tolvaptan (Jynarque™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO068

Description

Tolvaptan (Jynarque) is a selective vasopressin V(2)-receptor antagonist.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
tolvaptan (Jynarque)	15 mg tablets	Autosomal dominant polycystic kidney disease	28 tablets/28 days	206341
	30 mg tablets		60 tablets/30 days	206342
	45 & 15 mg tablet therapy pack		56 tablets/28 days (1 box/28 day)	202559
	60 & 30 mg tablet therapy pack		56 tablets/28 days (1 box/28 day)	202565
	90 & 30 mg tablet therapy pack		56 tablets/28 days (1 box/28 day)	202566

Initial Evaluation

I. Prescribed by prescribed by, or, in consultation with a nephrologist; **AND**

II. Tolvaptan (Jynarque) may be considered medically necessary when the following criteria below are met:

A. A diagnosis of **autosomal dominant polycystic kidney disease (ADPDK)** when the following are met:

1. Diagnosis is confirmed by imaging (e.g., ultrasound, CT, MRI) or genetic test; **AND**
2. Member has rapidly-progressing ADPKD (e.g., reduced or declining renal function, high or increasing total kidney volume [height adjusted]); **AND**
3. Member does not have Stage 5 chronic kidney disease (CKD) defined as a glomerular filtration rate {GFR} < 15 mL/min/1.73 m2, or receiving dialysis

III. Tolvaptan (Jynarque) is considered investigational when used for all other conditions, including but not limited to:
   A. Hyponatremia

Renewal Evaluation

I. Member experienced disease stability, or improvement
   - (e.g., reduction in number and/or rate of cyst production, change in renal function, reduction in rate of total kidney volume growth, slowed rate of kidney function decline)

AND

II. Documented lack of unacceptable toxicity

Supporting Evidence

I. Polycystic kidney disease (PKD) includes inherited diseases that cause irreversible decline in kidney function. PKD may be inherited as an autosomal dominant or recessive trait. The autosomal dominant form (autosomal dominant PKD [ADPKD]) is the most common genetic cause of chronic kidney disease (CKD). The majority of individuals with PKD eventually require renal replacement therapy.

II. The diagnosis of ADPKD is most commonly made via screening using ultrasound, CT scan or MRI. Genetic testing is available for definitive diagnosis, but is rarely performed. Confirmed diagnosis of ADPKD via one of these tests is required prior to coverage of Jynarque.

III. Tolvaptan (Jynarque) was shown to slow the rate of decline in renal function in adults at risk of rapidly-progressing ADPKD in two phase 3 randomized controlled trials, TEMPO and REPRISE.
   - TEMPO: Included 1445 adult patients with estimated creatinine clearance >60 mL/min and total kidney volume (TKV) >750 mL. The trial met the pre-specified primary endpoint of 3-year change in TKV ($p<0.0001$). The annual decline in eGFR was slower among patients who received tolvaptan compared to placebo (-2.72 versus -3.70 mL/min/1.73 m2 per year). Tolvaptan also reduced the rate of decline in kidney function at three years (hazard ratio [HR] 0.39, 95% CI 0.26-0.57), and the incidence of clinically significant kidney pain (HR 0.64, 95% CI 0.47-0.89).
   - REPRISE: Examined the effect of tolvaptan in patients with ADPKD who had reduced eGFR; such patients were generally not included in the TEMPO trial. At 12 months, the change from baseline eGFR was lower among those assigned tolvaptan as compared with placebo (-2.34 versus -3.61 mL/min/1.73 m^2); the group difference was 1.27 mL/min/1.73 m^2 (95% CI 0.86-1.68).

- The analysis of the REPRISE trial, and a post-hoc analysis of the TEMPO trial, showed that tolvaptan (Jynarque) may extend the time until stage 5 CKD (ie, eGFR <15 mL/min/1.73 m2) from six to nine years among patients who start tolvaptan with an eGFR <60 mL/min/1.73 m2, and, even longer among those who start tolvaptan earlier.
- Clinical trial criteria for rapidly progressive ADPKD
    i. Age 18-50 AND eGFR ≥60ml/min/1.73m2 AND Total Kidney Volume ≥750ml
    ii. Age 18-55 AND eGFR 25 to 65ml/min/1.73m2
    iii. Age 56-65 AND eGFR 25 to 44 ml/min/1.73m2 AND documented eFGR decline of more than 2.0 ml/min/1.73m2 per year
- The pivotal trials for Jynarque did not involve patients with Stage 5 CKD (glomerular filtration rate [GFR] < 15 mL/min/1.73 m2 or receiving dialysis).

IV. Tolvaptan (Jynarque) is a part of a Risk Evaluation and Mitigation Strategy (REMS) program to monitor for liver injury.

V. Tolvaptan (Jynarque) should not be used off-label for other diagnoses due to lack of evidence, and risk of adverse events.

VI. In clinical trials, outcomes included the reduction in rate of total kidney volume growth, the slowed rate of kidney function decline, improvement in renal function, a change in mean arterial blood pressure, and change in renal pain. Stability of disease, or improvement in at least one of these measures, is indicative of treatment response. Additionally, fatal liver injury is a significant safety concern of Jynarque; liver function tests should be monitored periodically.

Investigational or Not Medically Necessary Uses

I. Hyponatremia
    A. Samsca, is a tolvaptan formulation that is FDA approval for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium of less than 125 mEq/L or less marks hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure and syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Jynarque has not been evaluated for treatment of hyponatremia.

References

1. Jynarque [Prescribing Information]. Tokyo, Japan: Otsuka Pharmaceutical Co. April 2018
2. Muto S. Kawano H., Higashihara E., et al. The effect of tolvaptan on autosomal dominant polycystic kidney disease patients: a subgroup analysis of the Japanese patient subset from TEMPO 3:4 trial. Clin Exp Nephrol. 2015;19(5):867-877.
3. Torres, VE, Chapman, AB, Devuyst, O, et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. The New England journal of medicine. 2012 Dec 20;367(25):2407-18. PMID: 23121377

4. Torres VE., Chapman AB., Devuyst O., et al. Tolvaptan in later-stage autosomal dominant polycystic kidney disease. N Engl J Med. 2017;377:1930-1942.
5. UpToDate, Inc. Treatment of autosomal dominant polycystic kidney disease. UpToDate [database online]. Waltham, MA. Available at http://www.uptodate.com/home/index.html. Updated April 12, 2019

Policy Implementation/Update:

Date Created	May 2018
Date Effective	May 2018
Last Updated	May 2019
Last Reviewed	05/2019

Action and Summary of Changes	Date
Updated to policy format. Added the following: quantity limits for new 15 mg and 30 mg tablet, therapy to be prescribed by or in consultation with nephrologist, limited use to reflect patient population included in clinical trial (i.e. rapidly progressing ADPKD and do not have stage 5 CKD).	5/2019