

Under the Risk Evaluation and Mitigation Strategy (REMS) for JYNARQUE® (tolvaptan), baseline hepatic testing is required for all patients prior to initiation of treatment and then 2 weeks and 4 weeks following initiation. Monthly blood tests are required for the duration of the first 18 months of treatment and every 3 months thereafter.

The Laboratory Support Program for patients provides patients with no-cost hepatic testing for the duration of therapy. The hepatic tests covered by this program are inclusive of all the laboratory values relevant to the JYNARQUE REMS program, namely [1] aspartate aminotransferase (AST), [2] alanine transaminase (ALT), [3] total bilirubin (BT), and [4] alkaline phosphatase (ALP).

**Only patients treated with JYNARQUE are eligible for this program.**

When you enroll yourself/your practice in the Laboratory Support Program, you will receive a confirmation that your account has been set up. You will also receive test requisitions, both electronically and by mail, that you can give to your patients. These test requisitions will be prepopulated with your account information.

Patients may present their test requisition at any LabCorp Patient Service Center (PSC) in the United States for sample collection (phlebotomy) and the hepatic tests required by the JYNARQUE REMS. Samples may also be collected in-office. Office-based collections are eligible to participate in the complementary testing program; however, the Laboratory Support Program will not reimburse phlebotomy for in-office blood draws.

Laboratory results will be sent to the physician or physician practice associated with the test requisition using the preferred method of transmission indicated below.

This account setup form is required for physician enrollment in the Laboratory Support Program.

*All fields in this form are mandatory.*

## Account Information

Physician Name: \_\_\_\_\_ Contact Name: \_\_\_\_\_

Practice Name: \_\_\_\_\_

Practice Address: \_\_\_\_\_ City: \_\_\_\_\_

State: \_\_\_\_\_ Zip: \_\_\_\_\_ Phone: \_\_\_\_\_ Fax: \_\_\_\_\_

Email: \_\_\_\_\_

Current LabCorp Account No.: \_\_\_\_\_

Preferred method to receive test results:  Auto-Fax  Beacon (online reporting portal)

Preferred sample collection location:  In-office phlebotomy  LabCorp Patient Service Center

## Consent Statement

I understand and acknowledge that the Laboratory Support Program ("Program") is only available in the US for patients who are currently (a) being treated with JYNARQUE® (tolvaptan) for autosomal dominant polycystic kidney diseases (ADPKD), (b) enrolled in JYNARQUE Risk Evaluation and Mitigation Strategy (REMS) Program for hepatic monitoring, (c) over 18 years of age and (d) not covered in whole or in part by any state program or federal healthcare program, including but not limited to, Medicare or Medicaid (including Medicaid managed care), Medigap, VA, DOD, or TRICARE.

I certify that (a) any support provided through the Program on behalf of any of my patients is not given in exchange for any express or implied agreement or understanding that I would recommend, prescribe, or use any Otsuka product or service, and (b) my decision to prescribe the Otsuka product or service was based on my determination of medical necessity.

I agree that the Program and Otsuka may contact me for additional information relating to the Program or Otsuka product, including but not limited to email, fax, and telephone. I understand that Otsuka reserves the right, at any time and without notice, to modify or discontinue the Program.

Prescriber Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Please send completed form via fax to **(833) 581-3823** or via email to **mypass@labcorp.com**.

For questions, please call the Project Manager at **(984) 245-1041**. Hours of operation are 8:30 AM to 5:30 PM EST. If you call after 5:30 PM EST, please leave a voice message. Your call will be returned by 2:00 PM EST the following business day.

*Allow approximately 7-10 business days from receipt of completed form for account setup.*

Please see **IMPORTANT SAFETY INFORMATION** on next page.

## INDICATION and IMPORTANT SAFETY INFORMATION for JYNARQUE® (tolvaptan)

### INDICATION:

JYNARQUE is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

### IMPORTANT SAFETY INFORMATION:

#### WARNING: RISK OF SERIOUS LIVER INJURY

- **JYNARQUE (tolvaptan) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported**
- **Measure transaminases (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 hepatic injury can mitigate, but not eliminate, the risk of serious hepatotoxicity.**
- **Because of the risks of serious liver injury, JYNARQUE is available only through a Risk Evaluation and Mitigation Strategy program called the JYNARQUE REMS Program**

### CONTRAINDICATIONS:

- History, signs or symptoms of significant liver impairment or injury. This contraindication does not apply to uncomplicated polycystic liver disease
- Taking strong CYP3A inhibitors
- With uncorrected abnormal blood sodium concentrations
- Unable to sense or respond to thirst
- Hypovolemia
- Hypersensitivity (e.g., anaphylaxis, rash) to JYNARQUE or any component of the product
- Uncorrected urinary outflow obstruction
- Anuria

**Serious Liver Injury:** JYNARQUE can cause serious and potentially fatal liver injury. 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. To reduce the risk of significant or irreversible liver injury, assess ALT, AST and bilirubin prior to initiating JYNARQUE, at 2 weeks and 4 weeks after initiation, then monthly for 18 months and every 3 months thereafter.

**Hypertremia, Dehydration and Hypovolemia:** JYNARQUE therapy increases free water clearance which can lead to dehydration, hypovolemia and hypertremia. Instruct patients to drink water when thirsty, and throughout the day and night if awake. Monitor for weight loss, tachycardia and hypotension because they may signal dehydration. Ensure abnormalities in sodium concentrations are corrected before initiating therapy. If serum sodium increases above normal or the patient becomes hypovolemic or dehydrated and fluid intake cannot be increased, suspend JYNARQUE until serum sodium, hydration status and volume status parameters are within the normal range.

**Inhibitors of CYP3A:** Concomitant use of JYNARQUE with drugs that are moderate or strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, indinavir/ritonavir, ritonavir, and conivaptan) increases tolvaptan exposure. Use with strong CYP3A inhibitors is contraindicated; dose reduction of JYNARQUE is recommended for patients taking moderate CYP3A inhibitors. Patients should avoid grapefruit juice beverages while taking JYNARQUE.

**Adverse Reactions:** Most common observed adverse reactions with JYNARQUE (incidence >10% and at least twice that for placebo) were thirst, polyuria, nocturia, pollakiuria and polydipsia.

### Other Drug Interactions:

- **Strong CYP3A Inducers:** Co-administration with strong CYP3A inducers reduces exposure to JYNARQUE. Avoid concomitant use of JYNARQUE with strong CYP3A inducers
- **OATP1B1/3 and OAT3 Transporter Substrates:** Patients who take JYNARQUE should avoid concomitant use with OATP1B1/B3 and OAT3 substrates (e.g., statins, bosentan, glyburide, nateglinide, repaglinide, methotrexate, furosemide), as the plasma concentrations of these substrates may be increased
- **BCRP Transporter Substrates:** Tolvaptan is an inhibitor of BCRP. Patients who take JYNARQUE, should avoid concomitant use with BCRP substrates (e.g., rosuvastatin)
- **V<sub>2</sub>-Receptor Agonist:** Tolvaptan interferes with the V<sub>2</sub>-agonist activity of desmopressin (dDAVP). Avoid concomitant use of JYNARQUE with a V<sub>2</sub>-agonist.

**Pregnancy and Lactation:** Based on animal data, JYNARQUE may cause fetal harm. In general, JYNARQUE should be discontinued during pregnancy. Advise women not to breastfeed during treatment with JYNARQUE.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA-1088 ([www.fda.gov/medwatch](http://www.fda.gov/medwatch)).

Please see [FULL PRESCRIBING INFORMATION](#), including **BOXED WARNING**.



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.

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