Tolvaptan for ADPKD Shared System REMS (RISK EVALUATION AND MITIGATION STRATEGY) PROGRAM OVERVIEW

This overview describes the requirements of the Tolvaptan for ADPKD Shared System REMS and the responsibilities of prescribers, pharmacies, and patients.

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

TABLE OF CONTENTS

WHAT IS THE TOLVAPTAN FOR ADPKD SHARED SYSTEM 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 tolvaptan for ADPKD and is required by the Food and Drug Administration (FDA) to ensure the benefits of tolvaptan outweighs its risks.
- This REMS applies to tolvaptan products indicated for the treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD). This REMS does not apply to tolvaptan products that are indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia, including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone.
- **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.**

HOW DOES THE TOLVAPTAN FOR ADPKD SHARED SYSTEM REMS WORK?

	Before Prescribing/ Dispensing Tolvaptan For ADPKD	Before Starting Tolvaptan For ADPKD For Each Patient	While On Tolvaptan For ADPKD Treatment For Each Patient
Prescriber	Prescriber certification	• **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	• **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		• **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 -Dispense no more than a 30-days' supply • **Inpatient: Verify** the prescriber is certified and the patient is enrolled in the REMS -Dispense no more than a 15-days' supply at discharge
Patient		• Review **Patient Guide** • Patient Enrollment • **Get** a blood test before your first dose	• **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

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

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

WHAT ARE THE REQUIREMENTS OF THE TOLVAPTAN FOR ADPKD SHARED SYSTEM REMS?

- **In order to receive tolvaptan for ADPKD, prescribers, pharmacies, and patients must comply with the requirements of the Tolvaptan for ADPKD Shared System REMS.**

Prescriber	Pharmacy (Outpatient & Inpatient)	Patient
To prescribe tolvaptan for ADPKD: 1. **Become certified** by completing a one-time certification process 2. As you start patients on tolvaptan for ADPKD, **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 **Patient Status Form** for each patient every 3 months for the first 18 months of treatment and every 6 months thereafter	**To dispense tolvaptan for ADPKD *:** 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 -Dispense no more than a 30-days' supply 4. **Inpatient: Verify** the prescriber is certified and the patient is enrolled in the REMS -Dispense no more than a 15-days' supply at discharge	**To receive tolvaptan for ADPKD:** 1. **Understand the risks** associated with tolvaptan for ADPKD 2. **Enroll** in the REMS by completing the **Patient Enrollment Form** 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

*Tolvaptan for ADPKD is not available to all pharmacies. If you have any questions about the Tolvaptan for ADPKD Shared System REMS or how to obtain tolvaptan for ADPKD call **1-866-244-9446**.

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

PRESCRIBER REQUIREMENTS

Become Certified (One-time)	Enroll Your Patients	Monitor Your Patients
Before prescribing tolvaptan for ADPKD: 1. **Review** the following educational materials on tolvaptan for ADPKD to understand the risks of severe and potentially fatal liver injury: • Prescribing Information • **Program Overview** • **Prescriber Training** 2. **Complete** and **submit** the **Prescriber Knowledge Assessment** and the **Prescriber Enrollment Form** to the REMS • **Prescriber Knowledge Assessment** • **Prescriber Enrollment Form** 3. Upon completion of these steps, the REMS will notify you upon successful certification	**Before starting each patient on tolvaptan for ADPKD:** 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: • **Patient Guide** 2. **Order** and **evaluate** the baseline liver testing before each patient's first dose of tolvaptan for ADPKD 3. **Submit** a completed **Patient Enrollment Form** to the REMS and submit the prescription to the pharmacy. Provide a completed copy of the **Patient Enrollment Form** to the patient	**Once your patient is on tolvaptan for ADPKD:** 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 **Patient Status Form** 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 **Patient Status Form** 4. Inform the REMS if a patient is no longer under your care or has discontinued tolvaptan for ADPKD

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.
*The REMS will send a reminder to the certified prescriber of record when the **Patient Status Form** is due.
*If a patient has discontinued tolvaptan for ADPKD treatment, the prescriber/prescriber delegate must notify the REMS.
Completed forms should be submitted to the REMS online at **www.TolvaptanADPKDSharedREMS.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.

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

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

PHARMACY REQUIREMENTS

Become Certified	Ensure Compliance with REMS Requirements
Before dispensing tolvaptan for ADPKD for the first time: 1. **Designate** an authorized representative for the pharmacy. He or she will need to review the **Program Overview** and will oversee implementation and ensure compliance with the REMS requirements 2. **Have the authorized representative complete and submit** the **Outpatient Pharmacy Enrollment Form** or **Inpatient Pharmacy Enrollment Form** • Outpatient dispensing of tolvaptan for ADPKD is limited to contracted pharmacies that will be certified. The **Outpatient Pharmacy Enrollment Form** must be submitted via fax • Only inpatient pharmacies that are certified in the REMS may dispense tolvaptan for ADPKD for a specific enrolled patient being treated in the inpatient setting. The **Inpatient Pharmacy Enrollment Form** may be completed online or via fax 3. Have the authorized representative ensure that all relevant staff involved in dispensing of tolvaptan for ADPKD are trained on the REMS requirements and that a record of training is maintained by the pharmacy	**When dispensing tolvaptan for ADPKD:** 1. Before dispensing tolvaptan for ADPKD, **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 -Dispense no more than a 30-days' supply **Inpatient: Verify** the prescriber is certified and the patient is enrolled in the REMS -Dispense no more than a 15-days' supply at discharge 2. **Report** adverse events suggestive of serious and potentially fatal liver injury by contacting the REMS by phone 3. **Maintain** appropriate documentation that all processes and procedures are in place and are being followed 4. **Comply** with audits carried out by the Tolvaptan for ADPKD Applicants or third party acting on behalf of the Tolvaptan for ADPKD Applicants 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 **Outpatient Pharmacy Enrollment Form** or **Inpatient Pharmacy Enrollment Form**

Tolvaptan for ADPKD is not available to all pharmacies. If you have questions about the Tolvaptan for ADPKD Shared System REMS or how to obtain tolvaptan for ADPKD, call **1-866-244-9446**.

PATIENT REQUIREMENTS

Enroll and Complete Baseline Liver Testing	Complete Regular Liver Testing
Before starting tolvaptan for ADPKD: 1. **Discuss** and receive counseling from your healthcare provider on: a. The risk of serious and potentially fatal liver injury b. The need for required blood testing before my first dose and regularly during treatment 2. **Receive and read** the **Patient Guide** 3. **Complete** the **Patient Enrollment Form** with your healthcare provider 4. **Complete** liver testing before your first dose of tolvaptan for ADPKD	**Once your patient is on tolvaptan for ADPKD:** 1. **Complete** liver testing at 2 weeks, 4 weeks and monthly for the first 18 months of treatment and every 3 months thereafter 2. **Inform your healthcare provider** if you have any side effects, reactions, or symptoms after taking tolvaptan for ADPKD, such as signs and symptoms of serious liver injury 3. **Notify** the REMS if you **change your tolvaptan for ADPKD healthcare provider**, if your **contact information changes**, or if you **discontinue treatment with tolvaptan for ADPKD**

TOLVAPTAN FOR ADPKD SHARED SYSTEM REMS RESOURCES

	Before Prescribing/ Dispensing Tolvaptan For ADPKD	Before Starting Tolvaptan For ADPKD For Each Patient	While On Tolvaptan For ADPKD Treatment
Prescriber	• Prescribing Information • **Program Overview** • **Prescriber Training** • **Prescriber Knowledge Assessment** • **Prescriber Enrollment Form**		• **Patient Status Form**
Pharmacy	• **Program Overview** • **Inpatient Pharmacy Enrollment Form** • **Outpatient Pharmacy Enrollment Form**		
Patient		• **Patient Enrollment Form** • **Patient Guide**	

Tolvaptan is a selective vasopressin V_2-receptor antagonist indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

Tolvaptan is also indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia, including patients with heart failure and Syndrome of Inappropriate Antidiuretic Hormone.

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

ADDITIONAL QUESTIONS:

Please visit **www.TolvaptanADPKDSharedREMS.com** or call the Tolvaptan for ADPKD Shared System REMS at **1-866-244-9446** for more information about the Tolvaptan for ADPKD Shared System REMS.

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

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

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

Tolvaptan for ADPKD
Shared System REMS

Approval: 04/2025