# PRIOR AUTHORIZATION POLICY

**POLICY:** Tolvaptan Products – Tolvaptan tablets (Samsca® – Otsuka; generics)

**DATE REVIEWED:** 06/10/2020

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**OVERVIEW**

Samsca, 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 (HF) 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., HF, liver cirrhosis, SIADH).[1,2] Patients (aged ≥ 18 years) 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 ($P < 0.0001$) 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] Another long-term analysis (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]) showed that in 111 patients who received Samsca for approximately 1 year, increases in serum sodium were maintained.[1,3]

**POLICY STATEMENT**

Prior authorization is recommended for prescription benefit coverage of Samsca. All approvals are provided for up to 30 days.

**Automation:** None.

**RECOMMENDED AUTHORIZATION CRITERIA**

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

**FDA-Approved Indications**

1. **Hyponatremia.** Approve for up to 30 days if patient meets ONE of the following criteria (A, B, or C):
   - **A)** The patient has a serum sodium < 125 mEq/L at baseline; OR
   - **B)** The patient meets the following criteria (i and ii):
     - **i.** The patient has less marked hyponatremia, defined as serum sodium < 135 mEq/L at baseline; AND
     - **ii.** The patient has symptomatic hyponatremia.

Note: Symptoms of hyponatremia include nausea, vomiting, headache, lethargy, confusion; OR

**C)** The patient has already been started on Samsca and has received < 30 days of therapy.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Samsca has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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 REMS for ADPKD.

2. **Patient is Currently Receiving Jynarque® (tolvaptan tablets).** 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 for oral use [prescribing information]. Rockville, MD: Otsuka Pharmaceuticals; April 2018.
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 for oral use [prescribing information]. Rockville, MD: Otsuka Pharmaceuticals; January 2020.