Drug Coverage Policy

Effective Date……9/1/2025
Coverage Policy Number……IP0287
Policy Title…… Tolvaptan (Jynarque)

Tolvaptan Products – Tolvaptan (Jynarque)

- Jynarque® (tolvaptan tablets – Otsuka, generic)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Tolvaptan (Jynarque, generic), a selective vasopressin V_2-receptor antagonist, is indicated to slow kidney function decline in adults at risk of rapidly-progressing **autosomal dominant polycystic kidney disease** (ADPKD).[1]

Efficacy studies included patients with normal and reduced renal function. TEMPO 3:4 required patients to have an estimated creatinine clearance ≤ 60 mL/min, while REPRISE included patients with an estimated glomerular filtration rate $(eGFR)_{CKD\text{-}EPI}$ 25 to 65 mL/min/1.73 m^2.[1]

Disease Overview
ADPKD is a heterogeneous, inherited kidney disorder associated with the development of kidney cysts, which result in kidney pain, hypertension, renal failure, and other clinical sequelae.[2-5] The condition is a common cause of end-stage renal disease; however, other organs are also impacted (e.g., hepatic and vascular systems). Progressive kidney enlargement occurs; however, manifestations generally do not occur until later in life (fourth decade) due to compensatory renal mechanisms. If a parent has the condition, a child has a 50% chance of inheritance. Approximately 600,000 people in the US have this condition.

Guidelines
The European Renal Association Working Groups on Inherited Kidney Disorders, the European Rare Kidney Disease Reference Network, and the Polycystic Kidney Disease International published a consensus statement regarding use of tolvaptan in ADPKD (2022).[7] A confirmed annual eGFR decline ≥ 3.0 mL/min/1.73 m^2 over a period of ≥ 4 years defines rapid progression. Also, a Mayo Classification of 1D or 1E indicates rapid disease progression. Patients with Mayo Classification of 1C should be further evaluated for additional evidence of rapid disease progression. Total kidney volume changes should not be used as a marker of progression in individual patients. Finally, Jynarque should be discontinued when the patient approaches kidney failure (i.e., the need for renal replacement therapy).

The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Evaluation, Management, and Treatment of ADPKD (2025) address the role of tolvaptan.[9] Tolvaptan is recommended for adults with ADPKD with an eGFR ≥ 25 mL/min per 1.73 m^2, and who are at risk of disease progression. A historical rate of eGFR decline of ≥ 3.0 mL/min per 1.73 m^2 per year indicates rapid disease progression. Additionally, Mayo Classification 1C to 1E is indicative of rapid disease progression, but providers are encouraged to make case-by-case decisions for 1C classification.

The National Kidney Foundation and the Polycystic Kidney Disease Foundation list tolvaptan as an FDA-approved treatment option for patients with ADPKD.[5,8]

Safety
Tolvaptan (Jynarque, generic) is available only through a restricted distribution program called the Tolvaptan for ADPKD shared System Risk Evaluation and Mitigation Strategy (REMS) because of the risks of liver injury.[1]

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of tolvaptan. All approvals are provided for the duration noted below. Due to the specialized skills required for evaluation and diagnosis of patients treated with tolvaptan as well as the monitoring required for adverse events and long-term efficacy, approval requires tolvaptan to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Tolvaptan is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Autosomal Dominant Polycystic Kidney Disease.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
   A) Patient is ≥ 18 years of age; AND
   B) According to the prescriber, the patient has rapidly-progressing autosomal dominant polycystic kidney disease; AND
   Note: Examples of rapidly declining renal function include estimated glomerular filtration rate decline of ≥ 3.0 mL/min/1.73 m^2, and Mayo Classification of 1C, 1D or 1E.
   C) At baseline, the patient has an estimated glomerular filtration rate ≥ 25 mL/min/1.73 m^2; AND
   Note: This refers to baseline prior to treatment with any tolvaptan product.
   D) Patient is not on renal replacement therapy; AND
   Note: Renal replacement therapy is defined as dialysis or kidney transplantation.
   E) The medication is prescribed by or in consultation with a nephrologist.
   F) Preferred product criteria is met for the product(s) as listed in the below table(s)

Employer Plans:

Product	Criteria
Jynarque (tolvaptan) tablets	The patient has tried the bioequivalent generic product, **tolvaptan tablets**, AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which would result in, per the prescriber, a significant allergy or serious adverse reaction.
Jynarque (tolvaptan) tablet therapy pack	The patient has tried the bioequivalent generic product, **tolvaptan tablet therapy pack**, AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which would result in, per the prescriber, a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Tolvaptan for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

1. **Patient is Currently Receiving Samsca (tolvaptan tablets).** Samsca is a tolvaptan product that is indicated for the treatment of clinically-significant hypervolemic and euvolemic hyponatremia, including patients with heart failure and syndrome of inappropriate antidiuretic hormone (SIADH).[6] Concomitant use is not recommended.

2. **Hyponatremia.** Samsca is another tolvaptan product indicated for the treatment of clinically-significant hypervolemic and euvolemic hyponatremia (serum sodium < 125 mEq/L

or less marked hyponatremia that is symptomatic and has resisted correction and fluid restriction), including patients with heart failure and SIADH. Samsca should be used for this condition.

References

1. Jynarque® tablets [prescribing information]. Rockville, MD: Otsuka; March 2025.
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 Int*. 2015;88:17-27.
3. Ong ACM, Devuyst O, Knebelmann B, et al, on behalf of the ERA-EDTA Working Group for Inherited Kidney Diseases. Autosomal dominant polycystic kidney disease: the changing face of clinical management. *Lancet*. 2015;385:1993-2002.
4. Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. In Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. Last Updated: September 29, 2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1246/ Accessed on June 4, 2025.
5. National Kidney Foundation. Polycystic kidney disease. Available at: https://www.kidney.org/atoz/content/polycystic. Accessed on June 4, 2025.
6. Samsca® tablets [prescribing information]. Rockville, MD: Otsuka; April 2021.
7. Muller 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. *Nephrol Dial Transplant*. 2022;37:825-839.
8. Polycystic Kidney Disease Foundation. Tolvaptan. Available at: https://pkdcure.org/tolvaptan/. Accessed on June 4, 2025.
9. Kidney Disease: Improving Global Outcomes (KDIGO) ADPKD Work Group. KDIGO 2025 Clinical Practice Guideline for the Evaluation, Management, and Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD). *Kidney Int*. 2025;107(2S): S1-S239.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Policy Name Change: Updated** Policy Name from "Tolvaptan (Jynarque®)" to "Tolvaptan Products – Jynarque." **Autosomal Dominant Polycystic Kidney Disease: Added** a note listing examples of rapidly declining renal function, such as eGFR decline of ≥ 3.0 mL/min/1.73 m^2, and Mayo Classification of 1D or 1E. **Added** a note defining Stage 5 chronic kidney disease as having an eGFR < 15 mL/min/1.73 m^2 or receiving dialysis.	10/15/2024
Annual Revision	The policy was renamed to Tolvaptan Products – Tolvaptan (Jynarque) Prior Authorization Policy. Previously, the policy was named Tolvaptan Products – Jynarque. Jynarque tablets are now available as a generic product. **Autosomal Dominant Polycystic Kidney Disease.** Mayo Classification 1C was added to the	9/1/2025

	Note of examples for rapidly progressing autosomal dominant polycystic kidney disease. **Autosomal Dominant Polycystic Kidney Disease.** The requirement regarding kidney function was updated to state that the patient has an estimated glomerular filtration rate ≥ 25 mL/min/1.73 m^2. Previously, it stated that a patient did not have Stage 5 chronic kidney disease, which was defined in the Note as glomerular filtration rate < 15 mL/min/1.73 m^2. With the updated criterion, the related note was deleted. The requirement that a patient has an eGFR ≥ 25 mL/min^2 was clarified to state that this was a requirement at baseline. A corresponding Note was added to define baseline as prior to treatment with any tolvaptan product. Another requirement was also added that a patient on tolvaptan therapy cannot be on renal replacement therapy. A corresponding Note was added to define renal replacement therapy as dialysis or transplantation. **Employer Plans Preferred Product table.** **Added** preferred product requirement criteria for brand Jynarque tablets and brand Jynarque therapy pack.	

The policy effective date is in force until updated or retired.