Samsca (tolvaptan)
Policy Number: C8048-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
7/1/2015	6/3/2020	6/3/2021
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J8499 (NOC)- Prescription drug, oral, non chemotherapeutic, nos	RxPA	Q3 2020 20200722C8048-A

PRODUCTS AFFECTED:
Samsca (tolvaptan)

DRUG CLASS:
Vasopressin Antagonist

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Specialty Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and member self-administered

AVAILABLE DOSAGE FORMS:
Samsca TABS 15MG, Samsca TABS 30MG

FDA-APPROVED USES:
Hypervolemic and euvolemic hyponatremia

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Hypervolemic and euvolemic hyponatremia

REQUIRED MEDICAL INFORMATION:
A. HYPERVOLEMIC AND EUVOLEMIC HYPONATREMIA

1. Clinically significant hypervolemic or euvolemic hyponatremia as evidenced by:
   (a) Serum sodium less than 125 mEq/L [current or baseline value prior to beginning of therapy in hospital]
   OR
   (b) Serum sodium level ≥ 125 but patient is symptomatic and has resisted correction with fluid restriction
   AND
2. No concurrent use of strong CYP3A inhibitors [e.g., clarithromycin, ketoconazole, itraconazole,

ritonavir, indinavir, nelfinavir, saquinavir, nefazodone, telithromycin)]
AND

3. Confirmation that member does not have underlying liver disease (including cirrhosis) or a CrCl less than 10ml/minute
AND
4. Therapy will be (or was) initiate(d) or re-initiate(d) in a hospital within the past 30 days. If therapy has been initiated/re-initiated, member has not already received 30 days of Samsca therapy following the most recent hospitalization.

DURATION OF APPROVAL:
Initial authorization: 30 days. Continuation of Therapy: N/A. Therapy duration is limited to 30 days to limit hepatic injury risk associated with medication use.

QUANTITY:
60mg daily; 2 tablets per day

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a cardiologist, nephrologist, or endocrinologist

AGE RESTRICTIONS:
18 years of age and older

CONTINUATION OF THERAPY:
No renewal or continuation beyond 30 days. The duration of tolvaptan therapy should be limited to 30 days in order to minimize the risk of hepatic injury.
Additional authorization for treatment beyond 30 days is an EXCEPTION: [MOLINA MEDICAL DIRECTOR REVIEW REQUIRED]
A. HYPERVOLEMIC AND EUVOLEMIC HYPONATREMIA

1. Continuing/ongoing treatment to prevent clinically significant hypervolemic or euvolemic hyponatremia due to conditions such as heart failure or SIADH
AND
2. Samsca (tolvaptan) was initiated or re-initiated in a hospital (for close monitoring of serum sodium)
AND
3. Chart notes and medical records supporting the rationale for therapy beyond 30 days, including documentation of improvement in member's condition as a result of therapy
AND
4. Prescriber acknowledges that Samsca should not be used for more than 30 days in order to minimize the risk of hepatic injury; however, Prescriber is determined to proceed with continuation of therapy. NOTE: At the discretion of the Molina Medical Director, a peer-to-peer consultation may be necessary

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Samsca (tolvaptan) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Hypersensitivity (e.g., anaphylactic shock, generalized rash) to tolvaptan or any component of the formulation. History, signs, or symptoms of significant liver impairment or injury (avoid use in members with underlying liver disease); Uncorrected abnormal blood sodium concentrations. Inability to sense or respond to thirst; Hypovolemic hyponatremia. Urgent need to raise serum sodium acutely; uncorrected urinary outflow obstruction; Anuria; Concomitant use of strong CYP3A inhibitors (e.g., clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin); Creatinine clearance less than 10 mL/min (not recommended because drug effects on serum sodium levels are likely lost at very low levels of renal function).
Because of the risk of hepatotoxicity, tolvaptan (Samsca) should not be used for autosomal dominant

polycystic kidney disease (ADPKD) outside of the FDA-approved REMS

OTHER SPECIAL CONSIDERATIONS:
Therapy Limitations:
Individuals requiring intervention to raise serum sodium urgently to prevent or to treat serious neurological symptoms should not be treated with tolvaptan.

Black box warnings indicated the need to initiate and re-initiate only in a hospital setting where serum sodium can be monitored to prevent too rapid in correction of hyponatremia (greater than 12 mEq/L/24 hours). Too rapid correction of hyponatremia can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death. Slower rates of sodium correction may be advisable in susceptible individuals, including those with severe malnutrition, alcoholism or advanced liver disease.

It has not been established that raising serum sodium with tolvaptan provides a symptomatic benefit to members.

BACKGROUND:
Samsca (tolvaptan) is an oral non-peptide V2 vasopressin receptor antagonist indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia (i.e., serum sodium < 125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including in members with heart failure, cirrhosis, and syndrome of inappropriate antidiuretic hormone (SIADH). Tolvaptan is initiated and re-initiated in a hospital and then continued on an outmember basis, and has been shown to induce short-term clinical improvements but has not demonstrated improvement in long-term outcomes such as mortality or hospitalizations.

APPENDIX:
Agents known to cause hyponatremia (not an all-inclusive list): amiodarone, antipsychotics, amitriptyline, bromocriptine, carbamazepine, ciprofloxacin, cisplatin, chlorpropamide, clofibrate, cyclophosmamide, desmopressin, haloperidol, ifosfamide, imatinib (high doses) interferon-alpha, interferon-gamm lorcainide, melphalan, methotrexate, monoamine oxidase inhibitors, nicotine, narcotics, NSAIDs, opiate, selective serotonin reuptake inhibitors (SSRIs), sodium valproate, thioridazine, thiothixene, tricyclic antidepressants, vasopressin, vinblastine, vincristine, vinorelbine

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, member records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES:
1. Samsca (tolvaptan) [prescribing information]. Rockville, MD: Otsuka America Pharmaceutical Inc; May 2019

2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020 Available at: http://www.clinicalpharmacology.com. [via subscription only]
3. American Hospital Formulary Service (AHFS). Drug Information 2020 [STAT!Ref Web site]. Available at: http://online.statref.com. [via subscription only]
4. FDA Drug Safety Communications: FDA limits duration and usage of Samsca (tolvaptan) due to possible liver injury leading to organ transplant or death. Safety announcement April 30, 2013 UCM350084.
5. Gheorghiade M, Gottlieb SS, Udelson JE, et al; Tolvaptan Investigators. Vasopressin v(2) receptor blockade with tolvaptan versus fluid restriction in the treatment of hyponatremia. Am J Cardiol 2006;97(7):1064-7.
6. Konstam MA, Gheorghiade M, Burnett JC Jr, et al; Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan (EVEREST) Investigators. Effects of oral tolvaptan in members hospitalized for worsening heart failure: the EVEREST outcome trial. JAMA. 2007;297(12):1319-1331.
7. Schrier RW, Gross P, Gheorghiade M, et al; SALT Investigators. Tolvaptan, a selective oral vasopressin V2-receptor antagonist, for hyponatremia. N Engl J Med 2006;355(20):2099 112.
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