Drug Coverage Policy

Effective Date……10/15/2024
Coverage Policy Number……IP0471
Policy Title….. Tolvaptan (Samsca) for Individual and Family Plans

Tolvaptan Products – Tolvaptan (Samsca) for Individual and Family Plans

- Samsca® (tolvaptan tablets – Otsuka, generic)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW
Tolvaptan (Samsca, generic), a selective vasopressin V_2-receptor antagonist, 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). 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 raising serum sodium with Samsca provides a symptomatic benefit to patients.

Clinical Data
Two trials (Study of Ascending Levels of Tolvaptan in Hyponatremia 1 and 2 [SALT-1 and SALT-2; n = 424]) demonstrated that Samsca increased serum sodium effectively in patients with euvolemic or hypervolemic hyponatremia that was due to many underlying causes (e.g., heart failure, liver cirrhosis, SIADH).[1,2] Patients ≥ 18 years of age received therapy for 30 days with Samsca or placebo and were followed for an additional 7 days after study withdrawal. Patients in the trial had a serum sodium < 135 mEq/L at study entry (baseline 129 mEq/L). In both trials, Samsca therapy led to a greater increase in serum sodium compared with baseline for the measured endpoints at Day 4 and Day 30. The effects of sustained serum sodium were demonstrated for up to 1 year in an open-label study.[1]

SALTWATER (the Safety and sodium Assessment of Long-term Tolvaptan With hyponatremia: A year-long, open-label Trial to gain Experience under Real-world conditions [SALTWATER]) was an open-label extension study of the SALT-1 and SALT-2 trials.[1,3] Patients were eligible if they had completed either SALT-1 or SALT-2 and had a need and desire to continue therapy. There were 111 patients enrolled in the study with a mean baseline serum sodium concentration of 130.8 ± 4.4 mmol/L. Patients received Samsca for a mean of 701 days (1.92 years). Serum sodium concentrations increased to a mean of > 135 mmol/L by Day 14 and remained above this level at all observation time points going forward. Upon discontinuation of tolvaptan, the serum sodium concentration declined by ≥ 3 mmol/L in 68% of patients and an equal amount had serum sodium concentrations fall to < 135 mmol/L. One patient discontinued tolvaptan due to hypernatremia.

Medical Necessity Criteria

Tolvaptan is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Hyponatremia.** Approve for the duration noted if patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 30 days if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets ONE of the following criteria (a, b, or c):
       - **a)** Patient has a serum sodium < 125 mEq/L at baseline; OR
       - **b)** Patient meets the following criteria [(1) and (2)]:
         - **(1)** Patient has less marked hyponatremia, defined as serum sodium < 135 mEq/L at baseline; AND
         - **(2)** Patient has symptomatic hyponatremia; OR
           Note: Symptoms of hyponatremia include nausea, vomiting, headache, lethargy, confusion.
       - **c)** Patient has already been started on tolvaptan and has received < 30 days of therapy; AND
         Note: For a patient who has been started on tolvaptan and has received < 30 days of therapy, approve for a sufficient duration to complete 30 total days of therapy.
     - **iii.** Preferred product criteria is met for the product as listed in the below table
   - **B)** Patient is Currently Receiving Tolvaptan. Approve for 3 months if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has been established on therapy for at least 30 days; AND
       Note: A patient who has received < 30 days of therapy or is restarting therapy is reviewed under criterion A (Initial Therapy).
     - **ii.** Patient meets at least ONE of the following (a or b):
       - **a)** According to the prescriber, the serum sodium level has increased from baseline (prior to initiating the requested drug); OR

b) According to the prescriber, patient experienced improvement in at least one symptom, such as nausea, vomiting, headache, lethargy, or confusion.

Individual and Family Plans:

Product	Criteria
Samsca (tolvaptan tablets)	The patient has tried the bioequivalent generic product, **tolvaptan tablets [prior authorization required]**, AND cannot take due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which would result, per the prescriber, in a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Autosomal Dominant Polycystic Kidney Disease (ADPKD).** Jynarque® (tolvaptan tablets) is another tolvaptan product that is indicated to slow kidney function decline in adults at risk of rapidly-progressing ADPKD. The recommended dosing differs.[4] The Samsca prescribing information states that tolvaptan should not be prescribed or used to treat ADPKD outside of the FDA-approved Risk Evaluation and Mitigation Strategies for ADPKD.[1]

2. **Patient is Currently Receiving Jynarque.** Jynarque is another tolvaptan product that is indicated to slow kidney function decline in adults at risk of rapidly-progressing ADPKD. Concomitant use is not recommended.

3. **Patients Requiring Intervention to Raise Serum Sodium Urgently to Prevent or to Treat Serious Neurological Symptoms.** Samsca has not been studied in a setting of urgent need to raise serum sodium acutely.[1]

References

1. Samsca® tablets [prescribing information]. Rockville, MD: Otsuka; April 2021.
2. Schrier RW, Gross P, Gheorghiade M, et al, for the SALT Investigators. Tolvaptan, a selective oral vasopressin V_2-receptor antagonist, for hyponatremia. *N Engl J Med*. 2006;355:2099-2112.
3. Berl T, Quittnat-Pelletier F, Verbalis JG, et al, for the SALTWATER Investigators. Oral tolvaptan is safe and effective in chronic hyponatremia. *J Am Soc Nephrol*. 2010;21:705-712.
4. Jynarque® tablets [prescribing information]. Rockville, MD: Otsuka; October 2020.

Revision Details

Type of Revision	Summary of Changes	Date

Annual Revision	**Policy Name Change: Updated** Policy Name from "Tolvaptan (Samsca) for Individual and Family Plans" to "Tolvaptan Products – Tolvaptan (Samsca) for Individual and Family Plans." **Hyponatremia: Updated** the statement "individual has initiated a course of tolvaptan and requires further medication to complete the current course of therapy up to 30 days" to say "patient has already been started on tolvaptan and has received < 30 days of therapy." **Added** a note saying that for a patient who has been started on tolvaptan and has received < 30 days of therapy, approve for a sufficient duration to complete 30 total days of therapy.	10/15/2024

The policy effective date is in force until updated or retired.