
Title: Tolvaptan (Samsca®, Jynarque®)

Policy #: Rx.01.89

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **tolvaptan (Samsca®, Jynarque®)** as provided under the member's prescription drug benefit.

Description:

Hyponatremia is defined as a relative excess of water in relation to sodium. Treatment approaches depend on the duration, severity, and cause of hyponatremia.

Tolvaptan (Samsca®) is a selective vasopressin V2 receptor antagonist. Tolvaptan antagonizes the effect of vasopressin and causes an increase in urine water excretion that results in an increase in free water clearance, a decrease in urine osmolality and a resulting increase in serum sodium concentrations.

Tolvaptan (Samsca®) is indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium < 125meq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction) including patients with heart failure, cirrhosis, and syndrome of inappropriate antidiuretic hormone.

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disorder characterized by the growth of numerous fluid filled cysts in the kidneys which progressively decreases kidney function and lead to permanent kidney damage. It is the most common inherited disorder of the kidneys. Symptoms usually develop between the ages of 30 and 40, but they can begin earlier, even in childhood.

Tolvaptan (Jynarque®) is a selective vasopressin (V2) receptor antagonist. Patients with autosomal dominant polycystic kidney disease have elevated levels of vasopressin. Tolvaptan works by preventing vasopressin from binding to its receptor which then decreases the rate of cell proliferation and fluid secretion into the cystic lumen, ultimately inhibiting the growth of the fluid filled cysts in the kidneys and slows the worsening of kidney function.

Tolvaptan (Jynarque®) is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD).

Policy:

Tolvaptan (Samsca®) is approved when there is a diagnosis of ALL of the following:

- A. Member is 18 years of age or older; and
- B. Clinically significant hypervolemic or euvolemic hyponatremia and ONE of the following:
 1. Serum sodium less than 125meq/L; or
 2. Serum sodium 125-134meq/L with symptoms (ie nausea, vomiting, headache, lethargy, confusion, etc)

- and
- C. Inadequate response or inability to tolerate therapies to control hyponatremia (ie fluid restriction, diuretics, demeclocycline, etc); and
 - D. Prescriber is cardiologist, nephrologist, or endocrinologist

INITIAL CRITERIA

Tolvaptan (Jynarque®) is approved when there is documentation of ALL of the following:

- A. Member is 18 years of age or older; AND
- B. Diagnosis of autosomal dominant polycystic kidney disease with risk of rapidly progressing kidney disease; AND
- C. Baseline serum transaminases and bilirubin obtained prior to initiation of therapy; AND
- D. Prescribed by nephrologist or kidney transplant specialist

Initial authorization: 3 months

REAUTHORIZATION CRITERIA

Tolvaptan (Jynarque®) is re-approved when ALL of the following are met:

- A. ONE of the following
 1. Decline in kidney function has slowed; OR
 2. Kidney pain has improved
- And
- B. Serum transaminase less than 3 times the upper limit of normal; AND
 - C. Bilirubin less than 2 times upper limit of normal

Reauthorization duration: 12 months

Black Box Warning as shown in the drug Prescribing Information:

Tolvaptan (Samsca®)

INITIATE AND RE-INITIATE IN A HOSPITAL AND MONITOR SERUM SODIUM

Tolvaptan (Samsca®) should be initiated and re-initiated in patients only in a hospital where serum sodium can be monitored closely.

Too rapid correction of hyponatremia (e.g., >12 mEq/L/24 hours) can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death. In susceptible patients, including those with severe malnutrition, alcoholism or advanced liver disease, slower rates of correction may be advisable.

Tolvaptan (Jynarque®) can cause serious and potentially fatal liver injury. Acute liver failure requiring liver transplantation has been reported.

Measure ALT, AST and bilirubin before initiating treatment, at 2 weeks and 4 weeks after initiation, then monthly for the first 18 months and every 3 months or symptoms indicative of hepatic injury can mitigate, but not eliminate, the risk of serious hepatotoxicity.

Because of the risks of serious liver injury, Jynarque® is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) called the JYNARQUE REMS Program

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed

in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Jynarque® (tolvaptan) [package insert] Tokyo, Japan. Otsuka Pharmaceutical Co, Ltd. February 2019. Available at: <https://www.otsuka-us.com/media/static/JYNARQUE-PI.pdf>. Accessed January 16, 2020.

Samsca® (tolvaptan) [package insert]. Tokyo, Japan. Otsuka Pharmaceutical Co, Ltd. May 2019. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=5526617c-c7b9-4556-886d-729bbabbc566&type=display>. Accessed January 16, 2020.

Sterns RH. Overview of the treatment of hyponatremia in adults. UpToDate. April 2015. Available at: https://www.uptodate.com/contents/overview-of-the-treatment-of-hyponatremia-in-adults?source=search_result&search=hyponatremia&selectedTitle=2~150#H25. Accessed January 16, 2020.

Tolvaptan (Kidney Disease): MedlinePlus Drug Information." *MedlinePlus*, U.S. National Library of Medicine, 15 July 2018, medlineplus.gov/druginfo/meds/a609033.html.

Applicable Drugs:

i Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Samsca®	Tolvaptan
Jynarque®	Tolvaptan

Cross References:

Off Label Use Rx.01.33

Policy Version Number:	11.00
P&T Approval Date:	January 9, 2020
Policy Effective Date:	April 01, 2020
Next Required Review Date:	January 9, 2021

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

