PRIOR AUTHORIZATION POLICY

POLICY: Tolvaptan Products – Tolvaptan (Samsca) Prior Authorization Policy
- Samsca® (tolvaptan tablets – Otsuka, generic)

REVIEW DATE: 06/26/2024

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of tolvaptan. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of tolvaptan is recommended in those who meet the following criteria:

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 BOTH of the following (i and ii):
     - **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.
         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.
   - **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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of tolvaptan is not recommended in the following situations:

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]

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.