Clinical Policy: Tolvaptan (Jynarque, Samsca)

Reference Number: PA.CP.PHAR.27
Effective Date: 10.17.18
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Revision Log

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

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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 health plans affiliated with PA Health & Wellness® 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. 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;
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. 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 Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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: 12 months

B. Hyponatremia (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
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: up to a total duration of 30 days

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.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 policies – PA.CP.PMN.53 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:
    - Concomitant use of strong CYP 3A inhibitors (e.g., ketoconazole)
    - Uncorrected abnormal blood sodium concentrations
    - Hypovolemia
    - Anuria
    - Uncorrected urinary outflow obstruction
  - Samsca:
    - Use in patients with autosomal dominant polycystic kidney disease outside of FDA-Approved REMS
    - Urgent need to raise serum sodium acutely
    - Inability of the patient to sense or appropriate response to thirst
    - Hypovolemic hyponatremia
    - Concomitant use of strong CYP 3A inhibitors
    - Anuric patients
- 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 autosomal dominant polycystic kidney disease

Appendix D: General Information

- Samsca therapy should be initiated and re-initiated in a hospital setting to evaluate the therapeutic response and because too rapid correction of hyponatremia can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, and death.

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 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.	60 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Do not administer Samsca for more than 30 days to minimize the risk of liver injury.	

VI. Product Availability

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

VII. References

1. Torres V, Chapman A, et al. Tolvaptan in Patients with autosomal dominant polycystic kidney disease. N Engl J Med 2012; 367:2407-18.
2. Torres V, Chapman A, et al. Tolvaptan in later-stage autosomal dominant polycystic kidney disease. N Engl J Med. DOI: 10.1056/NEJMoa1710030.
3. Jynarque Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. April 2018. Available at: www.jynarque.com. Accessed April 25, 2018.
4. Samsca Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc. April 2018. Available at: www.samsca.com. Accessed August 24, 2018.
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.	10/18	
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	