OTSUKA LABORATORY SUPPORT PROGRAM ACCOUNT SETUP FORM

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 Otsuka 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 Otsuka Laboratory Support Program, you will receive a confirmation that your account has been set up. You will also receive test requisitions by mail, which you can give to your patients. These test requisitions will be prepopulated with your account information. Patients may present their test requisition at any QUEST Patient Service Center (PSC) in the United States for sample collection (phlebotomy) and the hepatic tests required by the JYNARQUE REMS. This account setup form is required for physician enrollment in the Otsuka Laboratory Support Program.

All fields in this form are mandatory.

Account Information

Physician Name: _____ Contact Name: _____

Physician NPI: _____ Practice Name: _____

Practice Address: _____ City: _____

State: _____ Zip: _____ Phone: _____ Fax: _____

Email: _____

Current QUEST Account No.: _____

Preferred method to receive test results: ☐ Auto-Fax ☐ Online reporting portal Quanum™

Preferred sample collection location: ☐ QUEST Patient Service Center ☐ Mobile

Consent Statement

I understand and acknowledge that the Otsuka Laboratory Support Program ("Program") is only available in the United States 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 **(610) 706-8775** or via email to **REMS@questdiagnostics.com**.

For questions please call the designated program line at **(866) 226-8046**, Monday - Friday, 7 AM to 7 PM CST, or you can reach the Account Manager at **(610) 454-4553**, Monday - Friday, 9 AM to 5 PM EST.

Allow approximately 5 business days from receipt of completed form for account setup.

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

JYNARQUE®
(tolvaptan) tablets

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.

Hypernatremia, Dehydration and Hypovolemia: JYNARQUE therapy increases free water clearance which can lead to dehydration, hypovolemia and hypernatremia. 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
- **V_2-Receptor Agonist:** Tolvaptan interferes with the V_2-agonist activity of desmopressin (dDAVP). Avoid concomitant use of JYNARQUE with a V_2-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).

Please see FULL PRESCRIBING INFORMATION, including **BOXED WARNING**.

Otsuka

Otsuka America Pharmaceutical, Inc.

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JYNARQUE®
(tolvaptan) tablets