Clinical Policy: Tolvaptan (Jynarque, Samsca)

Reference Number: PA.CP.PHAR.27
Effective Date: 10/2018
Last Review Date: 07/2025

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).

Limitatoin(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 PA Health & Wellness® 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/day.

Approval duration: 12 months

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, or endocrinologist;
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
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Autosomal Dominant Polycystic Kidney Disease (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;
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/day.

Approval duration: 12 months

B. Hyponatremia (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;
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/day.

Approval duration: Up to a total duration of 30 days

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies.

Approval duration: Duration of request or 12 months; or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

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 policy – PA.CP.PMN.53 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 REMSpatients 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/day administered PO as 45 mg in the morning and 15 mg 8 hours later. 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. 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. 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 • 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. October 2020. Available at: https://www.otsuka-us.com/sites/g/files/qhldwo10991/files/media/static/JYNARQUE-PI.pdf. Accessed April 14, 2025.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 14, 2025.
2. Torres V, Chapman A, et al. Tolvaptan in patients with autosomal dominant polycystic kidney disease. N Engl J Med 2012; 367:2407-18.
3. Torres V, Chapman A, et al. Tolvaptan in later-stage autosomal dominant polycystic kidney disease. N Engl J Med. DOI: 10.1056/NEJMoa1710030.
4. 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
Policy created.	10/2018
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/2019
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
3Q 2020 annual review: added age limit; updated product availability; updated Jynarque boxed warnings as per updated prescribing information; references reviewed and updated.	07/2020
3Q 2021 annual review: no significant changes; revised "medical justification" to "must use"; references reviewed and updated.	07/2021
3Q 2022 annual review: no significant changes; 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.	07/2022
3Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023
3Q 2024 annual review: no significant changes; references reviewed and updated.	07/2024
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.	07/2025