

IMPORTANT DRUG WARNING

[Month/Day/Year]

JYNARQUE REMS Letter for Healthcare Providers

Subject: Risk of serious and potentially fatal liver toxicity associated with JYNARQUE (tolvaptan)

Dear Healthcare Provider:

The purpose of this letter is to inform you about the risk of serious and potentially fatal liver injury associated with JYNARQUE (tolvaptan) and the need to monitor for this risk. JYNARQUE is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD). Tolvaptan, currently approved and marketed as SAMSCA, should not be used to treat ADPKD, as the risks associated with JYNARQUE require a REMS for safe use of the drug.

The U.S. Food and Drug Administration (FDA) has determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of JYNARQUE outweigh its risks. JYNARQUE is only available through a restricted distribution program — the JYNARQUE REMS. Only prescribers, pharmacies, and patients enrolled in the REMS can prescribe, dispense, and receive JYNARQUE.

Serious Risk of JYNARQUE:

JYNARQUE can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported in the postmarketing ADPKD experience. JYNARQUE is contraindicated in patients with a history, signs or symptoms of significant liver impairment or injury. This contraindication does not apply to uncomplicated polycystic liver disease.

As part of the JYNARQUE REMS:

- Healthcare providers must be trained and specially certified to prescribe JYNARQUE. REMS training materials and enrollment forms may be obtained by calling 1-866-244-9446 or visiting www.JYNARQUERems.com.
- Patients being treated with JYNARQUE must be enrolled in the REMS by completing a **Patient Enrollment Form** with their prescriber.
- Prescribers must measure ALT, AST and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months thereafter. Prompt action in response to laboratory abnormalities, signs, or symptoms indicative of liver injury can mitigate, but not eliminate, the risk of serious hepatotoxicity.
- During treatment, prescribers must also regularly complete and submit the **Patient Status Form**. A prescriber delegate acting on behalf of the prescriber may also complete and submit this form.

- Healthcare providers must promptly report any suspected adverse events suggestive of serious and potentially fatal liver injury by contacting the REMS by phone, using the **Liver Adverse Events Reporting Form**, or using the **Patient Status Form**.
- It is important for you to know that JYNARQUE will only be available through the JYNARQUE REMS, which will require distribution through certified pharmacies.

Adverse Events Reporting

To report negative side effects, contact Otsuka America Pharmaceutical, Inc. at **1-800-438-9927** or FDA at **1-800-FDA-1088** (www.fda.gov/medwatch)

Additional details about prescriber responsibilities, enrollment and educational materials for JYNARQUE REMS can be found at www.JYNARQUErems.com. For more information, contact the JYNARQUE REMS at **1-866-244-9446**.

The information in this letter is not intended as a complete description of benefits and risks associated with the use of JYNARQUE. Please see accompanying Prescribing Information.

Sincerely,

Robert McQuade, PhD
EVP, Chief Strategic Officer
Otsuka Pharmaceutical Development and Commercialization, Inc.



Otsuka America Pharmaceutical, Inc.

Manufactured by Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan.
Distributed and marketed by Otsuka America Pharmaceutical, Inc., Rockville, MD 20850 USA.
JYNARQUE is a registered trademark of Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan.

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JYNARQUE[®]
(tolvaptan) tablets