers
   - **D.** Prescription information
   - **E.** Shipment information
   - **F.** All of the above are entered

   (Answer: F)

9. In validating a prescription for XYWAV or XYREM, the Certified Pharmacy will verify that:

- The XYWAV Prescription Form or the XYREM Prescription Form was received from the prescriber's office, is complete and signed by the prescriber, and is dated within the last 6 months;
- The prescriber is enrolled in the XYWAV and XYREM REMS and has active DEA, state license, and NPI numbers;
- The patient is enrolled in the XYWAV and XYREM REMS and has no other active XYWAV or XYREM prescriptions;
- The prescription is for only a one-month supply (first fill) or no more than a 3-month supply (refills).

A. True
B. False

(Answer: A)

10. When must a healthcare provider complete and submit a XYWAV Prescription Form to the pharmacy (select all that apply)?

A. For a patient's initial prescription of XYWAV
B. For patients who are restarting XYWAV after a lapse in therapy of 6-months or longer
C. For all refills and renewals of XYWAV
D. If a patient changes from XYREM to XYWAV and has never had a previous prescription for XYWAV

(Answer: A, B and D)

11. In monitoring patients and prescribers for signs of inappropriate prescribing, abuse, misuse, and diversion, the pharmacy will:

A. Document early refill requests and instances of patient and prescriber behavior that suggest potential abuse, misuse, or diversion by completing a XYWAV and XYREM REMS Risk Management Report
B. Place an alert in the patient's profile within the Central Database for repeated reports of lost, stolen, destroyed, or spilled drug for review prior to shipping XYWAV or XYREM
C. Inform a XYWAV and XYREM REMS pharmacist immediately if pharmacy staff suspects a patient or prescriber of abuse, misuse, or diversion
D. A and B only
E. A, B, and C

(Answer: E)

12. All potential adverse events must be reported to Jazz Pharmaceuticals within one business day.

A. True
B. False

(Answer: A)

Pharmacy Staff Information

Name: _____

Job Title: _____

Knowledge Assessment: Module B

In-Depth Pharmacy Training for the XYWAV and XYREM REMS

1. Upon completion of formal training, a new pharmacist will perform which of the following assigned duties under the observation of a senior pharmacy mentor?
   - **A.** Execution of the XYWAV and XYREM REMS Patient Counseling Checklist with new patients (or their caregiver for pediatric patients) and patients (or their caregiver for pediatric patients) who have not received either XYWAV or XYREM for 6 months or longer
   - **B.** Detailed monitoring, including completion of a XYWAV and XYREM REMS Risk Management Report (RMR)
   - **C.** Follow-up interactions with patients, caregivers (for pediatric patients), and prescribers
   - **D.** A, B, and C

   (Answer: D)

2. The Central Pharmacy certified through the XYWAV and XYREM REMS will:
   - **A.** Limit the patient's first shipment of any oxybate-containing product within the XYWAV and XYREM REMS to a one-month supply and subsequent shipments to a three-month supply
   - **B.** Report potential adverse events to Jazz Pharmaceuticals
   - **C.** Notify prescribers when patients are taking sedative hypnotics, other CNS depressants, or other potentially interacting agents of which the prescriber is not already aware or there are signs of potential abuse or misuse
   - **D.** A, B, and C

   (Answer: D)

3. The XYWAV and XYREM REMS Central Database will contain the following information that must be available for ongoing review to ensure XYWAV and XYREM are dispensed to enrolled patients only after completion and documentation of safe use conditions:
   - **A.** Complete patient and prescriber enrollment information
   - **B.** Patient information, including two additional identifiers, current and previous prescribers, comorbid conditions and concomitant medications reported by the patient or caregiver (for pediatric patients), and prescription history
   - **C.** Caregiver information (for pediatric patients)
   - **D.** Prescription information, including whether the prescription is for XYWAV or XYREM, date, dose, titration instructions, number of refills, and total quantity
   - **E.** RMRs, shipment information, and documentation of interactions with patients, caregivers, and prescribers
   - **F.** All of the above

   (Answer: F)

4. XYWAV and XYREM contain the same amount of the active moiety, oxybate, per milliliter of solution.
   A. True
   B. False
   (Answer: A)

5. Prior to shipment of XYWAV or XYREM, the XYWAV and XYREM REMS Patient Counseling Checklist must be completed as follows (not all possible scenarios triggering use of the Patient Counseling Checklist are noted:
   - For initial prescriptions of XYWAV or XYREM and for patients restarting XYWAV or XYREM after not receiving either XYWAV or XYREM for 6 months or more, complete the entire checklist
   - For prescription renewals and refills, if the patient or caregiver indicates a change in the patient's health or medications, transfer the patient or caregiver to the pharmacist to determine if further counseling and prescriber outreach is required. Steps 1, 3, 4, and 5 of the XYWAV and XYREM REMS Patient Counseling Checklist must be completed if the patient or caregiver indicates that the patient is taking a new medication or has a new comorbid medical condition that is listed in Step 4 of the XYWAV and XYREM REMS Patient Counseling Checklist.
   - For new caregivers of already enrolled pediatric patients, complete the entire checklist

   A. True
   B. False
   (Answer: A)

6. When the patient is transitioning from XYWAV to XYREM and is on a salt-restricted diet or has comorbidities such as high blood pressure, heart failure, or kidney problems, the certified pharmacy will have to counsel the patient utilizing the XYWAV and XYREM REMS Patient Counseling Checklist.
   A. True
   B. False
   (Answer: A)

7. If patient use of a contraindicated medication (e.g. sedative hypnotics or alcohol) is confirmed and the prescriber has not indicated prior knowledge, the pharmacist will contact and consult the prescriber prior to shipping XYWAV or XYREM.
   A. True
   B. False
   (Answer: A)

8. If there are any clinical usage clarifications needed for a prescription, the pharmacist will:
   A. Refuse to fill the prescription
   B. Notify and consult the prescriber
   C. Fill out an RMR
   D. Disenroll the prescriber
   (Answer: B)

9. Which of the following is NOT true for the prescription refill process?
   A. Up to 5 refills are allowed on a XYWAV or XYREM prescription
   B. Refill prescriptions can be submitted electronically
   C. Refill orders are opened when the patient has approximately 10 days of therapy remaining from the previous prescription
   D. All refills must be countersigned by the prescriber
   (Answer: D)

10. As part of processing a prescription refill, the pharmacist may discuss the following with the patient or caregiver (for pediatric patients) EXCEPT:
- **A.** Use of sedative hypnotics (e.g., diazepam, phenobarbital, or zolpidem)
- **B.** Use of alcohol
- **C.** History of sleep apnea
- **D.** Choice of prescriber
- **E.** History of asthma, COPD, or other conditions affecting breathing

(Answer: D)

11. If the pharmacist identifies that the patient is taking a potentially interacting agent that may present a risk to the patient, the pharmacist should consider which of the following actions before filling the prescription?
- **A.** Notifying law enforcement
- **B.** Taking no action
- **C.** Consulting the prescriber
- **D.** Consulting the insurance provider

(Answer: C)

12. In monitoring and assessing for signs of abuse, misuse, or diversion, a pharmacist must document risk management events in the Central Database by completing a Risk Management Report. Events that should generate an RMR include, but are not limited to (choose BEST answer):
- **A.** Early refill requests (excluding requests to accommodate shipment logistics)
- **B.** Lost, stolen, destroyed, or spilled drug
- **C.** Patient or caregiver claims that product was not delivered while carrier shows receipt of delivery
- **D.** Counterfeit or contaminated product
- **E.** All of the above

(Answer: E)

13. When is weight required on the prescription form?
- **A.** For all patients on every prescription form
- **B.** For all patients on initial and restart fills only
- **C.** For adult patients on every prescription form
- **D.** For adult patients on initial and restart fills only
- **E.** For pediatric patients on every prescription form
- **F.** For pediatric patients on initial and restart fills only

(Answer: F)

XYWAV and XYREM REMS

XYREM PRESCRIPTION FORM

XYREM® (sodium oxybate) oral solution 0.5 g/mL

Form available online at www.XYWAVXYREMREMS.com. Either submit online OR print, sign, and:
Fax to XYWAV and XYREM REMS: 1-866-470-1744 (toll free)
OR mail to XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589.
For more information, call the XYWAV and XYREM REMS at 1-866-997-3688 (toll free).

Please Print (*denotes required field; †denotes required field for pediatric patients on initial fill and restarts)

Prescriber Information

*First Name: _____ M.I.: _____ *Last Name: _____

*Street Address: _____ *Phone: _____

*City: _____ *State: _____ *Zip Code: _____ *Fax: _____

*DEA No.: _____ *NPI No.: _____

Office Contact: _____ Office Contact Phone: _____ *State License No.: _____

Patient Information

*First Name: _____ M.I.: _____ *Last Name: _____ *Primary Phone: _____

*Date of Birth (MM/DD/YYYY): _____ † Weight (if under age 18): _____ kg *Gender: ☐ M ☐ F Cell Phone: _____

*Address: _____ Work Phone: _____

*City: _____ *State: _____ *Zip Code: _____ E-mail: _____

*MEDICATIONS: (list all known current prescription and non-prescription medications and dosages or submit as a separate page)	COMORBIDITIES: (list known comorbidities or submit as a separate page)

Total Quantity	Refills:
1 2 3 month(s) supply (circle one)	0 1 2 3 4 5 (circle one)

Dispensing Instructions
Directions: Take first dose p.o., diluted in ¼ cup of water, at bedtime. Take second dose p.o., diluted in ¼ cup of water 2.5 to 4 hours later.
Note: Prepare both doses at the same time prior to bedtime. The XYREM shipment does not include water for dilution.

Initial prescription fill cannot exceed 1 month of therapy. Refills cannot exceed 3 months supply.
Please complete EITHER the titrated dosing OR fixed dosing section.
Please see the Prescriber Brochure and the full Prescribing Information for additional dosing instructions.

Titrated XYREM Dosing: Titrate to Effect

Starting Dose:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____	days
1st Titration:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____	days
2nd Titration:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____	days
3rd Titration:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____	days

First dose is ordinarily taken at bedtime; second dose is taken 2.5 to 4 hours later.
***For patients who sleep more than 8 hours per night, the first dose of XYREM may be given at bedtime or after an initial period of sleep.**
****If XYREM is used in patients 7 years of age and older who weigh less than 20 kg, a lower starting dosage, lower maximum weekly dosage increases, and lower total maximum nightly dosage should be considered. Some patients may achieve better responses with unequal doses at bedtime and 2.5 to 4 hours later.**

Fixed XYREM Dosing

Dose:	First dose: _____ g	+	Second dose (2.5 to 4 hours later):: _____ g	=	_____ g	Total Nightly Dose

Special Dosing Instructions

Prescriber Verification—My signature below signifies that: I understand the statements and agree to the REMS requirements, which are found on the back of this form; XYREM is medically appropriate for this patient; and I have informed the patient and/or caregiver that the XYWAV and XYREM REMS will send him or her the appropriate educational material (XYREM Patient Quick Start Guide for adult patients and XYREM Brochure for Pediatric Patients and their Caregivers for pediatric patients) with the first prescription fill.

***Prescriber Signature:** _____ ***Date:** _____

Supervising Physician Signature: _____ **Date:** _____
(If required by state law)

XYREM® (sodium oxybate) oral solution

Reference ID: 4644289

XYWAV and XYREM REMS

XYREM PRESCRIPTION FORM

XYREM® (sodium oxybate) oral solution 0.5 g/mL

Prescriber: Signature verification is required on the **FRONT** page of this XYREM Prescription Form as acknowledgment that you have an understanding of and/or agree to the following:

I understand that XYREM is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

I understand that:

- XYREM is a CNS depressant and can cause obtundation and clinically significant respiratory depression at recommended doses
- Alcohol and sedative hypnotics are contraindicated in patients who are using XYREM
- Concurrent use of XYREM with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptics, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death
  - If use of these CNS depressants in combination with XYREM is required, dose reduction or discontinuation of one or more CNS depressants (including XYREM) should be considered
  - If short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with XYREM should be considered
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with XYREM use
- XYREM is a Schedule III controlled substance with potential for abuse and misuse
- Safe use and handling by patients is important in order to prevent abuse/misuse and accidental exposure to family/friends, including children
- XYREM is to be prescribed only to patients enrolled in the XYWAV and XYREM REMS

I have read and understand the Prescribing Information and XYWAV and XYREM REMS Prescriber Brochure.

I have screened this patient for:

- History of alcohol or substance abuse
- History of sleep-related breathing disorders
- History of compromised respiratory function
- Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
- History of depression or suicidality

I have counseled this patient and/or caregiver on:

- The serious risks associated with XYREM
- Contraindications (alcohol and sedative hypnotics)
- Risk of concomitant use of XYREM with alcohol, other CNS depressants, or other potentially interacting agents
- Preparation and dosing instructions for XYREM
- Risk of abuse and misuse associated with use of XYREM
- Risk of operating hazardous machinery, including automobiles or airplanes, for the first 6 hours after taking a dose of XYREM
- Preparation and dosing instructions for XYREM
- Safe use, handling, and storage of XYREM

XYREM® (sodium oxybate) oral solution

XYWAV and XYREM REMS

XYWAV PRESCRIPTION FORM

XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

Form available online at www. XYWAVXYREMREMS.com. Either submit online, OR print, sign, and:
Fax to XYWAV and XYREM REMS: 1-866-470-1744 (toll free)
OR mail to XYWAV and XYREM REMS, PO Box 66589, St. Louis, MO 63166-6589.
For more information, call the XYWAV and XYREM REMS at 1-866-997-3688 (toll free).

Please Print (*denotes required field; †denotes required field for pediatric patients on initial fill and restarts)

Prescriber Information

*First Name: _____ M.I.: _____ *Last Name: _____

*Street Address: _____ *Phone: _____

*City: _____ *State: _____ *Zip Code: _____ *Fax: _____

*DEA No.: _____ *NPI No.: _____

Office Contact: _____ Office Contact Phone: _____ *State License No.: _____

Patient Information

*First Name: _____ M.I.: _____ *Last Name: _____ *Primary Phone: _____

*Date of Birth (MM/DD/YYYY): _____ † Weight (if under age 18): _____ kg *Gender: ☐ M ☐ F Cell Phone: _____

*Address: _____ Work Phone: _____

*City: _____ *State: _____ *Zip Code: _____ E-mail: _____

*MEDICATIONS: (list all known current prescription and non-prescription medications and dosages or submit as a separate page)	COMORBIDITIES: (list known comorbidities or submit as a separate page)

Total Quantity	Refills:
1 2 3 month(s) supply (circle one)	0 1 2 3 4 5 (circle one)

Dispensing Instructions
Directions: Take first dose p.o., diluted in ¼ cup of water, at bedtime. Take second dose p.o., diluted in ¼ cup of water 2.5 to 4 hours later.
Note: Prepare both doses at the same time prior to bedtime. The XYWAV shipment does not include water for dilution.

Initial prescription fill cannot exceed 1 month of therapy. Refills cannot exceed 3 months supply.
Please complete EITHER the titrated dosing OR fixed dosing section.
Please see the Prescriber Brochure and the full Prescribing Information for additional dosing instructions.

Titrated XYWAV Dosing: Titrate to Effect

Starting Dose:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____ days
1st Titration:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____ days
2nd Titration:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____ days
3rd Titration:	First dose: _____ g	+	Second dose: _____ g	=	_____ g	Total Nightly Dose for _____ days

First dose is ordinarily taken at bedtime; second dose is taken 2.5 to 4 hours later.
***For patients who sleep more than 8 hours per night, the first dose of XYWAV may be given at bedtime or after an initial period of sleep.**
****If XYWAV is used in patients 7 years of age and older who weigh less than 20 kg, a lower starting dosage, lower maximum weekly dosage increases, and lower total maximum nightly dosage should be considered.**
Note: Some patients may achieve better responses with unequal doses at bedtime and 2.5 to 4 hours later.

Fixed XYWAV Dosing

Dose:	First dose: _____ g	+	Second dose (2.5 to 4 hours later): _____ g	=	_____ g	Total Nightly Dose

Special Dosing Instructions

Prescriber Verification—My signature below signifies that: I understand the statements and agree to the REMS requirements, which are found on the back of this form; XYWAV is medically appropriate for this patient; and I have informed the patient and/or caregiver that the XYWAV and XYREM REMS will send him or her the appropriate educational material XYWAV Patient Quick Start Guide for adult patients and XYWAV Brochure for Pediatric Patients and their Caregivers for pediatric patients) with the first prescription fill.

***Prescriber Signature:** _____ ***Date:** _____

Supervising Physician Signature: _____ **Date:** _____
(If required by state law)

xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

Reference ID: 4644289

XYWAV and XYREM REMS

XYWAV PRESCRIPTION FORM

XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution, 0.5 g/mL

Prescriber: Signature verification is required on the **FRONT** page of this XYWAV Prescription Form as acknowledgment that you have an understanding of and/or agree to the following:

I understand that XYWAV is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

I understand that:

- XYWAV is a CNS depressant and can cause obtundation and clinically significant respiratory depression at recommended doses
- Alcohol and sedative hypnotics are contraindicated in patients who are using XYWAV
- Concurrent use of XYWAV with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating anti-epileptics, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death
  - If use of these CNS depressants in combination with XYWAV is required, dose reduction or discontinuation of one or more CNS depressants (including XYWAV) should be considered
  - If short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with XYWAV should be considered
- Patients who have sleep apnea or compromised respiratory function (e.g., asthma, COPD, etc.) may be at higher risk of developing respiratory depression, loss of consciousness, coma, and death with XYWAV use
- XYWAV is a Schedule III controlled substance with potential for abuse and misuse
- Safe use and handling by patients is important in order to prevent abuse/misuse and accidental exposure to family/friends, including children
- XYWAV is to be prescribed only to patients enrolled in the XYWAV and XYREM REMS

I have read and understand the Prescribing Information and XYWAV and XYREM REMS Prescriber Brochure.

I have screened this patient for:

- History of alcohol or substance abuse
- History of sleep-related breathing disorders
- History of compromised respiratory function
- Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents
- History of depression or suicidality

I have counseled this patient and/or caregiver on:

- The serious risks associated with XYWAV
- Contraindications (alcohol and sedative hypnotics)
- Risk of concomitant use of XYWAV with alcohol, other CNS depressants, or other potentially interacting agents
- Preparation and dosing instructions for XYWAV
- Risk of abuse and misuse associated with use of XYWAV
- Risk of operating hazardous machinery, including automobiles or airplanes, for the first 6 hours after taking a dose of XYWAV
- Preparation and dosing instructions for XYWAV
- Safe use, handling, and storage of XYWAV

XYWAV and XYREM REMS Patient Counseling Checklist

(Prior to dispensing XYWAV or XYREM, the XYWAV and XYREM REMS Certified Pharmacy ensures the completion of the checklist and its requirements and documents the information received in the XYWAV and XYREM REMS Central Database. Include additional requirements (if any) per federal or state requirements that need to be collected as part of the patient counseling process.)

STEP 1: PATIENT INFORMATION

Prescription for:

- ☐ XYWAV
- ☐ XYREM

(Complete this section for new patients [first shipment of any oxybate-containing product within the XYWAV and XYREM REMS], existing patients who are restarting XYWAV or XYREM treatment after not receiving either of the drug products for 6 months or longer, and patients who report a new medication or new comorbid medical condition listed in Step 4 of this checklist)

- ☐ New/restart
- ☐ Scheduled refill
- ☐ Early refill approved through RMR process
- ☐ Change of care responsibility

Patient Name: _____ **Patient ID Number:** _____

Prescriber Name: _____ **Prescriber ID Number:** _____

For pediatric patients, include caregiver information below.

Caregiver Name: _____ **Caregiver ID Number:** _____

Include Pharmacist name and date time stamp for each section completed.

STEP 2: COUNSELING

(Complete this section ONLY for new patients and existing patients who are restarting XYWAV or XYREM treatment after not receiving XYWAV or XYREM for 6 months or longer)

- ☐ Ask if the prescriber reviewed the appropriate XYWAV and XYREM REMS material with the patient/caregiver (XYWAV or XYREM Patient Quick Start Guide for adult patients, XYWAV or XYREM Brochure for Pediatric Patients and Their Caregivers for pediatric patients) and explain that this material will be included with the first shipment.

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

- ☐ Verify that the patient/caregiver has been counseled on **Therapy Expectations** below

  - During clinical trials with XYWAV and XYREM, many patients with narcolepsy saw some improvement with excessive daytime sleepiness and/or cataplexy in the first weeks after beginning therapy. However, the response varies from patient to patient. It may also take time to find the right dose that works for the patient. The prescriber will determine the dose that is appropriate.

- The patient/caregiver should talk to the prescriber about any troubling side effects or if the patient does not feel any benefits while taking XYWAV or XYREM.
- For any prescription changes, the prescriber should call or fax the new prescription change to the pharmacy; patients or caregivers should NEVER attempt to change the dose themselves.

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

☐ Verify that the patient/caregiver has been counseled on **Preparation and Administration** information below

- XYWAV/XYREM should be prepared and taken only as directed by the prescriber (review prescriber's instructions with patient/caregiver). Prepare the first dose by placing _____ grams of XYWAV/XYREM into one of the provided pharmacy containers. Add 1/4 cup of water to the container and turn the cap clockwise (to the right) until it clicks and locks into its child-resistant position. Then, prepare the second dose by placing _____ grams of XYWAV/XYREM into the second pharmacy container, adding about 1/4 cup of water, and closing the pharmacy container. The water does not come with XYWAV/XYREM. The patient/caregiver can use either tap or bottled water. The solution should remain clear, and it will taste salty. Place the containers in a safe place, out of the reach of children or pets.
  - For adult patients, the recommended location for the second dose is a safe place near the patient's bed.
  - For pediatric patients, it is recommended that the caregiver ensure that all XYWAV/XYREM doses are kept in a safe place until given.
- The patient/caregiver should call the XYWAV and XYREM REMS with any questions regarding how XYWAV/XYREM is to be prepared or taken. The pharmacy is available Monday through Friday, from 7 AM to 8 PM Central Time, at 1-866-997-3688, and a pharmacist is always available, 24 hours a day, 7 days a week, if needed.
- The patient/caregiver should refer to the product Medication Guide for additional information on preparation of doses.
- When the patient is ready to go to sleep, the first dose of XYWAV/XYREM should be taken while sitting in bed and the patient should lie down immediately after dosing.
  - Doses should be taken at least 2 hours after eating.
  - The time that it takes to fall asleep might be different from night to night. The patient may fall asleep quickly, in about 5 to 15 minutes, although some patients have reported falling asleep more quickly (without first feeling drowsy) and others may take longer to fall asleep.
  - The patient/caregiver may want to set an alarm to make sure the patient wakes up to take the second dose. The second dose of XYWAV/XYREM should be taken 2.5 to 4 hours after the first dose of XYWAV/XYREM is taken.
  - If a dose is missed, the patient should NEVER take two doses of XYWAV/XYREM at once.
- The diluted medication MUST be used within 24 hours of preparation. Discard any unused medication down the sink or toilet drain.
- When XYWAV/XYREM can no longer be drawn out of the bottle with the dispensing device, the patient/caregiver should dispose of the bottle. Remind the patient/caregiver to mark out information on the prescription label, including all personal information and the XYWAV/XYREM name, to make it unreadable before throwing out the empty bottle or other empty medicine packaging.
- The patient/caregiver should be sure to store both the XYWAV/XYREM bottle and all prepared doses in a safe and secure place out of the reach of children and pets. Emergency medical help should be sought right away if a child who has not been prescribed XYWAV/XYREM drinks XYWAV/XYREM.
- XYWAV/XYREM should be stored at room temperature.

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

☐ Verify that the patient/caregiver has been counseled on **Precautions Needed for XYWAV/XYREM Use**

- XYWAV/XYREM is classified as a controlled substance medication. XYWAV/XYREM must be used only by the person for whom it is prescribed and as directed by the physician. All lost or stolen medication must be reported.
- Federal law prohibits the transfer of this drug to any person other than the patient for whom it was prescribed.
- XYWAV/XYREM contains oxybate, which is a form of gamma-hydroxybutyrate (GHB). GHB has been used as a substance of abuse and has been associated with drug-facilitated sexual assault (date rape).
- Abuse of GHB can lead to dependence (a physical need to take the drug), craving for the medicine, and severe withdrawal symptoms (symptoms that start when the drug is stopped, especially when it is stopped suddenly). Abuse of GHB, with or without other central nervous system (CNS) depressants (e.g., nortriptyline, oxycodone, or heroin), including alcohol, can lead to seizure, trouble breathing, decreases in the level of consciousness, coma, and death.

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

☐ Verify that the patient/caregiver has been counseled on **Side Effects**

- In clinical trials:
  - in adult patients, the most commonly observed side effects associated with the use of XYWAV included: headache, nausea, dizziness, decreased appetite, parasomnia, diarrhea, hyperhidrosis, anxiety, and vomiting.
  - in adult patients, the most commonly observed side effects associated with the use of XYREM included: nausea, dizziness, vomiting, somnolence, enuresis, and tremor.
  - in pediatric patients, the most commonly observed side effects associated with the use of XYWAV/XYREM included: enuresis, nausea, headache, vomiting, weight decreased, decreased appetite, and dizziness. Some side effects may be more likely to be observed with higher doses of XYWAV/XYREM.
- XYWAV/XYREM can cause serious side effects, including trouble breathing while asleep, confusion, unusual or disturbing thoughts, depression, and passing out, even at recommended doses. The patient/caregiver should consult with the prescriber if the patient has any of these problems while taking XYWAV/XYREM.
- Patients should not participate in hazardous activities requiring complete mental alertness or motor coordination within the first 6 hours of dosing or after first initiating treatment until certain that XYWAV/XYREM does not affect them adversely.
- When taking XYWAV/XYREM, patients should not drink alcohol or take medicines that make them sleepy, including antidepressants, antipsychotics, anti-epileptics, opioids, general anesthetics, muscle relaxants, and/or illicit CNS depressants (e.g., heroin or GHB).
- These are not all of the side effects that patients may experience. The patient/caregiver should contact the prescriber if there are concerns about any possible side effects. Refer to the product Medication Guide for additional information on possible side effects.

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

☐ Instruct patients/caregivers to call the prescriber if:
- Patient is pregnant or plans to become pregnant. It is not known if XYWAV/XYREM can affect an unborn baby.
- Patient is breastfeeding. XYWAV/XYREM passes into breast milk. The patient/caregiver should talk to the prescriber to decide if the patient will take XYWAV/XYREM or breastfeed.
- Patient has or has had depression or tried to harm him- or herself. Patients should be watched for new signs of depression.
- Patient has liver problems. The dose may need to be adjusted.
- Patient has sleep apnea (short periods of not breathing while asleep), snoring, or breathing or lung problems. Patients with these may have a higher chance of serious breathing problems with XYWAV/XYREM.
- Patient has mental health problems.
- Patient walks during sleep.
- For patients taking XYREM: Patient is on a salt-restricted diet, has high blood pressure, heart failure, or kidney problems. XYREM is a drug with a high sodium (salt) content and may not be right for patients with these conditions.

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

☐ For situations involving a change of care responsibility:
- Inform caregiver/patient that this completes this section of the checklist. Confirm that the caregiver/patient has asked any questions he or she has about XYWAV/XYREM.

STEP 3: SCREENING

(Complete this section for new patients, existing patients who are restarting XYWAV or XYREM treatment after not receiving either of the drug products for 6 months or longer, and patients who report a new medication or new comorbid medical condition listed in Step 4 of this checklist)

1. Is the patient taking sedative hypnotics (e.g., diazepam, phenobarbital, or zolpidem)?

☐ Yes ☐ Counseled Patient/Caregiver
☐ No

Please list the drug(s) and dose of each: _____

_____

_____

2. Is the patient taking sedating antidepressants, antipsychotics, or anti-epileptics such as divalproex sodium (Depakote); general anesthetics; muscle relaxants; opioid analgesics; or illicit CNS depressants (e.g., heroin or gamma-hydroxybutyrate [GHB])?

☐ Yes ☐ Counseled Patient/Caregiver
☐ No

Please list the drug(s) and dose of each: _____

_____

_____

3. What other prescription and non-prescription medications is the patient taking?
Please list the drug(s) and dose of each: _____

_____

_____

4. Does the patient drink alcohol?
☐ Yes ☐ Counseled Patient/Caregiver
☐ No

5. Has the patient been diagnosed with sleep apnea (short periods of not breathing while asleep)?
☐ Yes ☐ Counseled Patient/Caregiver
☐ No

6. Does the patient have a diagnosis of or suffer from asthma, chronic obstructive pulmonary disease (COPD), or other conditions affecting his/her breathing (slower breathing, trouble breathing)?
☐ Yes ☐ Counseled Patient/Caregiver
☐ No

Please list the drug(s) used to treat, and dose of each, if known:

_____

_____

7. Does the patient have any other current medical conditions for which the patient is under a healthcare provider's care?
☐ Yes ☐ Counseled Patient/Caregiver
☐ No

Please list the conditions(s) if known: _____

_____

_____

8. Does the patient/caregiver have any clinical questions about XYWAV and/or XYREM?
☐ Yes ☐ Counseled Patient/Caregiver
☐ No ☐ Referred Patient/Caregiver to Prescriber

Please list the question(s): _____

_____

_____

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

STEP 4: CONCOMITANT MEDICATION & COMORBIDITY SUMMARY

(Complete this section for new patients, existing patients who are restarting XYWAV or XYREM treatment after not receiving either of the drug products for 6 months or longer, and patients who report a new medication or new comorbid medical condition listed in Step 4 of this checklist)

Medication Type

- ☐ Sedative hypnotics
- ☐ Alcohol
- ☐ Other potentially interacting agents:
  - ☐ Sedating antidepressants, antipsychotics, or anti-epileptics
  - ☐ General anesthetics
  - ☐ Muscle relaxants
  - ☐ Opioid analgesics
  - ☐ Divalproex sodium or other valproate drug (e.g., valproic acid)
  - ☐ Illicit CNS depressants (e.g., heroin or gamma-hydroxybutyrate [GHB])

Medical Conditions

- ☐ Sleep apnea
- ☐ Asthma
- ☐ COPD
- ☐ Other conditions affecting the patient's breathing
- ☐ History of depression or suicidality
- ☐ History of drug or alcohol abuse
- ☐ Seizure disorders
- ☐ Hepatic impairment
- ☐ High blood pressure, heart problems, kidney problems, or a salt-restricted diet [Prescriber consult may be required for patients taking XYREM]

If any medication types or medical conditions listed above are checked, or any questions in Step 3 were answered yes and there is no confirmation of prior prescriber knowledge, call the prescriber to consult:

Is a prescriber consult required?

- ☐ Yes
- ☐ No

If no, please provide reason: _____

If yes, action(s) taken (check all that apply and document details in prescriber consult outcome section below):

- ☐ Called prescriber: _____ / _____ / _____
- ☐ Other: _____ / _____ / _____

Prescriber consult outcome: _____

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

STEP 5: COMPLETION SUMMARY

(Complete this section for new patients, existing patients who are restarting XYWAV or XYREM treatment after not receiving either of the drug products for 6 months, and patients who report a new medication or new comorbid medical condition listed in Step 4 of this checklist)

Checklist Completed

- ☐ Yes
- ☐ No (XYWAV or XYREM is not shipped until checklist is completed.)

If yes, date checklist completed: _____ / _____ / _____ (Date Time)
If no, reason for non-completion: _____

_____

_____

_____ **(Pharmacist Name)** _____ / _____ / _____ **(Date/Time)**

XYWAV and XYREM REMS Risk Management Report

Risk Management Reports (RMRs) are filled out by the central Certified Pharmacy to document and report events that give rise to a reasonable suspicion of abuse, misuse, diversion, or any behavior or information that may indicate the drug is not being used according to the prescriber's instructions. The RMR history of a patient allows for the review of prior events of suspected abuse, misuse, or diversion and gives the pharmacist a more complete picture of the patient's history. The availability of individual patient RMRs enables the pharmacist to track and monitor for trends suggesting abuse, misuse, or diversion in individual patients. A trend or pattern of behavior in a patient's RMR history can be an indicator of abuse, misuse, or diversion and identifies patients who may require additional scrutiny when another event, such as an early refill request, occurs. In these cases, the RMR history informs actions of the pharmacist.

Examples of events that would require completion of an RMR under the XYWAV and XYREM REMS include, but are not limited to, the following:

- Patient requests for early refills.
- Patient's loss/misuse of the product.
- Patient claim that he or she did not receive the product but the delivery service shows receipt of delivery, or that the shipment was lost or stolen or delivered to an incorrect address and was not returned.
- Tampering with or counterfeiting or contaminating the product.
- Inquiries and/or arrests by law and regulatory enforcement agencies associated with the misuse or diversion of the product, or crimes related to the product.
- Prescribers whose DEA and/or state license numbers cannot be validated and the prescriber is submitting a REMS Prescriber Enrollment Form, REMS Patient Enrollment Form, XYWAV Prescription Form, or XYREM Prescription Form.

To complete an RMR:

- Assign a unique Control Number to each report in the Central Database.
- Complete investigation of the event, which may include contacting the patient, prescriber, law enforcement agency, or other parties.
- Attach any additional documentation required to support the investigation, including but not limited to the following: DEA 106 Form, police or fire report, or report from the shipping service.
- Complete review, follow up, and sign-off on the RMR.
  - When the event involves suspected abuse, misuse, or diversion, the prescriber will be contacted and an alert may be placed in the prescriber or patient profile of the Central Database to ensure prescriber and pharmacist awareness.
  - The Certified Pharmacy will monitor any associated patient or prescriber activity in the XYWAV and XYREM REMS during the course of the investigation and for a period after the investigation, where appropriate.
  - The Certified Pharmacy will work with Jazz Pharmaceuticals to determine the need to notify local, state, or federal agencies.
- Ensure that the information contained in the RMR is maintained in the Central Database.
- Send the RMR to Jazz Pharmaceuticals within one business day.

If the RMR includes a potential adverse event, the potential adverse event is reported through the Jazz Pharmaceuticals adverse event reporting system. If the RMR includes a product complaint, the event is also reported through the Jazz Pharmaceuticals product complaint system.

XYWAV and XYREM REMS Risk Management Report

Date: _____ **Control No.:** JRM- _____
Addendum: Yes ☐ No ☐

Type of reporter (e.g., patient, pharmacist, physician): _____

If not patient, name of reporter: _____

Nature of report (e.g., early refill request, lost or stolen bottle, package not received, other):

_____

Identification number(s) (patient and/or prescriber ID associated with RMR): _____

Date enrolled in program (from patient or prescriber record): _____

Reviewed alerts and RMR history for individual? Yes ☐ No ☐

RMR event (please provide detail): _____

_____

Date(s) of RMR event: Start: _____ End: _____

Early refill requested? Yes ☐ No ☐
If yes, reason for early refill request (e.g., dose increase, spilled medication, lost/stolen product):

_____

Prescriber contacted? Yes ☐ No ☐
If yes, outcome: _____ If no, reason: _____

Early refill status: Approved ☐ Denied ☐ Early refill status reason: _____

Potential adverse event associated with report? Yes ☐ No ☐ If yes, AE number: _____

Summary of investigation: _____

_____

Attachments (check all that apply):
DEA 106 Form ☐ Police/Fire Report ☐ Shipping Service Report ☐
Other ☐ (specify) _____

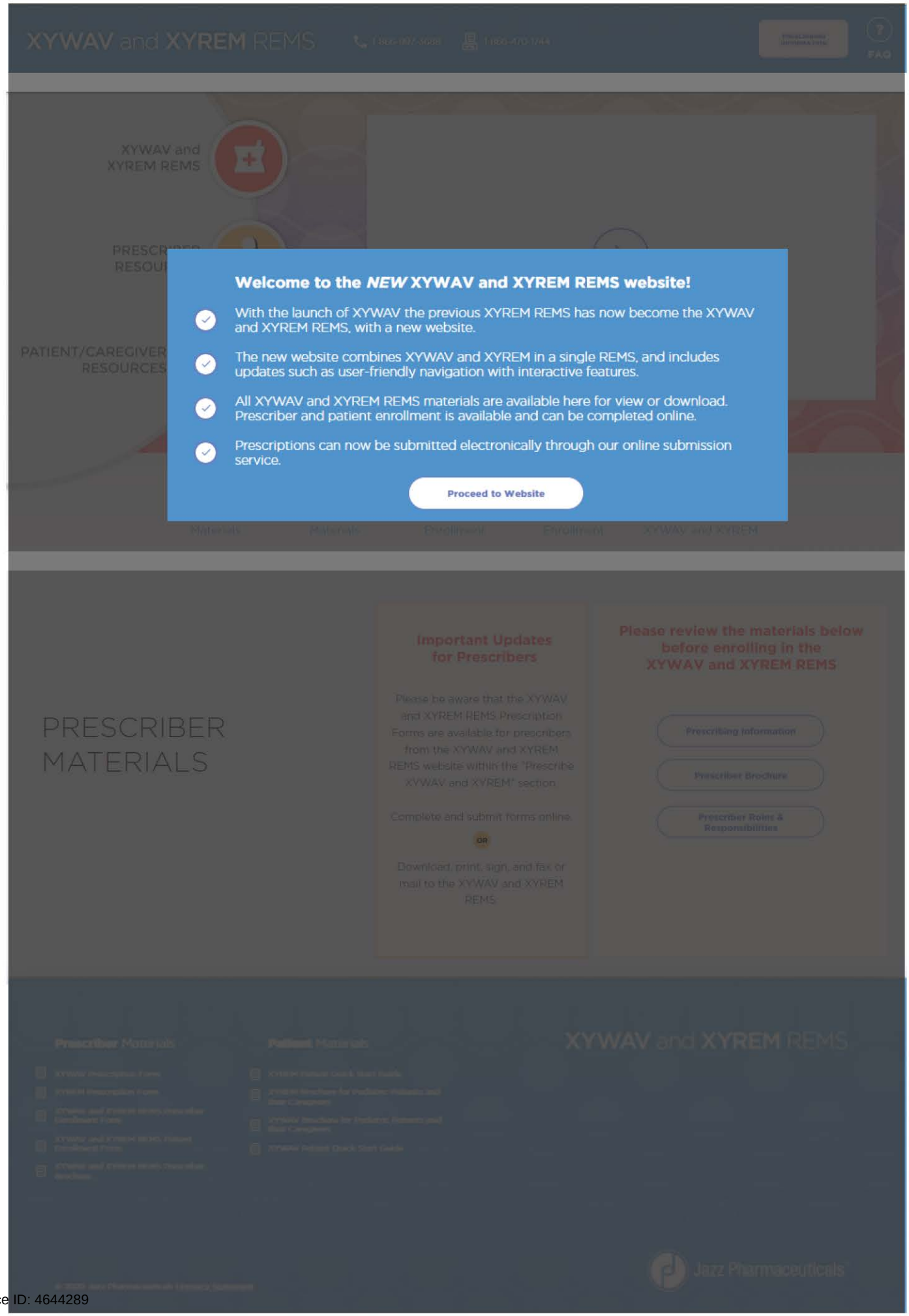
Monitor (alert placed): Yes ☐ No ☐ N/A ☐

Report closed: Yes ☐ No ☐

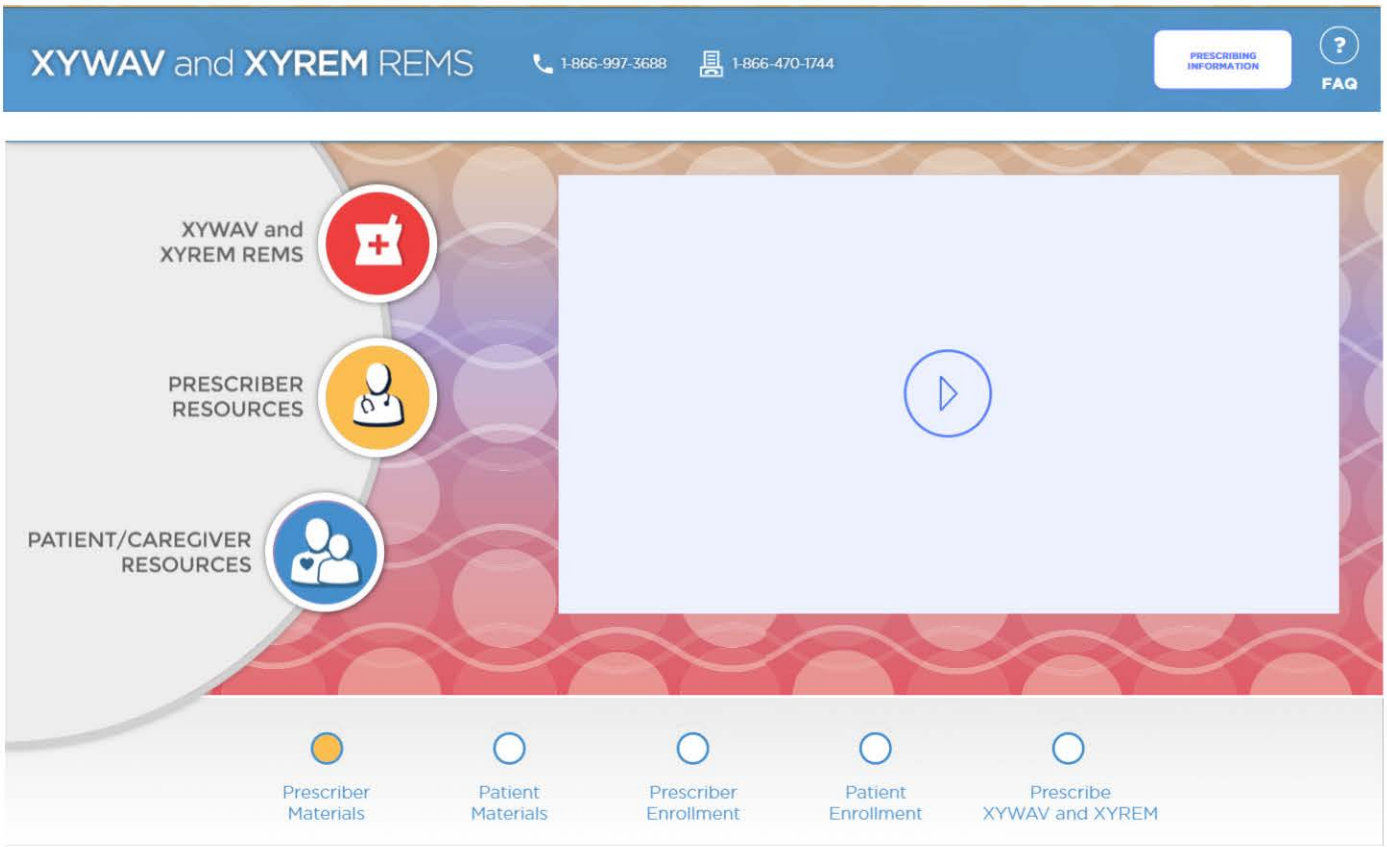
Operations Director (or designee): _____ Signature (date/time) _____

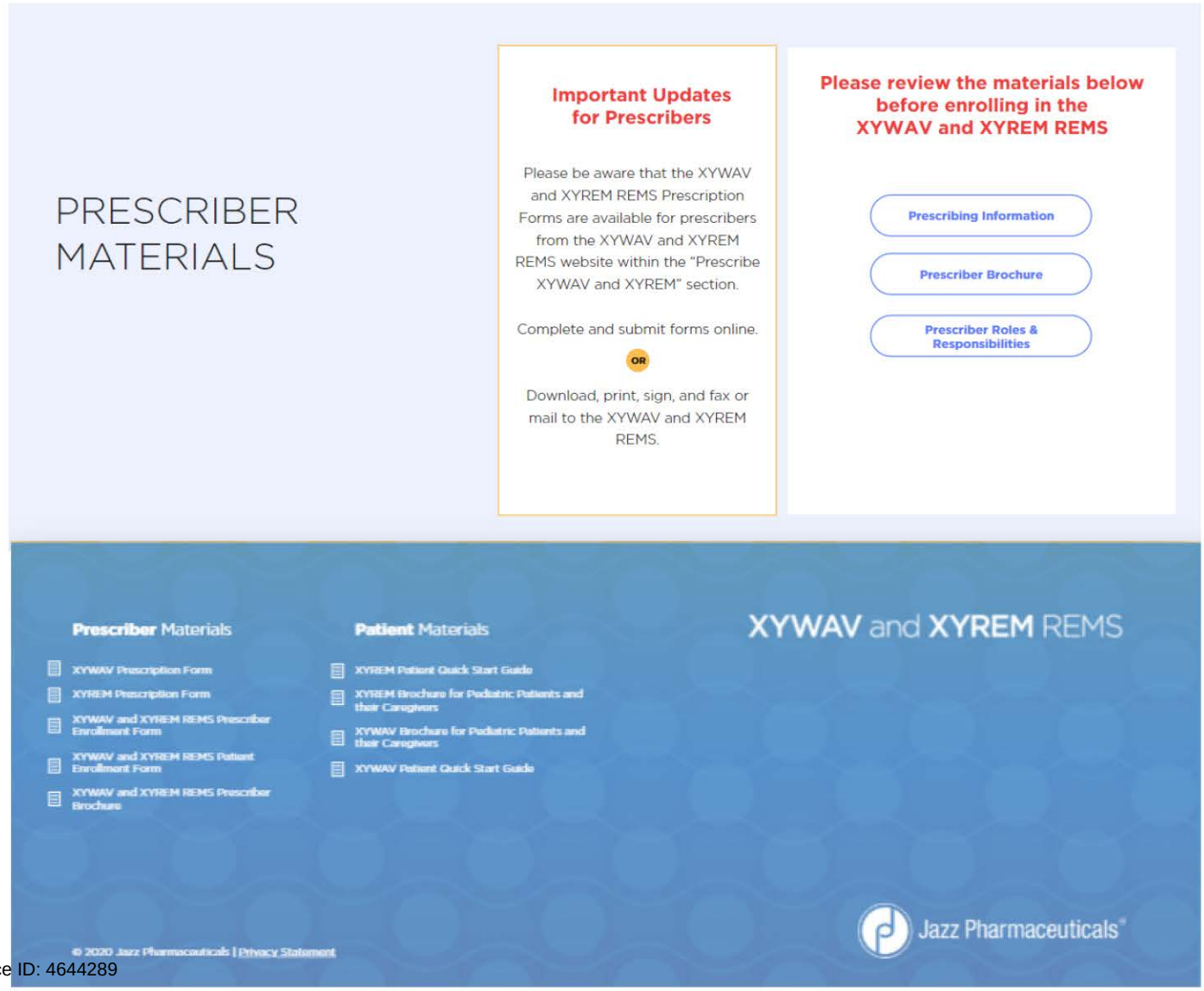
Pharmacist in Charge (or designee): _____ Signature (date/time) _____

Home Page (Info Pop-up)



Home Page


XYWAV and XYREM REMS
1-866-997-3688
1-866-470-1744
PRESCRIBING INFORMATION
FAQ
XYWAV and XYREM REMS
PRESCRIBER RESOURCES
PATIENT/CAREGIVER RESOURCES
Prescriber Materials
Patient Materials
Prescriber Enrollment
Patient Enrollment
Prescribe XYWAV and XYREM


PRESCRIBER MATERIALS
Important Updates for Prescribers
Please be aware that the XYWAV and XYREM REMS Prescription Forms are available for prescribers from the XYWAV and XYREM REMS website within the "Prescribe XYWAV and XYREM" section.
Complete and submit forms online.
OR
Download, print, sign, and fax or mail to the XYWAV and XYREM REMS.
Please review the materials below before enrolling in the XYWAV and XYREM REMS
Prescribing Information
Prescriber Brochure
Prescriber Roles & Responsibilities
Prescriber Materials
XYWAV Prescription Form
XYREM Prescription Form
XYWAV and XYREM REMS Prescriber Enrollment Form
XYWAV and XYREM REMS Patient Enrollment Form
XYWAV and XYREM REMS Prescriber Brochure
Patient Materials
XYREM Patient Quick Start Guide
XYREM Brochure for Pediatric Patients and their Caregivers
XYWAV Brochure for Pediatric Patients and their Caregivers
XYWAV Patient Quick Start Guide
XYWAV and XYREM REMS
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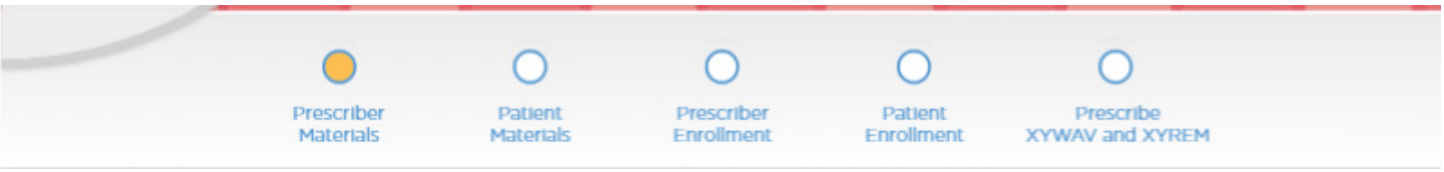
Top Carousel (1 of 4)

Top Carousel (2 of 4)

Top Carousel (3 of 4)

Bottom Carousel (1 of 5)



PRESCRIBER MATERIALS

Important Updates for Prescribers

Please be aware that the XYWAV and XYREM REMS Prescription Forms are available for prescribers from the XYWAV and XYREM REMS website within the "Prescribe XYWAV and XYREM" section.

Complete and submit forms online.

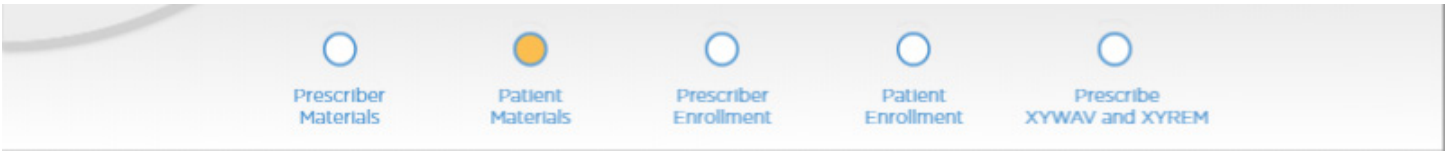
OR

Download, print, sign, and fax or mail to the XYWAV and XYREM REMS.

Please review the materials below before enrolling in the XYWAV and XYREM REMS

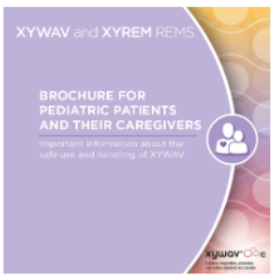
- Prescribing Information
- Prescriber Brochure
- Prescriber Roles & Responsibilities

Bottom Carousel (2 of 5)



PATIENT MATERIALS

Before enrolling, patients can use the Quick Start Guide and Brochure for Pediatric Patients and Their Caregivers on the right to find out more concerning the use of XYWAV and XYREM.



Brochure for Pediatric Patients And their Caregivers

Use the Caregiver Brochure to counsel caregivers of pediatric patients.

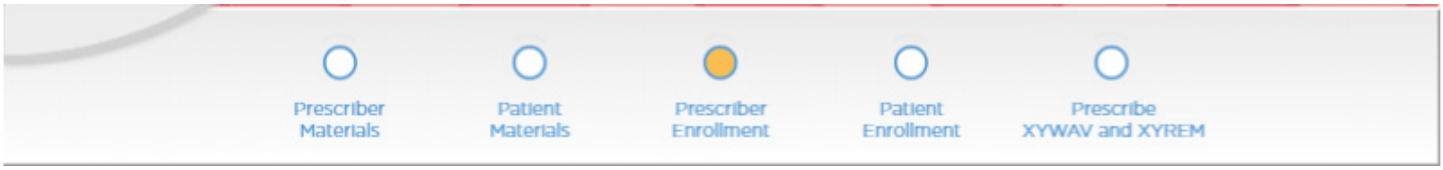
For XYWAV | For XYREM

Patient Quick Start Guide

Click below to read the Patient Quick Start Guide for counseling adult patients

For XYWAV | For XYREM

Bottom Carousel (3 of 5)



For Prescriber Use Only

PRESCRIBER ENROLLMENT

To become certified, each prescriber must complete a XYWAV and XYREM REMS Prescriber Enrollment Form once and submit it to the XYWAV and XYREM REMS via the options shown on the right.

Before enrolling in the XYWAV and XYREM REMS, ensure you're familiar by reading the XYWAV and XYREM Prescribing Information, Prescriber Roles & Responsibilities and the Prescriber Brochure.

The enrollment process for prescribers is quick, easy, and secure. Choose one of the two methods described below. Complete your enrollment form and submit it to the Certified Pharmacy for processing.

Option 1

Download:
Prescriber Enrollment Form

Scan and Email to:
ESSDSPrescribers@express-scripts.com

OR

Fax to:
XYWAV and XYREM REMS
1-866-470-1744 (toll free)

OR

Mail to:
XYWAV and XYREM REMS
PO Box 66589
St. Louis, MO 63166-6589

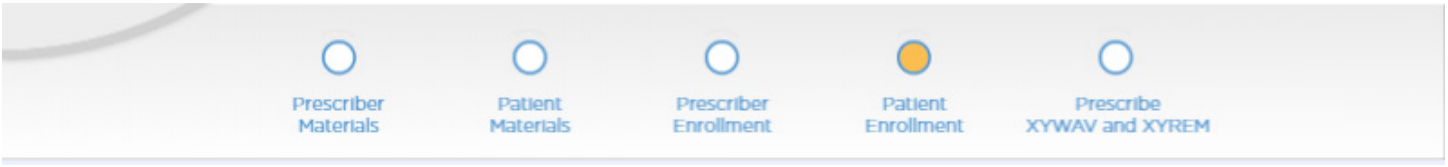
OR

Option 2

Submit using DocuSign
By using DocuSign, the XYWAV and XYREM REMS can ensure that your personal information can stay safe, secure, and protected.

ACCESS ONLINE PRESCRIBER ENROLLMENT FORM

Bottom Carousel (4 of 5)



For Prescriber Use Only

PATIENT ENROLLMENT

If you begin patient enrollment online, your patient will receive an e-mail to complete his/her portions of the form, including an e-signature. Then, you will submit the form to the Certified Pharmacy. Both you and your patient will be notified when enrollment in the program is successful.

If you choose Option 1, have your patient sign the enrollment form in your office. You will then submit it to the Certified Pharmacy by e-mail, fax, or mail.

Option 1

Download:
Patient Enrollment Form

Scan and Email to:
ESSDSPrescribers@express-scripts.com

OR

Fax to:
XYWAV and XYREM REMS
1-866-470-1744 (toll free)

OR

Mail to:
XYWAV and XYREM REMS
PO Box 66589
St. Louis, MO 63166-6589

OR

Option 2

Submit using DocuSign
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ACCESS ONLINE PATIENT ENROLLMENT FORM

Bottom Carousel (5 of 5)

FAQ

Is it still possible to enroll offline?
Yes, you can still enroll offline. Please download the PDF version of this form and follow the submission instructions.

How do I add my signature to an online enrollment?
This is done securely and easily through DocuSign.

Do I need a DocuSign account to complete the online enrollment process?
No. You do not need a DocuSign account to complete the online enrollment process.

Do I need to complete the online version of the prescriber enrollment form if I am already enrolled into the XYWAV and XYREM REMS?
No. If you are already enrolled into the newly approved XYWAV and XYREM REMS or the XYREM REMS or have completed the prescriber enrollment process offline and faxed it to the Certified Pharmacy, you do not need to complete the online version of the prescriber enrollment form.

You can still use the online enrollment form to enroll your patients.

How long does it take to process my enrollment so I can enroll patients?
Generally, the Certified Pharmacy will process your enrollment within 2 to 3 business days.

How will patients be notified that they need to complete their portion of the enrollment form?
Once you initiate the patient enrollment form, an email notification will be sent to your patient. The email will include a link to the enrollment form on DocuSign, where your patient can securely complete their portion of the enrollment process.

If your patient does not complete their portion of the enrollment form, we will send them a series of notification reminder emails.

How can I help my patient complete their portion of the enrollment form?
Due to security and privacy reasons, patients must fill out the entire portion of their form. If additional assistance is needed, we recommend you assist them with the process through a phone call.

Will a patient be able to include a copy of their insurance identification card?
If a patient confirms that they have prescription coverage on the enrollment form, they will be able to include a copy of their insurance identification card as an attachment.

If patients are completing the enrollment form on a mobile device, they will be able to use the camera to take a picture of their identification card.

How do I know my patient's information is safe?
DocuSign provides full document encryption to ensure the security and privacy of your data. Documents stored in their ISO 27001 and SSAE 16 data centers are encrypted with the highest levels of encryption.

Will my or my patient's information be shared with any third parties?
No. Your or your patient's information will be kept strictly confidential and never be shared or sold to third parties.

Prescriber Roles & Responsibilities

Prescribers enrolled in the XYWAV and XYREM REMS agree to perform the following:

1. Review the Prescribing Information (PI) and the XYWAV and XYREM REMS Prescriber Brochure.

2. Screen each patient for:

- History of alcohol or substance abuse

- History of sleep-related breathing disorders

- History of compromised respiratory function

- Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents

- History of depression or suicidality

3. Counsel each patient prior to initiating therapy with XYWAV or XYREM on the serious risks and safe use and handling of XYWAV and XYREM using the XYWAV and XYREM REMS Quick Start Guide.

4. Enroll each patient in the XYWAV and XYREM REMS by completing the XYWAV and XYREM REMS Patient Enrollment Form and submitting the form to the XYWAV and XYREM REMS.

5. Evaluate each patient within the first 3 months of starting XYWAV and XYREM therapy, including an evaluation of the following. It is recommended that patients be re-evaluated every 3 months thereafter while taking XYWAV and XYREM.

- Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents

- Serious adverse events

- Signs of abuse and misuse, including:
  i. an increase in dose or frequency of dosing
  ii. reports of lost, stolen, or spilled medication
  iii. drug-seeking behavior

6. Report all potential serious adverse events, including CNS depression, respiratory depression, loss of consciousness, coma, death, and any cases of suspected abuse, misuse, or diversion to Jazz Pharmaceuticals.

Each time a new prescription is written the prescriber will complete the XYWAV and XYREM REMS Prescription Form and submit it to the XYWAV and XYREM REMS. By completing and signing this form, the prescriber acknowledges:

1. Having an understanding of:

- The approved indications for XYWAV and XYREM:

  i. Treatment of cataplexy in narcolepsy

  ii. Treatment of excessive daytime sleepiness in narcolepsy

- The serious risks associated with XYWAV and XYREM

- The Prescribing Information and XYWAV and XYREM REMS Prescriber Brochure

2. Having screened the patient for the following:

- History of alcohol or substance abuse

- History of sleep-related breathing disorders

- History of compromised respiratory function

- Concomitant use of sedative hypnotics, other CNS depressants, or other potentially interacting agents

- History of depression or suicidality

3. Having counseled the patient on:

- The serious risks associated with XYWAV and XYREM Contraindications (alcohol and sedative hypnotics) and implications of concomitant use of XYWAV and XYREM with other potentially interacting agents

- Preparation and dosing instructions for XYWAV and XYREM

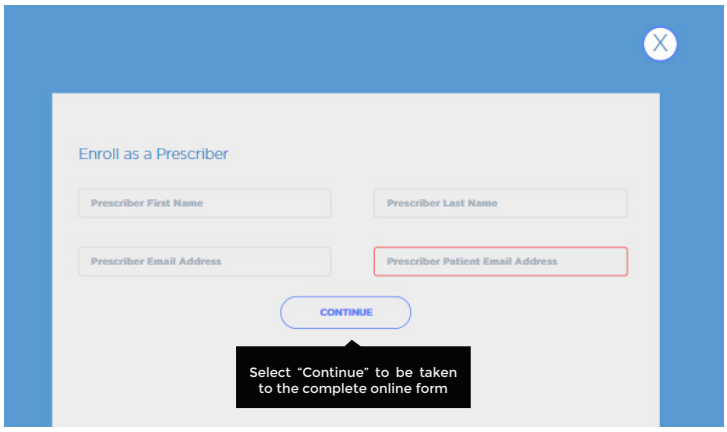
- Risk of abuse and misuse associated with XYWAV and XYREM

- Risk of operating hazardous machinery including automobiles or airplanes for the first 6 hours after taking a dose of XYWAV and XYREM

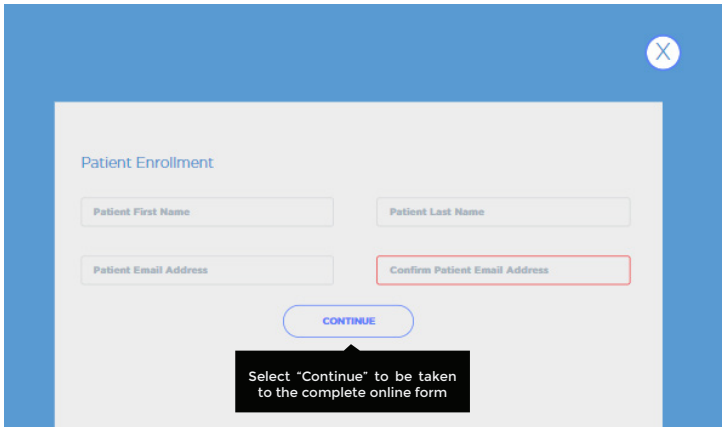
- Safe use, handling, and storage of XYWAV and XYREM

4. That XYWAV and XYREM is medically appropriate for the patient

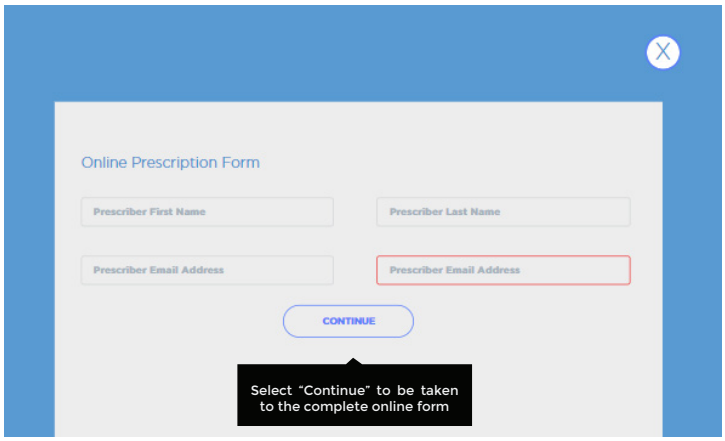
5. Having listed all known prescription and nonprescription medications and doses on the XYWAV and XYREM REMS Prescription Form



Online version of PDF Prescriber Enrollment Form



Online version of PDF Patient Enrollment Form



Online version of PDF Prescription form

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ERIC P BASTINGS
07/21/2020 05:40:10 PM