



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

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Subject Tolvaptan (Samsca™)

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INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), 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 supercedes** 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. 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. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers tolvaptan (Samsca™) as medically necessary for the treatment of hypervolemic or euvolemic hyponatremia [serum sodium < 125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction]

NOTE: Per FDA dosing recommendations, therapy initiation should begin in a hospital setting to allow for close inpatient monitoring.

FDA Approved Indications

Samsca is a selective vasopressin V2-receptor antagonist 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, cirrhosis, and Syndrome of Inappropriate Antidiuretic Hormone (SIADH). Important limitations - 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 Samsca provides a symptomatic benefit to patients.

FDA Recommended Dosing

Samsca should be initiated and re-initiated in a hospital. The recommended starting dose is 15 mg once daily. Dosage may be increased at intervals ≥24 hr to 30 mg once daily, and to a maximum of 60 mg once daily as needed to raise serum sodium.

Black Box 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., >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.

Drug Availability

Samsca tablets are available in the following strengths and packages: 15 mg tablets are non-scored, blue, triangular, shallow-convex, debossed with "OTSUKA" and "15" on one side in blisters of 10. Samsca 30 mg tablets are non-scored, blue, round, shallow-convex, debossed with "OTSUKA" and "30" on one side in blisters of 10.

General Background

Pharmacology

Tolvaptan is an oral selective vasopressin receptor antagonist approved to treat euvolemic and hypervolemic hyponatremia. Hyponatremia is the most common electrolyte abnormality in both ambulatory and hospitalized patients. Other hyponatremia treatment options include fluid restriction, hypertonic saline, loop diuretics, lithium, urea, and demeclocycline. Tolvaptan is 29 times more selective for vasopressin V₂ over V_{1a} receptors promoting aquaresis and increased serum sodium. Approximately 40% of the dose is absorbed with peak concentrations occurring 2 to 4 hours after administration. Absorption is not affected by food. Metabolism occurs via CYP 3A. Tolvaptan is an inhibitor and substrate of P-glycoprotein. Elimination occurs primarily in feces.

Clinical Efficacy

No clinical trials compare tolvaptan to the other available vasopressin antagonist, conivaptan. In two placebo-controlled, randomized, double-blind trials, sodium concentrations increased more with tolvaptan than placebo (p<0.001). The percentage of patients with marked hyponatremia at day 30 compared to baseline was less with tolvaptan (baseline=48-52%; day 30=7-15%) than placebo (baseline: 48-50%; day 30: 32-35%). In heart failure patients, tolvaptan increased sodium concentrations (p<0.001), decreased body weight after one day of therapy (p<0.001), and improved edema (p=0.003) more than placebo, but did not reduce all-cause mortality.

Adverse Reactions

The most common adverse events reported with tolvaptan are thirst, dry mouth, and polyuria. In cirrhosis patients, gastrointestinal bleeding occurred more often with tolvaptan than placebo. Concomitant administration of tolvaptan and CYP3A inhibitors is contraindicated. Co-administration with CYP3A inducers may decrease tolvaptan concentrations and is not recommended. Tolvaptan administration with digoxin increased digoxin exposure.

Coding/Billing Information

Note: This section not in use.

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