

JYNARQUE® (tolvaptan) REMS LIVER ADVERSE EVENTS REPORTING FORM

Adverse events suggestive of serious and potentially fatal liver injury must be reported to the REMS. Healthcare providers can complete and submit this form to the REMS by fax or online or they can report the information by calling the JYNARQUE REMS. Adverse events can also be reported to the REMS when the **JYNARQUE REMS Patient Status Form** is due. If an event is submitted via the **Liver Adverse Event Report Form**, it is not necessary to also submit **the same event** on the **Patient Status Form** or contact the REMS Program Coordinating Center by phone. The **Patient Status Form** should still be submitted per the regular schedule outlined in the REMS.

*Indicates required field

Patient Information

First Name*: _____ Last Name*: _____
Birthdate*: _____ REMS ID: _____
Address Line 1*: _____
Address Line 2: _____
City*: _____ State*: _____ Zip code*: _____

Prescriber Information

First Name*: _____ Last Name*: _____ REMS ID: _____
National Provider Identifier No. (NPI)*: _____ Practice/Facility Name: _____
Address Line 1: _____
Address Line 2: _____
City: _____ State: _____ Zip code: _____
Phone*: _____ Fax*: _____ Email*: _____

Serious Adverse Event Reporting

*My patient experienced a serious and potentially fatal liver injury event Yes No

Liver injury events meeting any of the following criteria should be considered and reported as serious and potentially fatal liver injury.

- Development of any liver injury events leading to liver transplantation or resulting in a fatal outcome or considered to be life-threatening, or
- Development of any liver injury events meeting any of the laboratory criteria presented below:
 - ALT (Alanine aminotransferase) or AST (Aspartate aminotransferase) $>8 \times$ ULN (Upper limit of normal), or
 - ALT or AST $>5 \times$ ULN for more than 2 weeks, or
 - ALT or AST $>3 \times$ ULN and (TBL [Total Bilirubin] $>2 \times$ ULN or International Normalized Ratio [INR] >1.5) (TBL measurement can be within 30 days of the ALT elevation), or
 - ALT or AST $>3 \times$ ULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia ($>5\%$)

Event Information:

****Please see definition of seriousness criteria on page 2****

*Please select Yes or No for each seriousness criteria below:

Death* Yes No Life-threatening* Yes No
Hospitalization* Yes No Important Medical event* Yes No

*Treatment was discontinued due to this event Yes No Not available

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

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Serious Adverse Event Reporting (continued)

Liver Laboratory Information:

Were the liver enzymes (ALT/AST) elevated > 3 x ULN?*

Yes No Not available

Were there Symptoms of Liver Injury?*

Yes No

The patient's prescriber will be contacted for further information regarding this report of a serious and potentially fatal liver injury event. Pertinent laboratory results will be requested.

Signature*: _____ Date*: _____

Print Name*: _____

If the patient has been discontinued from JYNARQUE treatment, the prescriber/prescriber delegate must notify the REMS.

Definition of seriousness criteria:

Death

Report if you suspect that the death was an outcome of the liver event, and include the date if known.

Life-threatening

Report if suspected that the patient was at substantial risk of dying at the time of the liver event, or use or continued use of product might have resulted in the death of the patient.

Hospitalization (initial or prolonged)

Report if admission to the hospital or prolongation of hospitalization was a result of the liver event. Emergency room visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

Important Medical Events

Report when the liver event does not fit the other outcomes, but the liver event may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other outcomes. Examples include allergic bronchospasm (a serious problem with breathing) requiring treatment in an emergency room, serious blood dyscrasias (blood disorders) or seizures/convulsions that do not result in hospitalization. The development of drug dependence or drug abuse would also be examples of important medical events.



Otsuka

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Manufactured by Otsuka Pharmaceutical Co., Ltd., Tokyo, 101-8535 Japan.

Distributed and marketed by Otsuka America Pharmaceutical, Inc., Rockville, MD 20850 USA.

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[Month Year of Approval]

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