Clinical Policy: Tolvaptan (Jynarque, Samsca)

Reference Number: ERX.SPA.252
Effective Date: 09.01.18
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Tolvaptan (Jynarque®, Samsca®) is an oral non-peptide V2 vasopressin 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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: 12 months

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. Recent (within the last 7 days) serum sodium level < 125 mEq/L, unless hyponatremia is symptomatic and has resisted correction with fluid restriction;
5. Age ≥ 18 years;
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
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Autosomal Dominant Polycystic Kidney Disease (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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: 12 months

B. Hyponatremia (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by increased sodium level since baseline;
3. Member must use generic tolvaptan, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed 60 mg per day.

Approval duration: up to a total treatment duration of 30 days

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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; need to raise serum sodium acutely; 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 QD, then 30 mg PO QD after 24 hours, to a maximum of 60 mg PO QD as needed to achieve the desired level of serum sodium. 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 www.jynarque.com. Accessed March 22, 2021.
2. Samsca Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. June 2018. Available at: www.samsca.com. Accessed March 22, 2021.
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 R, Haas C, et al. Practical approaches to the management of autosomal dominant polycystic kidney disease patients in the era of tolvaptan. Clinical Kidney Journal, 2018, vol. 11, no. 1, 62-69.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	06.05.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.01.19	08.19
3Q 2020 annual review: added Samsca and hyponatremia criteria to policy; updated Jynarque 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
3Q 2021 annual review: no significant changes; revised "medical justification" to "must use"; references reviewed and updated.	03.22.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.