


An evidence-based answer to a common clinical question about JYNARQUE® (tolvaptan)



**How can I determine
the optimal dose
of JYNARQUE
for my patient
that is tolerable
and efficacious?**

**Are the aquaretic
side effects of
JYNARQUE reduced
with a lower dose?**

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 Program**

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

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




Dosing recommendations for JYNARQUE® (tolvaptan)

	 Immediately upon waking		 8 hours later		 Total daily dose
INITIAL DOSE	45 mg	+	15 mg	=	60 mg
TITRATION STEP	60 mg	+	30 mg	=	90 mg
TARGET DOSE	90 mg	+	30 mg	=	120 mg

The pill shape and color are graphical representations and are not actual size.

- The starting dose for JYNARQUE is 45 mg upon waking and 15 mg 8 hours later and should be titrated up to 60/30 and 90/30 mg based on tolerability
- Whereas the Full Prescribing Information for JYNARQUE specifies an up-titration interval of at least 1 week, there is no limit on how long the titration interval can be extended

If patients are unable to tolerate the JYNARQUE starting dose of 45/15 mg, patients may down-titrate based on tolerability

		
15/15 mg, 30/15 mg, 45/15 mg, 60/30 mg, 90/30 mg Blister cards	30 mg tablets 30-count bottle	15 mg tablets 30-count bottle

JYNARQUE is provided in several dosage forms

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

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

Titrating JYNARQUE® (tolvaptan) by urine osmolality



Chebib and colleagues suggested that JYNARQUE needs to be titrated only to the **dose required to achieve persistent suppression of the vasopressin effect on the kidney** (ie, urine hypotonicity relative to plasma, a urine osmolality [Uosm] of ≤ 280 mOsm/kg in a first-void morning sample before the morning dose)¹

In the early dose-finding studies of tolvaptan for ADPKD, efficacy was defined by the capacity to achieve a sustained Uosm of < 300 mOsm/kg¹



In addition to dose titration, dietary changes that aim to reduce daily osmolar loads (eg, moderate reductions in the ingestion of protein and sodium) may help to mitigate aquaretic effects of therapy¹

SELECT IMPORTANT SAFETY INFORMATION:

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.



INDICATION and IMPORTANT SAFETY INFORMATION for JYNARQUE® (tolvaptan)

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IMPORTANT SAFETY INFORMATION (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.

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
- **V₂-Receptor Agonist:** Tolvaptan interferes with the V₂-agonist activity of desmopressin (dDAVP). Avoid concomitant use of JYNARQUE with a V₂-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**.

An evidence-based answer to a common clinical question about JYNARQUE® (tolvaptan)

Determining the optimal dose of JYNARQUE



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Reference: 1. Chebib FT, Perrone RD, Chapman AB, et al. *J Am Soc Nephrol*. 2018;29(10):2458-2470.

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Otsuka America Pharmaceutical, Inc.

