Jynarque (tolvaptan) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date 08-01-2025

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Jynarque® (tolvaptan) Tablet*	To slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD)	*generic available	1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

ADPKD	Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease that affects approximately 12.5 million people worldwide. It is characterized by continuous development and growth of cysts causing progressive kidney enlargement associated with hypertension, abdominal fullness and pain, episodes of cyst hemorrhage, gross hematuria, nephrolithiasis, cyst infections, and reduced quality of life. End stage renal disease (ESRD) eventually occurs typically after the fourth decade of life. ADPKD is a systemic disorder affecting other organs with potentially serious complications such as massive hepatomegaly and intracranial aneurysm rupture. Mutations in two genes (PKD1, PKD2) are responsible for the majority of ADPKD cases.(2) Widely accepted practice guidelines do not currently exist for ADPKD diagnosis, evaluation, prevention, or treatment. However, the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Evaluation, Management, and Treatment of ADPKD represents the first KDIGO guideline on this subject. The guideline was recently made available for public review and will be published in early 2025.(4) The European Renal Association (ERA) Working Group on Inherited Kidney Disorders, the European Rare Kidney Disease Reference Network, and the Polycystic Kidney Disease International published a consensus statement update on the use of tolvaptan for ADPKD. Rapid disease progression is defined as a confirmed annual estimated glomerular filtration rate (eGFR) decline of greater than or equal to 3 mL/min/1.73m^2. The estimation of eGFR loss should be reliable and based on at least five measurements over a period of at least 4 years. Mayo Classes 1D and 1E indicate rapid disease progression. Mayo Class 1C patients should be carefully considered due to the overlap with slowly progressive disease and additional evidence for rapid disease progression should be sought in these patients. The PROPKD score should be used in cases in which the eGFR and/or Mayo Classification estimates are inconclusive or contradictory. A score greater than 6 is an indicator of rapid disease progression. Total kidney volume (TKV) changes over time should not be used as a marker of progression in individual patients. Tolvaptan should be started as soon as rapid disease progression can be determined in patients 18 years of age or older, and

	tolvaptan should be discontinued when patients approach kidney failure (the need for renal replacement therapy).(2) Tolvaptan treatment must be initiated and monitored under the supervision of physicians with expertise in managing ADPKD and a full understanding of the risks of tolvaptan therapy, including hepatotoxicity and monitoring requirements.(2)
Efficacy	Jynarque was shown to slow the rate of decline in renal function in patients at risk of rapidly progressing ADPKD in two trials; TEMPO 3:4 in patients at earlier stages of disease and REPRISE in patients at later stages. The findings from these trials, when taken together, suggest that Jynarque slows the loss of renal function progressively through the course of the disease.(1) TEMPO 3:4 was a phase 3, double-blind, placebo-controlled, randomized trial which included 1445 adult patients (age greater than 18 years) with early (estimated creatinine clearance [eCrCl] greater than or equal to 60 mL/min), rapidly progressing (TKV greater than or equal to 750 mL and age less than 51 years) ADPKD (diagnosed by modified Ravine criteria). The trial met its prespecified primary endpoint of 3-year change in TKV (p less than 0.0001). Over the 3-year period, TKV increased by 2.8% per year (95% confidence interval [CI], 2.5 to 3.1) with tolvaptan versus 5.5% per year (95% CI, 5.1 to 6.0) with placebo. The relative rate of ADPKD-related events was decreased by 13.5% in tolvaptan-treated patients, (44 vs. 50 events per 100 person-years; hazard ratio, 0.87; 95% CI, 0.78 to 0.97; p=0.0095).(1) REPRISE was a phase 3, double-blind, placebo-controlled, randomized withdrawal trial in 1519 adult patients (age 18-65) with chronic kidney disease (CKD) with an eGFR between 25 and 65 mL/min/1.73 m^2 if younger than age 56; or eGFR between 25 and 44 mL/min/1.73 m^2, plus eGFR decline greater than 2.0 mL/min/1.73 m^2/year if between age 56-65. Subjects were to be treated for 12 months; after completion of treatment, patients entered a 3-week follow-up period to assess renal function. In the randomized period, the change of eGFR from pretreatment baseline to post-treatment follow-up was –2.3 mL/min/1.73 m^2/year with tolvaptan as compared with – 3.6 mL/min/1.73 m^2/year with placebo, corresponding to a treatment effect of 1.3 mL/min/1.73 m^2/year (p less than 0.0001). The key secondary endpoint (eGFR slope in ml/min/1.73 m^2/year assessed using a linear mixed effect model of annualized eGFR [CKD-EPI]) showed a difference between treatment groups of 1.0 ml/min/m^2/year that was also statistically significant (p less than 0.0001).(1)
Safety	Jynarque has a boxed warning for risk of serious liver injury:(1) • Jynarque can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported. • Measure 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. • Jynarque is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) called the Jynarque REMS Program. Jynarque is contraindicated in the following:(1) • Patients with a history, signs or symptoms of significant liver impairment or injury. This contraindications does not apply to uncomplicated polycystic liver disease. • Concomitant use with strong CYP 3A inhibitors • Uncorrected abnormal blood sodium concentrations • Unable to sense or respond to thirst • Hypovolemia • Hypersensitivity to tolvaptan or components of the product • Uncorrected urinary outflow obstruction

	• Anuria

REFERENCES

Number	Reference
1	Jynarque prescribing information. Otsuka America Pharmaceuticals, Inc. October 2020.
2	Chapman AB, Devuyst O, Eckardt KU, et al. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney International*. 2015;88(1):17-27. doi:10.1038/ki.2015.59
3	Müller RU, Messchendorp AL, Birn H, et al. An update on the use of tolvaptan for autosomal dominant polycystic kidney disease: consensus statement on behalf of the ERA Working Group on Inherited Kidney Disorders, the European Rare Kidney Disease Reference Network and Polycystic Kidney Disease International. *Nephrology Dialysis Transplantation*. 2021;37(5):825-839. doi:10.1093/ndt/gfab312
4	KDIGO ADPKD Guideline available for public review - KDIGO. KDIGO - KIDNEY DISEASE | IMPROVING GLOBAL OUTCOMES. https://kdigo.org/kdigo-adpkd-guideline-available-for-public-review/

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Jynarque	tolvaptan tab	15 MG ; 30 MG	M ; N ; O ; Y	O ; Y		
Jynarque	tolvaptan tab therapy pack	15 MG ; 30 & 15 MG ; 45 & 15 MG ; 60 & 30 MG ; 90 & 30 MG	M ; N ; O ; Y	O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Jynarque	tolvaptan tab	15 MG	60	Tablets	30	DAYS			59148008213;70748023806
Jynarque	tolvaptan tab	30 MG	30	Tablets	30	DAYS			59148008313;70748023906
Jynarque	tolvaptan tab therapy pack	15 MG ; 30 & 15 MG ; 45 & 15 MG ; 60 & 30 MG ; 90 & 30 MG	56	Tablets	28	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Jynarque	tolvaptan tab	15 MG ; 30 MG	Commercial ; HIM ; ResultsRx
Jynarque	tolvaptan tab therapy pack	15 MG ; 30 & 15 MG ; 45 & 15 MG ; 60 & 30 MG ; 90 & 30 MG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Jynarque	tolvaptan tab	30 MG	Commercial ; HIM ; ResultsRx
Jynarque	tolvaptan tab	15 MG	Commercial ; HIM ; ResultsRx
Jynarque	tolvaptan tab therapy pack	15 MG ; 30 & 15 MG ; 45 & 15 MG ; 60 & 30 MG ; 90 & 30 MG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has a diagnosis of autosomal dominant polycystic kidney disease (ADPKD) and BOTH of the following: 1. The patient does not have stage 5 chronic kidney disease (CKD) **AND** 2. The patient is not on dialysis **OR** B. The patient has another FDA labeled indication for the requested agent and route of administration **OR** C. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. The patient will NOT be using the requested agent in combination with another tolvaptan agent for the requested indication **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS or DrugDex 1 or 2a level of evidence **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met:

Module	Clinical Criteria for Approval
	1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient will NOT be using the requested agent in combination with another tolvaptan agent for the requested indication **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	**Quantity Limit for Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **Length of Approval:** up to 12 months