Jynarque (tolvaptan)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Jynarque
- **Generic name:** Tolvaptan
- **Pharmacological class:** Selective vasopressin V_2-receptor antagonist
- **Strength and Formulation:** 15mg, 30mg, 45mg, 60mg, 90mg; tabs
- **Manufacturer:** Otsuka America
- **How supplied:** Tabs—14, 56
- **Legal Classification:** Rx

Jynarque


JYNARQUE
(tolvaptan) tablets
90mg
30mg
60mg
30mg
45 mg
15 mg
56 Tablets
Monthly Carton contains
4 child resistant Weekly Packs each
containing 1 blister card with 14 tablets
DISPENSE THE ENCLOSED MEDICATION GUIDE TO EACH PATIENT
NDC 59148-089-07
NDC 59148-088-28
NDC 59148-087-28
Rx only
DISENSE THE ENCLOSED MEDICATION GUIDE TO EACH PATIENT

Indication

- **To slow kidney function decline** in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD)

Dosage & Administration

- Initially 60mg/day (45mg on waking + 15mg taken 8hrs later)
- Titrate to 60mg + 30mg, then to 90mg + 30mg per day if tolerated; separate titrations at least weekly
- Concomitant **moderate CYP3A inhibitors**: reduce Jynarque dose (see full labeling); temporarily interrupt if recommended reduced doses are not available

Considerations for Special Populations

- **Pregnancy:** May cause fetal harm
- **Nursing mothers:** Not recommended
- **Pediatric:** Not established
- **Elderly:** Caution with dose selection; start low
- **Hepatic impairment:** See Contraindications

Contraindications

- History, signs or symptoms of significant **liver impairment or injury** except uncomplicated polycystic liver disease
- Concomitant **strong CYP3A inhibitors**
- Uncorrected abnormal blood sodium concentrations or urinary outflow obstruction
- Unable to sense or respond to thirst
- Hypovolemia
- Anuria

Boxed Warning

- Can cause serious and potentially fatal **liver injury**

Warnings/Precautions

- Assess ALT/AST, bilirubin prior to treatment, at 2 and 4 weeks after initiation, then monthly for 18 months, and every 3 months thereafter
- **Discontinue immediately** if signs/ symptoms of hepatic injury occur, ALT/AST or bilirubin >2XULN; if resolves, may reinitiate (with more monitoring) if ALT/AST remains <3XULN

Warnings/Precautions

- Do not restart if hepatic injury occurs or ALT/AST >3XULN
- Ensure adequate hydration
- Correct sodium concentration prior to initiation

Warnings/Precautions

- Monitor for weight loss, tachycardia, hypotension
- Suspend therapy until normalized if serum sodium increases above normal range, or hypovolemia or dehydration occurs and fluid intake cannot be increased

Interactions

- See **Contraindications**
- Concomitant **moderate CYP3A inhibitors**: dose adjustment is needed (see Dosing)

Interactions

- **Avoid** concomitant grapefruit juice, strong CYP3A inducers, OATP1B1/3 and OAT3 substrates (eg, statins, bosentan, glyburide, nateglinide, repaglinide, methotrexate, furosemide), BCRP substrates (eg, rosuvastatin), and V_2-receptor agonists (eg, desmopressin)

Adverse Reactions

- Thirst
- Polyuria
- Nocturia
- Pollakiuria
- Polydipsia
- Serious hepatic injury
- Hypernatremia
- Dehydration
- Hypovolemia

Mechanism of Action

- Tolvaptan is a selective V_2-receptor antagonist
- In human ADPKD cyst epithelial cells, tolvaptan inhibited AVP-stimulated *in vitro* cyst growth and chloride-dependent fluid secretion into cysts

Clinical Studies

- Jynarque was evaluated in 2 trials: **TEMPO 3:4** and **REPRISE**
- Pooled findings suggest Jynarque slows the loss of renal function progressively through the course of the disease

Clinical Studies

- In the Phase 3, double-blind, placebo-controlled study, **TEMPO 3:4** (N=1445), adults with early, rapidly-progressing ADPKD were randomized to tolvaptan or placebo for up to 3 years

Clinical Studies

- The **primary endpoint** was the intergroup difference for rate of change of total kidney volume (TKV) normalized as a percentage
- Relative rate of ADPKD-related events was reduced by **13.5%** in the tolvaptan group (hazard ratio [HR] 0.87, 95% CI, 0.78–0.97; *P* =.0095)

Clinical Studies

- In the Phase 3, double-blind, placebo-controlled, randomized withdrawal trial, **REPRISE** (N=1370), adults with chronic kidney disease (CKD) were treated for 12 months followed by a 3-week follow-up period to assess renal function

Clinical Studies

- The **primary endpoint** was the treatment difference in the change in eGFR from pre-treatment baseline to post-treatment follow-up
- Change of eGFR from pretreatment baseline to post-treatment was smaller with tolvaptan vs placebo
  - **Tolvaptan:** -2.3mL/min/1.73m^2
  - **Placebo:** -3.6mL/min/1.73m^2

Clinical Studies

- Treatment effect: 1.3mL/min/1.73m^2 (*P* <.0001)
- The efficacy profile was generally consistent across different subgroups for this indication

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/jynarque/drug/34834/