Clinical Policy Title:	tolvaptan
Policy Number:	RxA.277
Drug(s) Applied:	Jynarque®, Samsca®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

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.

Dosing Information

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. Do not administer Samsca® for more than 30 days to minimize the risk of liver injury.	60 mg/day

Dosage Forms

- 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.
- Tolvaptan (Samsca®) Tablets: 15 mg and 30 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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/day.

Approval duration
Commercial: 12 months
Medicaid: 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. Dose does not exceed 60 mg per day.

Approval duration
Commercial: 30 days
Medicaid: 30 days

II. **Continued Therapy Approval**

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 120 mg/day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

B. **Hyponatremia** (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by increased sodium level since baseline;
3. If request is for a dose increase, new dose does not exceed 60 mg/day.

Approval duration
Commercial: 30 days
Medicaid: 30 days

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
ADPKD: Autosomal Dominant Polycystic Kidney Disease
SIADH: Syndrome of inappropriate antidiuretic hormone

APPENDIX B: Therapeutic Alternatives
- Not applicable.

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Jynarque®:
    - History of signs or symptoms of significant liver impairment or injury, does not include uncomplicated polycystic liver disease;
    - Concomitant use of strong CYP3A inhibitors is contraindicated;
    - Uncorrected abnormal blood sodium concentrations;
    - Unable to sense or respond to thirst;
    - Hypovolemia;
    - Uncorrected urinary outflow obstruction;
    - Hypersensitivity to tolvaptan or any of its components;
    - 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 CYP3A inhibitors;
    - Anuria;
    - Hypersensitivity.

- Boxed warning(s):
  - Jynarque®: Risk of serious liver injury.
  - Samsca®:
    - Initiate and re-initiate in a hospital and monitor serum sodium;
    - Not for use for ADPKD.

Appendix D: General Information
- Not applicable.

References

1. Jynarque Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. November 2020. Available at: www.jynarque.com. Accessed May 06, 2021.
2. Samsca Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. April 2021. Available at: www.samsca.com. Accessed May 06, 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 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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated. 3. Initial and Continued approval duration was updated to include Medicaid, Commercial & HIM approval duration. 4. Continued therapy criteria II.A.1. & II.B.1. was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. References were reviewed and updated.	07/17/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample, ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. HIM approval duration was removed from Initial and continued approval criteria. 3. Appendix B: Therapeutic Alternatives header verbiage was changed to "Below are suggested therapeutic alternatives based on..." 4. Hypersensitivity to tolvaptan was added to Appendix C: Contraindication. 5. References were reviewed and updated.	04/02/2021	06/10/2021