Identify appropriate patients with ADPKD for JYNARQUE® (tolvaptan), like Julia

Julia, 40—Stage 2 CKD

Julia is a 4th grade teacher who also enjoys painting. She hopes to pass that passion down to her daughters, Charlotte and Nora.

Julia's many risk factors, along with her age, led her nephrologist to request an ultrasound to determine her kidney length.

Physical Findings and Labs:

- **Age:** 40 • **Height:** 5'4" • **Weight:** 177 lbs • **BMI:** 30
- **BP:** 105/70 mm/Hg, controlled on an ACE-inhibitor
- **Creatinine:** 1.1 mg/dL
- **eGFR:** 77 mL/min/1.73 m^2
- **Ultrasound kidney length:** markedly enlarged kidneys, each with a length of >17 cm

Medical History:

- Diagnosed with ADPKD as a young adult when an ultrasound showed innumerable, bilateral cysts
- Hyperlipidemia
- Proteinuria
- Obesity
- Hypertension before age 35

Family History:

- Father had ADPKD, which later progressed to ESKD at age 70

Patient image and patient case are fictional.

ACE=angiotensin-converting enzyme; ADPKD=autosomal dominant polycystic kidney disease; BMI=body mass index; BP=blood pressure; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease.

JYNARQUE®
(tolvaptan)
15, 30, 45, 60, 90 mg tablets

INDICATION:

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

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 Tolvaptan for ADPKD Shared System REMS**

Please see **IMPORTANT SAFETY INFORMATION** on pages 4 and 5.

Assessing ADPKD progression and treatment consideration

- Julia presented with **several risk factors associated with rapid disease progression**, including obesity, proteinuria, and hypertension before age 35

- Because of her **young age**, her nephrologist decided to request a **kidney length measurement via ultrasound**

- Because her kidney length was **greater than 17 cm at 40 years of age with CKD Stage 2**, Julia's nephrologist determined that she was **at risk for rapidly progressing ADPKD**[1,2]

- After further assessment, Julia's nephrologist determined she was an appropriate patient and recommended she start treatment with JYNARQUE® (tolvaptan)

SELECT IMPORTANT SAFETY INFORMATION:

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

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Starting JYNARQUE® (tolvaptan)

- Julia has taken her doctor's advice of exercising more regularly and living a more healthy lifestyle to get her weight under control
- Julia's nephrologist **explained the benefits and risks** associated with treatment, including the risk of serious liver injury, the requirements of the REMS program, and they also reviewed the medication guide prior to starting treatment
- Julia's nephrologist explained that JYNARQUE may cause aquaretic side effects and advised to **drink more water to avoid thirst and dehydration**
- Because she is a teacher, frequent urination is a concern for Julia. Therefore, the nurse counseled her on ways to help manage aquaretic side effects, including going on a **low sodium and protein diet** and **scheduling bathroom breaks**
- Julia's nephrologist told her about the **Peer Mentor Program**. She spoke to a Peer Mentor who shared his **experience integrating JYNARQUE into his lifestyle and job**, and she felt more comfortable after hearing his JYNARQUE experience
- Based on Julia's commercial insurance coverage, her specialty pharmacy determined she was eligible for **$10/month copay support***

*Assumes one 28-day supply prescription per month. If more than one prescription is filled in a calendar month, patients may pay more than $10 in that month. Other terms and conditions may apply.
REMS=Risk Evaluation and Mitigation Strategy.

SELECT IMPORTANT SAFETY INFORMATION:

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.

References: 1. Gansevoort RT, Arici M, Benzing T, et al. Recommendations for the use of tolvaptan in autosomal dominant polycystic kidney disease: a position statement on behalf of the ERA-EDTA Working Groups on Inherited Kidney Disorders and European Renal Best Practice. *Nephrol Dial Transplant*. 2016;31(3):337-348. **2.** Magistroni R, Corsi C, Martí T, Torra R. A review of the imaging techniques for measuring kidney and cyst volume in establishing autosomal dominant polycystic kidney disease progression. *Am J Nephrol*. 2018;48:67-78. **3.** Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Intern Suppl*. 2013;3(1):1-150. **4.** Irazabal MV, Rangel LJ, Bergstralh EJ, et al. Imaging classification of autosomal dominant polycystic kidney disease: a simple model for selecting patients for clinical trials. *J Am Soc Nephrol*. 2015;26(1):160-172.

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- 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.

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

(continued on next page)

IMPORTANT SAFETY INFORMATION for JYNARQUE® (tolvaptan) (cont'd)

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.

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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).

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Talk to your sales representative or visit JYNARQUEhcp.com to learn more about appropriate patient types for JYNARQUE® (tolvaptan)

Tim, 31—Stage 2 CKD

Mayo Classification of 1C (high risk) and TKV greater than expected for his age point to risk of rapidly progressing ADPKD[4]

Julia, 40—Stage 2 CKD

Multiple risk factors as well as her concerning kidney length are signs of risk of rapidly progressing ADPKD[1,2]

Patient images and patient cases are fictional.

TKV=total kidney volume.

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