

JYNARQUE®
(tolvaptan) tablets

JYNARQUE REMS (RISK EVALUATION AND MITIGATION STRATEGY) PROGRAM OVERVIEW

This overview describes the requirements of the JYNARQUE REMS and the responsibilities of prescribers, pharmacies and patients.

If you have any questions regarding the REMS, please visit www.JYNARQUErems.com
or call **1-866-244-9446**.

Phone: 1-866-244-9446 | www.JYNARQUErems.com | Fax: 1-866-750-6820

Healthcare providers must report cases of liver injury to the REMS Program Coordinating Center.

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WHAT IS THE JYNARQUE REMS?

- This Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage the risk of serious and potentially fatal liver injury associated with use of JYNARQUE and is required by the Food and Drug Administration (FDA) to ensure the benefits of JYNARQUE outweighs its risks.
- **Acute liver failure requiring liver transplantation has been reported in the post-marketing ADPKD experience. Discontinuation in response to laboratory abnormalities or signs or symptoms of liver injury (such as fatigue, anorexia, nausea, right upper abdominal discomfort, vomiting, fever, rash, pruritus, icterus, dark urine or jaundice) can reduce the risk of severe hepatotoxicity.**

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HOW DOES THE JYNARQUE REMS WORK?

	Before Prescribing/Dispensing JYNARQUE	Before Starting JYNARQUE for each Patient	While on JYNARQUE Treatment for Each Patient
Prescriber	Prescriber certification	<ul style="list-style-type: none"> • Counsel the patient on the risk of serious and potentially fatal liver injury and the requirement for liver function monitoring at baseline and specific intervals during treatment • Assess the patient's liver function and appropriateness of initiating treatment • Enroll the patient 	<ul style="list-style-type: none"> • Assess the patient's liver function and appropriateness of continuing treatment at 2 weeks, 4 weeks and monthly for the first 18 months of treatment and every 3 months thereafter • Document appropriateness of continuing treatment and submit to the REMS using the Patient Status Form every 3 months for the first 18 months of treatment and every 6 months thereafter
Pharmacy (Outpatient & Inpatient)	Pharmacy certification		<ul style="list-style-type: none"> • Outpatient: Obtain authorization to dispense each prescription by contacting the REMS online or by phone to verify prescriber is certified, and patient is enrolled and authorized to receive the drug <ul style="list-style-type: none"> — Dispense no more than a 30-day supply • Inpatient: Verify the prescriber is certified and the patient is enrolled in the REMS Program <ul style="list-style-type: none"> — Dispense no more than a 15-day supply at discharge
Patient		<ul style="list-style-type: none"> • Review Patient Guide • Patient Enrollment • Get a blood test before your first dose 	<ul style="list-style-type: none"> • Get a blood test at 2 weeks and 4 weeks after you start treatment • Get a blood test every month for the first 18 months of treatment and then every 3 months thereafter

WHAT ARE THE REQUIREMENTS OF THE JYNARQUE REMS?

• In order to receive JYNARQUE, prescribers, pharmacies, and patients must comply with the requirements of the JYNARQUE REMS.

Prescriber	Pharmacy (Outpatient & Inpatient)	Patient
<p>To prescribe JYNARQUE:</p> <ol style="list-style-type: none"> 1. Become certified by completing a one-time certification process 2. As you start patients on JYNARQUE, counsel and evaluate baseline liver testing prior to enrolling them into the REMS, and complete the prescription 3. Perform ongoing patient monitoring, evaluate liver testing at 2 weeks, 4 weeks and monthly for the first 18 months of treatment and every 3 months thereafter 4. Complete a <i>Patient Status Form</i> for each patient every 3 months for the first 18 months of treatment and every 6 months thereafter 	<p>To dispense JYNARQUE*:</p> <ol style="list-style-type: none"> 1. Designate an authorized representative, become certified, and recertify if there is a change in the authorized representative 2. Train staff and comply with REMS requirements 3. Outpatient: Obtain authorization to dispense each prescription by contacting the REMS online or by phone to verify prescriber is certified, and the patient is enrolled and authorized to receive the drug <ul style="list-style-type: none"> — Dispense no more than a 30-day supply 4. Inpatient: Verify the prescriber is certified and the patient is enrolled in the REMS Program <ul style="list-style-type: none"> — Dispense no more than a 15-day supply at discharge 	<p>To receive JYNARQUE:</p> <ol style="list-style-type: none"> 1. Understand the risks associated with JYNARQUE 2. Enroll in the REMS by completing the <i>Patient Enrollment Form</i> with your healthcare provider 3. Complete baseline liver testing before your first dose, 2 weeks and 4 weeks after your first dose and monthly for the first 18 months of treatment and every 3 months thereafter

*JYNARQUE is not available to all pharmacies. If you have any questions about the REMS or how to obtain JYNARQUE call **1-866-244-9446**.

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PRESCRIBER REQUIREMENTS

Become Certified (One-time)	Enroll Your Patients	Monitor Your Patients
<p>Before prescribing JYNARQUE:</p> <ol style="list-style-type: none"> 1. Review the following educational materials on JYNARQUE to understand the risks of severe and potentially fatal liver injury: <ul style="list-style-type: none"> • <i>Prescribing Information</i> • <i>JYNARQUE REMS Program Overview</i> • <i>JYNARQUE REMS Prescriber Training</i> 2. Complete and submit the <i>Prescriber Knowledge Assessment</i> and the <i>Prescriber Enrollment Form</i> to the REMS <ul style="list-style-type: none"> • <i>JYNARQUE REMS Prescriber Knowledge Assessment</i> • <i>JYNARQUE REMS Prescriber Enrollment Form</i> 3. Upon completion of these steps, the REMS will notify you upon successful certification 	<p>Before starting each patient on JYNARQUE:</p> <ol style="list-style-type: none"> 1. Counsel your patients on the risk of serious and potentially fatal liver injury and the requirement for liver function monitoring at baseline, 2 weeks, 4 weeks and monthly for the first 18 months of treatment and every 3 months thereafter and share the resources below: <ul style="list-style-type: none"> • <i>JYNARQUE REMS Patient Guide</i> 2. Order and evaluate the baseline liver testing before each patient's first dose of JYNARQUE 3. Submit a completed <i>Patient Enrollment Form</i> to the REMS and submit the prescription to the pharmacy. Provide a completed copy of the <i>Patient Enrollment Form</i> to the patient 	<p>Once your patient is on JYNARQUE:</p> <ol style="list-style-type: none"> 1. Monitor your patients on an ongoing basis. Assess the patient's liver function and appropriateness of continuing treatment 2 weeks and 4 weeks after treatment initiation, then monthly for the first 18 months and every 3 months thereafter 2. Submit a completed <i>Patient Status Form</i> to the REMS for each patient every 3 months for the first 18 months of treatment and every 6 months thereafter* 3. Report adverse events suggestive of serious and potentially fatal liver injury by contacting the REMS by phone or submitting a completed <i>Liver Adverse Events Reporting Form</i> or a completed <i>Patient Status Form</i> 4. Inform the REMS if a patient is no longer under your care or has discontinued JYNARQUE

The completion of the laboratory test and the submission of the **Patient Status Form** are done at different intervals. At the time that the **Patient Status Form** is due, this form may also be used to report serious or potentially fatal liver injury events. However, the **Patient Status Form** must still be submitted regularly – even if liver adverse events were already reported on the **Liver Adverse Event Reporting Form**.

*The REMS will send a reminder to the certified prescriber of record when the **Patient Status Form** is due.

*If a patient has discontinued JYNARQUE treatment, the prescriber/prescriber delegate must notify the REMS.

Completed forms should be submitted to the REMS online at www.JYNARQUErems.com or via fax to **1-866-750-6820**. Patient Status Forms may be submitted by certified Prescribers or their delegate online or via fax.

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PHARMACY REQUIREMENTS

Become Certified	Ensure Compliance with REMS Requirements
<p>Before dispensing JYNARQUE for the first time:</p> <ol style="list-style-type: none"> 1. Designate an authorized representative for the pharmacy. He or she will need to review the <i>REMS Program Overview</i> and will oversee implementation and ensure compliance with the REMS requirements 2. Have the authorized representative complete and submit the <i>Outpatient Pharmacy Enrollment Form</i> or <i>JYNARQUE REMS Inpatient Pharmacy Enrollment Form</i> <ul style="list-style-type: none"> • Outpatient dispensing of JYNARQUE is limited to a small number of contracted pharmacies that will be certified. The <i>Outpatient Pharmacy Enrollment Form</i> must be submitted via fax • Only inpatient pharmacies that are certified in the REMS may dispense JYNARQUE for a specific enrolled patient being treated in the inpatient setting. The <i>Inpatient Pharmacy Enrollment Form</i> may be completed online or via fax 3. Have the authorized representative ensure that all relevant staff involved in dispensing of JYNARQUE are trained on the REMS requirements and that a record of training is maintained by the pharmacy 	<p>When dispensing JYNARQUE:</p> <ol style="list-style-type: none"> 1. Before dispensing JYNARQUE, <ul style="list-style-type: none"> Outpatient: Obtain authorization to dispense each prescription by contacting the REMS online or by phone to verify prescriber is certified, and the patient is enrolled and authorized to receive the drug <ul style="list-style-type: none"> — Dispense no more than a 30-day supply Inpatient: Verify the prescriber is certified and the patient is enrolled in the REMS Program <ul style="list-style-type: none"> — Dispense no more than a 15-day supply at discharge 2. Report adverse events suggestive of serious and potentially fatal liver injury by contacting the REMS by phone or submitting a completed <i>Liver Adverse Events Reporting Form</i> 3. Maintain appropriate documentation that all processes and procedures are in place and are being followed 4. Comply with audits carried out by Otsuka Pharmaceuticals or third party acting on behalf of the manufacturer to ensure that all processes and procedures are in place and being followed 5. Recertify in the REMS if a new authorized representative is designated by completing and submitting the <i>Outpatient Pharmacy Enrollment Form</i> or <i>Inpatient Pharmacy Enrollment Form</i>

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PATIENT REQUIREMENTS

Enroll and Complete Baseline Liver Testing	Complete Regular Liver Testing
<p>Before starting JYNARQUE:</p> <ol style="list-style-type: none">1. Discuss and receive counseling from your healthcare provider on:<ol style="list-style-type: none">a. The risk of serious and potentially fatal liver injuryb. The need for required blood testing before my first dose and regularly during treatment2. Receive and read the <i>Patient Guide</i>3. Complete the <i>Patient Enrollment Form</i> with your healthcare provider4. Complete liver testing before your first dose of JYNARQUE	<p>Once your patient is on JYNARQUE:</p> <ol style="list-style-type: none">1. Complete liver testing at 2 weeks, 4 weeks and monthly for the first 18 months of treatment and every 3 months thereafter2. Inform your healthcare provider if you have any side effects, reactions, or symptoms after taking JYNARQUE, such as signs and symptoms of serious liver injury3. Notify the REMS if you change your JYNARQUE healthcare provider, if your contact information changes, or if you discontinue treatment with JYNARQUE

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JYNARQUE REMS RESOURCES

	Before Prescribing/ Dispensing JYNARQUE	Before starting JYNARQUE for each Patient	While on JYNARQUE Treatment
Prescriber	<ul style="list-style-type: none"> • <i>Prescribing Information</i> • <i>JYNARQUE REMS Program Overview</i> • <i>JYNARQUE REMS Prescriber Training</i> • <i>JYNARQUE REMS Prescriber Knowledge Assessment</i> • <i>JYNARQUE REMS Prescriber Enrollment Form</i> 		<ul style="list-style-type: none"> • <i>JYNARQUE REMS Patient Status Form</i> • <i>JYNARQUE REMS Liver Adverse Events Reporting Form</i>
Pharmacy	<ul style="list-style-type: none"> • <i>JYNARQUE REMS Program Overview</i> • <i>JYNARQUE REMS Inpatient Pharmacy Enrollment Form</i> • <i>JYNARQUE Outpatient Pharmacy Enrollment Form</i> 		<ul style="list-style-type: none"> • <i>JYNARQUE REMS Liver Adverse Events Reporting Form</i>
Patient		<ul style="list-style-type: none"> • <i>JYNARQUE REMS Patient Guide</i> 	

JYNARQUE is a selective vasopressin V₂-receptor antagonist indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD)

Please see the Prescribing Information, including **BOXED WARNING**, for more information.

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ADDITIONAL QUESTIONS:

Please visit www.JYNARQUErems.com or call the JYNARQUE REMS at **1-866-244-9446** for more information about the JYNARQUE REMS.

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