# Clinical Policy: Tolvaptan (Jynarque, Samsca)

Reference Number: CP.PHAR.27
Effective Date: 06.05.18
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

Tolvaptan (Jynarque®, Samsca®) is a selective vasopressin $V_2$-receptor antagonist.

## FDA Approved Indication(s)

Jynarque is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

Samsca is 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 with fluid restriction), including patients with heart failure and syndrome of inappropriate antidiuretic hormone (SIADH).

Limitation(s) of use:

- Patients requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with Samsca.
- It has not been established that Samsca provides a symptomatic benefit to patients.

## Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that tolvaptan, Jynarque, and Samsca are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Autosomal Dominant Polycystic Kidney Disease** (must meet all)**:**

1. Diagnosis of ADPKD;
2. Request is for Jynarque or generic tolvaptan;
3. Prescribed by or in consultation with a nephrologist;
4. Age ≥ 18 years;
5. Estimated glomerular filtration rate (eGFR) ≥ 25 mL/min/1.73 $m^2$;
6. Member is at risk of rapidly progressive disease as evidenced by one of the following (a or b):
   a. Mayo Image Classification (MIC) class 1C to 1E (*see Appendix D*);
   b. Historical rate of eGFR decline ≥ 3 mL/min/1.73 $m^2$ per year;
7. If request is for Jynarque, member must use generic tolvaptan, unless contraindicated or clinically significant adverse effects are experienced;

8. Dose does not exceed 120 mg per day.

**Approval duration:**
**Medicaid/HIM/ICHRA –** 12 months
**Commercial –** 12 months or duration of request, whichever is less.

**B. Hyponatremia** (must meet all)**:**
1. Diagnosis of hypervolemic or euvolemic hyponatremia;
2. Request is for Samsca or generic tolvaptan;
3. Prescribed by or in consultation with a nephrologist, cardiologist, endocrinologist, or acute care physician (e.g., hospitalist);
4. Age ≥ 18 years;
5. One of the following (a or b):
   a. Recent (within the last 7 days) serum sodium level < 125 mEq/L;
   b. Hyponatremia is symptomatic and has resisted correction with fluid restriction;
6. If request is for Samsca, member must use generic tolvaptan, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed 60 mg per day.

**Approval duration: 30 days**

**C. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

**A. Autosomal Dominant Polycystic Kidney Disease** (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Request is for Jynarque or generic tolvaptan;

3. Member is responding positively to therapy;
4. If request is for Jynarque, member must use generic tolvaptan, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, new dose does not exceed 120 mg per day.

**Approval duration:**
**Medicaid/HIM/ICHRA –** 12 months
**Commercial –** 12 months or duration of request, whichever is less.

**B. Hyponatremia** (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Request is for Samsca or generic tolvaptan;
3. Member is responding positively to therapy as evidenced by increased sodium level since baseline;
4. Member has not received more than 30 days of Samsca treatment;
5. If request is for Samsca, member must use generic tolvaptan, unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for a dose increase, new dose does not exceed 60 mg per day.

**Approval duration: Up to a total duration of 30 days**

**C. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

ADPKD: autosomal dominant polycystic kidney disease
eGFR: estimated glomerular filtration rate
FDA: Food and Drug Administration
htTKV: height-adjusted total kidney volume
MIC: Mayo Image Classification

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Jynarque:
    - History, signs or symptoms of significant liver impairment or injury, does not include uncomplicated polycystic liver disease; concomitant use of strong CYP 3A inhibitors is contraindicated; uncorrected abnormal blood sodium concentrations; unable to sense or respond to thirst; hypovolemia; hypersensitivity to tolvaptan or any of its components; uncorrected urinary outflow obstruction; anuria
  - Samsca:
    - Use in patients with ADPKD outside of FDA-Approved REMS; patients who are unable to respond appropriately to thirst; hypovolemic hyponatremia; concomitant use of strong CYP 3A inhibitors; anuria; hypersensitivity
- Boxed warning(s):
  - Jynarque:
    - Risk of serious liver injury, acute liver failure requiring liver transplantation has been reported; measure transaminases and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then continuing monthly for the first 18 months and every 3 months thereafter, Jynarque is only available through a restricted distribution program called Tolvaptan for ADPKD Shared System REMS
  - Samsca:
    - Initiate and re-initiate in a hospital and monitor serum sodium; not for use for ADPKD

*Appendix D: Mayo Image Classification*

- Strong evidence indicates that height-adjusted total kidney volume (htTKV) is the best existing prognostic biomarker in ADPKD, and that calculating the MIC is the easiest and simplest means to interpret and employ such data. The MIC divides htTKV/age into 5 different classes, 1A to 1E, reflecting kidney size and related to the severity of the kidney disease. Starting at a theoretical starting value of 150 mL/m at birth, annual htTKV growth rates are as follows: 1A: < 1.5%; 1B: 1.5-3%; 1C: 3-4.5%; 1D: 4.5-6%; 1E: > 6%.

- The MIC can be calculated using a web-based application: https://www.mayo.edu/research/documents/pkdcenter-adpkd-classification/doc-20094754

## V. Dosage and Administration

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| Tolvaptan (Jynarque) | ADPKD | 60 mg PO per day administered as 45 mg in the morning and 15 mg 8 hours later.<br><br>If dose is tolerated after at least a week, the total daily dose of 90 mg (60 mg in the morning and 30 mg 8 hours later) can be given.<br><br>The target dose is 120 mg/day (90 mg in the morning and 30 mg 8 hours later), if tolerated. | 120 mg/day |
| Tolvaptan (Samsca) | Hyponatremia | 15 mg PO once daily, then 30 mg PO once daily after 24 hours, to a maximum of 60 mg PO once daily as needed to achieve the desired level of serum sodium.<br><br>Samsca initiation and re-initiation should occur in a hospital. Do not administer Samsca for more than 30 days to minimize the risk of liver injury. | 60 mg/day |

## VI. Product Availability

| Drug Name | Availability |
|---|---|
| Tolvaptan (Jynarque) | • Tablets (7-day and 28-day blister-packs): 45 mg with 15 mg, 60 mg with 30 mg, 90 mg with 30 mg<br>• Tablets (30 pack): 15 mg, 30 mg |
| Tolvaptan (Samsca) | • Tablets: 15 mg, 30 mg |

## VII. References

1. Jynarque Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. March 2025. Available at: https://www.otsuka-us.com/sites/g/files/qhldwo10991/files/media/static/JYNARQUE-PI.pdf. Accessed April 16, 2026.
2. Samsca Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. April 2021. Available at: https://www.otsuka-us.com/sites/g/files/qhldwo10991/files/media/static/Samsca-PI.pdf. Accessed April 16, 2026.
3. Torres V, Chapman A, et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. N Engl J Med. 2012; 367:2407-18.

4. Torres V, Chapman A, et al. Tolvaptan in later-stage autosomal dominant polycystic kidney disease. N Engl J Med. DOI: 10.1056/NEJMoa1710030.
5. 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(Suppl 25): S1-S239.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 3Q 2022 annual review: no significant changes; changed Commercial length of benefit to " 12 months or duration of request, whichever is less", updated Section V to state "Samsca initiation and re-initiation should occur in a hospital"; updated Samsca contraindication section removing "need to raise serum sodium acutely" to align with prescribing information; provided duration clarification for continued hyponatremia treatment with Samsca; references reviewed and updated. | 03.25.22 | 08.22 |
| Template changes applied to other diagnoses/indications and continued therapy section. | 10.11.22 | |
| 3Q 2023 annual review: no significant changes; references reviewed and updated. | 04.14.23 | 08.23 |
| 3Q 2024 annual review: no significant changes; revised policy/ criteria section to also include generic tolvaptan; references reviewed and updated. | 05.14.24 | 08.24 |
| 3Q 2025 annual review: for ADPKD, added requirements for minimum eGFR and high risk for rapidly progressive disease per 2025 KDIGO guidelines and in alignment with pivotal study design and FDA labeling, respectively; for Jynarque, added redirection to generic tolvaptan; references reviewed and updated. | 06.17.25 | 08.25 |
| 3Q 2026 annual review: for hyponatremia, added option for acute care physician prescriber since Samsca is initiated in a hospital setting; added ICHRA line of business; references reviewed and updated. | 04.23.26 | 08.26 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note:**
**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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