Clinical Policy: Tolvaptan (Jynarque, Samsca)

Reference Number: CP.PHAR.27
Effective Date: 06.05.18
Last Review Date: 08.23
Line of Business: Commercial, HIM, 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 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;
3. Prescribed by or in consultation with a nephrologist;
4. Age ≥ 18 years;
5. Dose does not exceed 120 mg per day.

Approval duration:
Medicaid/HIM – 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;
3. Prescribed by or in consultation with a nephrologist, cardiologist, or endocrinologist;
4. Age ≥ 18 years;
5. Recent (within the last 7 days) serum sodium level < 125 mEq/L, unless hyponatremia is symptomatic and has resisted correction with fluid restriction;
6. 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 120 mg per day.

Approval duration:
Medicaid/HIM – 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. Member is responding positively to therapy as evidenced by increased sodium level since baseline;
3. Member has not received more than 30 days of Samsca treatment;
4. 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 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) 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, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) 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, 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, 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, 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
FDA: Food and Drug Administration

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 Jynarque REMS program.
    - Samsca:
        - Initiate and re-initiate in a hospital and monitor serum sodium; not for use for ADPKD.

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. 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 (generic available)

VII. References

1. Jynarque Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. October 2020. Available at: https://www.otsuka-us.com/sites/g/files/qhldwo6966/files/media/static/JYNARQUE-PI.pdf. Accessed April 14, 2023.
2. Samsca Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. April 2021. Available at: https://www.otsuka-us.com/sites/g/files/qhldwo6966/files/media/static/Samsca-PI.pdf. Accessed April 14, 2023.
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. Muller RU, Haas CS, Sayer JA. Practical approaches to the management of autosomal dominant polycystic kidney disease patients in the era of tolvaptan. Clin Kidney J, 2018 Feb; 11(1):62-69.
6. 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: 88:17-27.
7. Eckardt KU, Alper SL, Antignac C, et al. Kidney Disease: Improving Global Outcomes. Autosomal dominant tubulointerstitial kidney disease: diagnosis, classification, and management--A KDIGO consensus report. Kidney Int. 2015 Oct;88(4):676-83.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	06.05.18	08.18
Added HIM line of business; added Samsca and hyponatremia criteria to policy; references reviewed and updated.	09.04.18	11.18
4Q 2019 annual review: no significant changes; added to contraindications and boxed warnings per updated prescribing information; references reviewed and updated.	08.25.19	11.19
3Q 2020 annual review: no significant changes; updated product availability; updated Jynarque boxed warnings as per updated prescribing information; added criterion for medical justification supporting inability to use generic tolvaptan for brand Samsca request; references reviewed and updated.	07.22.20	08.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: no significant changes; revised "medical justification" to "must use"; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.22.21	08.21
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

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.