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.

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