Samsca (tolvaptan) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
8/1/2023	7/1/2018

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Samsca® (tolvaptan) tablet*	Treatment of clinically significant hypervolemic and euvolemic hyponatremia (serum sodium less than 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) Limitations 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 raising serum sodium with Samsca provides a symptomatic benefit to patients	*generic available	1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Hyponatremia	Hyponatremia is the most common disorder of body fluid and electrolyte balance in clinical practice, occurring in up to 15-30% of acute and chronically hospitalized patients. While many cases are considered mild and relatively asymptomatic, hyponatremia is clinically important for the following reasons: untreated acute severe hyponatremia can cause substantial morbidity and mortality; adverse outcomes, including mortality, are higher in patients with a wide range of underlying conditions; and correction of serum sodium that is too fast may cause severe neurologic damage and death.(2,3) Hyponatremia can be classified as hypotonic, hypertonic, or isotonic. Hypotonic hyponatremia being further classified based on a patient's extracellular fluid volume as hypovolemic hyponatremia, hypervolemic hyponatremia, or euvolemic hyponatremia. Hypovolemic hyponatremia is associated with fluid depletion and can arise from a number of conditions. Hypervolemic hyponatremia is caused by fluid overload, as in advanced cirrhosis, renal disease, or congestive heart failure. Euvolemic hyponatremia is most commonly associated with Syndrome of Inappropriate Antidiuretic Hormone (SIADH).(2) Appropriate treatment should be based on the type of hyponatremia, the underlying etiology, the serum sodium (Na+) level, and the severity of symptoms. Treatment strategies can include fluid restriction, diuretic therapy, sodium supplementation, demeclocycline, urea, and vasopressin receptor antagonists (vaptans). The 2013 expert panel recommendations note that, at the time that fluid restriction is first started, medications known to be associated with SIADH should be discontinued or changed.(2)

	Medications associated with SIADH are: antidepressants (SSRIs, tricyclics, MAOIs, venlafaxine), anticonvulsants (carbamazepine, oxcarbazepine, sodium valproate, lamotrigine), antipsychotics (phenothiazines, butyrophenones), anticancer (vinca alkaloids, platinum compounds, ifosfamide, melphalan, cyclophosphamide, methotrexate, pentostatin), antidiabetic (chlorpropamide, tolbutamide), vasopressin analogues (desmopressin, oxytocin, terlipressin, vasopressin), miscellaneous (amiodarone, clofibrate, interferon, NSAIDs, levamisole, linezolid, monoclonal antibodies, nicotine, opiates, PPIs). Discontinuing these medications can lead to the rapid reversal of SIADH.(3)
Efficacy (1)	Samsca is a selective vasopressin V2-receptor antagonist approved for the treatment of patients with hypervolemic or euvolemic hyponatremia. Binding of tolvaptan to the V2-receptor increases serum sodium concentrations by antagonizing the effect of vasopressin, increasing urine water excretion, increasing free water clearance (aquaresis), and decreasing urine osmolality.
Safety (1)	**Boxed Warning** 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., greater than 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. Due to the risk of hepatotoxicity, tolvaptan should not be used for ADPKD outside of the FDA-approved REMS program. **Contraindications** • Use in patients with autosomal dominant polycystic kidney disease (ADPKD) outside of FDA-approved REMS • Inability of patient to sense or respond to thirst • Hypovolemic hyponatremia • Concomitant use with strong CYP3A inhibitors (e.g., ketoconazole, clarithromycin, itraconazole, ritonavir, indinavir, nelfinavir, saquinavir, nefazodone, and telithromycin) • Anuria • Hypersensitivity to tolvaptan or any component of the product **Warnings and Precautions** • Too rapid correction of serum sodium can cause serious neurologic sequelae • Liver injury: Limit treatment duration to 30 days. If hepatic injury is suspected, discontinue Samsca. Avoid use in patients with underlying liver disease. • Dehydration and hypovolemia • Co-administration with hypertonic saline • Drug interactions including use with moderate-to-strong CYP3A inhibitors. Do not use Samsca with strong inhibitors of CYP3A and avoid concomitant use with moderate CYP3A inhibitors. • Hyperkalemia or drugs that increase serum potassium • Acute urinary retention with outflow obstruction

REFERENCES

Number	Reference
1	Samsca Prescribing Information. Otsuka Pharmaceutical Co., Ltd. April 2021.
2	Verbalis, J. G., Goldsmith, S. R., Greenberg, A., Korzelius, C., Schrier, R. W., Sterns, R. H., & Thompson, C. J. (2013). Diagnosis, evaluation, and treatment of hyponatremia: Expert panel recommendations. *The American Journal of Medicine*, *126*(10). https://doi.org/10.1016/j.amjmed.2013.07.006
3	Spasovski, G., Vanholder, R., Allolio, B., Annane, D., Ball, S., Bichet, D., Decaux, G., Fenske, W., Hoorn, E. J., Ichai, C., Joannidis, M., Soupart, A., Zietse, R., Haller, M., van der Veer, S., Van Biesen, W., & Nagler, E. (2014). Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Nephrology Dialysis Transplantation*, *29*(suppl_2), i1–i39. https://doi.org/10.1093/ndt/gfu040

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Samsca	tolvaptan tab	15 MG ; 30 MG	M ; N ; O ; Y	M ; N ; O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Samsca	tolvaptan tab	15 MG	30	Tablets	365	DAYS			31722086803 ; 31722086831 ; 49884076852 ; 49884076854 ; 59148002050 ; 60505431700 ; 60505470400 ; 60505470402 ; 67877063502 ; 67877063533
Samsca	tolvaptan tab	30 MG	60	Tablets	365	DAYS			31722086903 ; 49884077052 ; 49884077054 ; 59148002150 ; 60505431800 ; 60505470500 ; 60505470501 ; 67877063602 ; 67877063633

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Samsca	tolvaptan tab	15 MG ; 30 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Samsca	tolvaptan tab	30 MG	Medicaid
Samsca	tolvaptan tab	15 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The requested agent was initiated (or re-initiated) in the hospital **AND** 2. Prior to initiating the requested agent, the patient has/had a diagnosis of clinically significant hypervolemic or euvolemic hyponatremia defined by one of the following: A. serum sodium less than 125 mEq/L **OR** B. serum sodium greater than or equal to 125 mEq/L and has symptomatic hyponatremia that has resisted correction with fluid restriction **AND** 3. The patient does NOT have underlying liver disease, including cirrhosis **AND** 4. Medications known to cause hyponatremia (e.g., antidepressants [SSRIs, tricyclics, MAOIs, venlafaxine], anticonvulsants [carbamazepine, oxcarbazepine, sodium valproate, lamotrigine], antipsychotics [phenothiazines, butyrophenones], anticancer [vinca alkaloids, platinum compounds, ifosfamide, melphalan, cyclophosphamide, methotrexate, pentostatin], antidiabetic [chlorpropamide, tolbutamide], vasopressin analogues [desmopressin, oxytocin, terlipressin, vasopressin], miscellaneous [amiodarone, clofibrate, interferon, NSAIDs, levamisole, linezolid, monoclonal antibodies, nicotine, opiates, PPIs]) have been evaluated and discontinued when appropriate **AND** 5. The patient will NOT be using the requested agent in combination with another tolvaptan agent for the requested indication **AND** 6. The patient does not have any FDA labeled contraindications to the requested agent **AND** 7. The patient has not already received 30 days of therapy with the requested agent for the current hospitalization **Length of Approval:** 30 tablets/365 days of the 15 mg tablets 60 tablets/365 days of the 30 mg tablets NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Evaluation** **Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose and/or duration of therapy) does NOT exceed the program quantity limit **OR** 2. BOTH of the following: A. The requested quantity (dose and/or duration of therapy) is greater than the program quantity limit **AND** B. The patient has had an additional hospitalization for hyponatremia for initiation of the requested agent **Length of Approval:** 30 tablets/365 days of the 15 mg tablets 60 tablets/365 days of the 30 mg tablets

