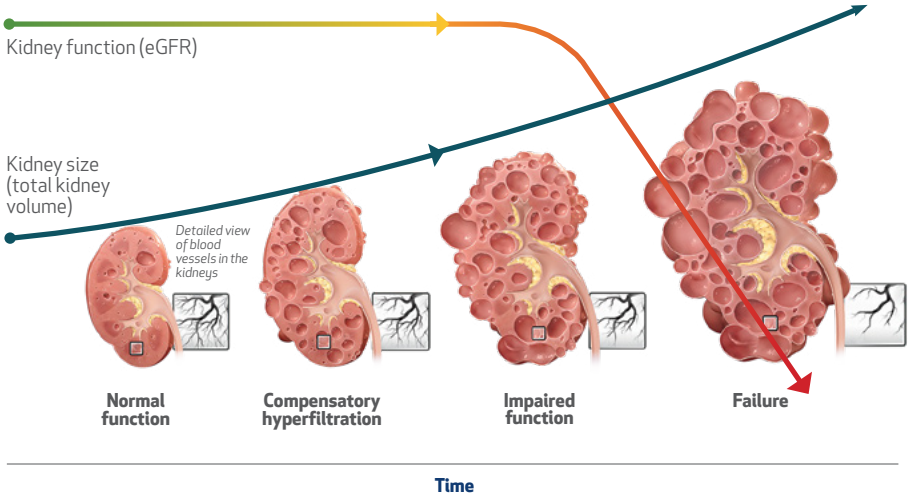
With ADPKD, there is a lot to consider

Patients with stable eGFR could be at risk of rapid progression[1-3]



ADPKD=autosomal dominant polycystic kidney disease; eGFR=estimated glomerular filtration rate.

INDICATION AND IMPORTANT SAFETY INFORMATION

JYNARQUE® (tolvaptan) 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 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**

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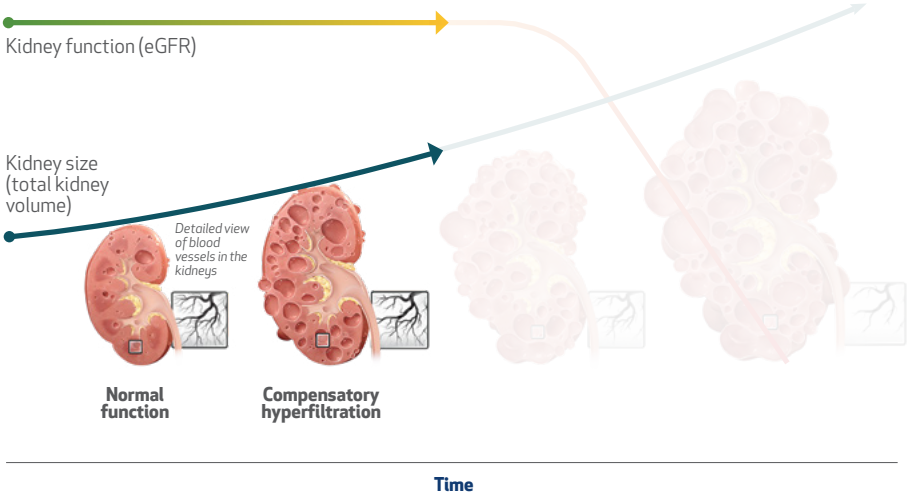
Stable eGFR

Even when eGFR appears stable, irreversible kidney damage may still be occurring[1,2]

Kidney growth and damage often occur before kidney function declines[1,3,4]



IMPORTANT SAFETY INFORMATION (CONT'D)

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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Determine if your patient with stable eGFR is at risk for rapid ADPKD progression with 2-step risk identification

STEP 1: Identify risk factors

Identify the presence of any of these independently validated risk factors, which could indicate the risk of rapid progression[5]:

- Proteinuria and microalbuminuria[5]
- Truncating *PKD1* mutation[6]
- Urologic events before age 35 (gross hematuria, cyst infection, or flank pain related to cysts)[6]
- Hypertension before age 35[6]
- Overweight and obesity (BMI ≥25 kg/m^2)[7]
- Family history of ESKD at or before age 58[8]

STEP 2: Get kidney measurements

If at least ONE risk factor is identified, a kidney measurement should be ordered

Kidney size is a strong predictor of rapid ADPKD progression before eGFR begins to decline.[9]

Talk to the radiologist to get a height-adjusted TKV (htTKV) measurement. Then scan the QR code to find out how to use htTKV to determine your patient's risk of progression and appropriateness for treatment.

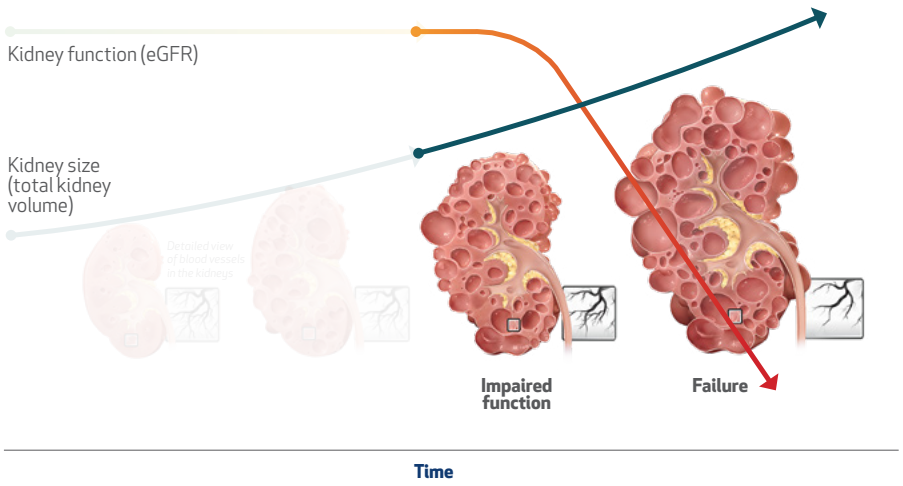
A CRISP cohort analysis, published in *Kidney International*, showed that a one-time TKV measurement can help assess the rate of future kidney function decline.[10]

The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) is an NIH-funded, 14-year observational study (N=241) of adult ADPKD patients. The primary goal was to determine the extent to which TKV forecasts development of renal insufficiency in ADPKD. [10,11]

BMI=body mass index; ESKD=end-stage kidney disease ; TKV=total kidney volume.

Rapidly declining eGFR

Rapid eGFR decline may indicate rapid disease progression[4,8,*]



*Rapid disease progression is defined as historical annual eGFR decline of ≥3 mL/min/1.73 m^2 (determined by multiple measurements of eGFR over 3-5 years).[4]

If your patients are showing evidence of rapidly progressing ADPKD, consider whether JYNARQUE® (tolvaptan) may be an appropriate treatment choice.

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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Recognize these patients in your practice? They could be appropriate for JYNARQUE

Tim, 31—Stage 2 CKD

Tim had a relatively stable eGFR, but his family history of early ESKD led his nephrologist to scan his kidneys for a TKV measurement.

Scan the QR code to learn more about Tim.

Julia, 40—Stage 2 CKD

Julia presented with several risk factors associated with rapid disease progression before age 35. Because of her young age, her nephrologist decided to request a kidney length measurement via ultrasound.[12]

Scan the QR code to learn more about Julia.

Patient images and patient cases are fictional.

CKD=chronic kidney disease.

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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**.

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Otsuka is committed to making JYNARQUE® (tolvaptan) affordable and available

>83% of patients with commercial insurance have coverage for JYNARQUE.[12]

94% of all patients pay **$10** or less per month for JYNARQUE, regardless of coverage type.[12,*,†]

*Assumes one 28-day supply prescription per month. If more than one prescription is filled in a calendar month, patient may pay more than $10 in that month. Offer is not transferable. Patients are not eligible if they are under 18 years of age, or are 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. Only valid in US and Puerto Rico. Offer void where prohibited by law, taxed or restricted. Other restrictions may apply. This program is not health insurance. Otsuka America Pharmaceutical, Inc. has the right to rescind, revoke or amend this program at any time without notice. Your participation in this program confirms that this offer is consistent with your insurance coverage and that you will report the value received if required by your insurance provider. When you use this program, you are certifying that you understand and comply with the program rules, terms and conditions.

†Managed Markets Insight & Technology, LLC database as of July 2023. Commercial lives exclude Health Insurance Exchanges Program (HIX) data.

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