



Otsuka

Otsuka America Pharmaceutical, Inc.

You are invited to participate in an educational program:

Understanding and Treating Hyponatremia

presented by

Harminder S Sandhu

Capital Area Renal Associates-Associate
Washington Hospital Center

Tuesday, August 10, 2010

6:30 PM

McCormick & Schmick's Seafood Restaurant

7401 Woodmont Avenue
Bethesda, MD 20814
(301) 961-2626

Carolyn Altieri
Otsuka Representative
Program Host

Please register by faxing your reply to Advanced Health Media at (866) 921-4497 before Tuesday, August 10, 2010.

Registration Form

YES, I will attend the program for Samsca™ (tolvaptan).

Name: _____ Specialty: _____

Address: _____

Phone: _____ Fax: _____ Email: _____

NO, I cannot attend the program.

Space is limited.

Please fax your reply to AHM before Tuesday, August 10, 2010 to confirm your reservation.

If you have any questions, please call AHM at 866-703-6292

Program code: USCEA02C05S-27

In accordance with the PhRMA Code on Interactions with Healthcare Professionals, attendance at this educational program is limited to Healthcare Professionals. Accordingly, attendance by guests or spouses is not permitted.

This is a promotional program and no CME credits are offered. This educational program may include the provision of a modest meal. Otsuka does not offer such a meal to healthcare professionals (HCPs) whose institutions prohibit such hospitality, nor does Otsuka offer such meal where federal or state laws limit an HCP's ability to accept such a meal. Accordingly, please consult your legal or ethics advisor regarding any applicable limitation before attending this educational program.

Please see INDICATION and IMPORTANT SAFETY INFORMATION on the back.

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INDICATION and IMPORTANT SAFETY INFORMATION for SAMSCA™ (tolvaptan)

INDICATION

SAMSCA is indicated for the treatment of clinically significant hypervolemic and euvoletic 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 raising serum sodium with SAMSCA provides a symptomatic benefit to patients.

IMPORTANT SAFETY INFORMATION

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.

SAMSCA is contraindicated in the following conditions:

- Urgent need to raise serum sodium acutely
 - Inability of the patient to sense or appropriately respond to thirst
 - Hypovolemic hyponatremia
 - Concomitant use of strong CYP 3A inhibitors
 - Anuric patients
- **Too Rapid Correction of Serum Sodium Can Cause Serious Neurologic Sequelae** – During initiation and after titration monitor patients to assess serum sodium concentrations and neurologic status. Subjects with SIADH or very low baseline serum sodium concentrations may be at greater risk for too-rapid correction of serum sodium. In patients receiving SAMSCA who develop too rapid a rise in serum sodium, discontinue or interrupt treatment with SAMSCA and consider administration of hypotonic fluid. Fluid restriction during the first 24 hours with SAMSCA may increase the likelihood of overly-rapid correction of serum sodium, and should generally be avoided
 - **Gastrointestinal Bleeding in Patients with Cirrhosis** – Use only when need to treat outweighs this risk
 - **Dehydration and Hypovolemia** – In patients who develop medically significant signs or symptoms of hypovolemia, discontinuation is recommended. Dehydration and hypovolemia can occur, especially in potentially volume-depleted patients receiving diuretics or those who are fluid restricted
 - **Co-administration with Hypertonic Saline** – Not recommended
 - **Other Drugs Affecting Exposure to SAMSCA**
 - **CYP 3A Inhibitors** – Do not use with strong inhibitors of CYP 3A; avoid concomitant use with moderate CYP 3A inhibitors
 - **CYP 3A Inducers** – Avoid concomitant use with CYP 3A inducers. If co-administered, the dose of SAMSCA may need to be increased
 - **P-gp Inhibitors** – The dose of SAMSCA may have to be reduced if co-administered with P-gp inhibitors
 - **Hyperkalemia or Drugs that Increase Serum Potassium** – Monitor serum potassium levels in patients with a serum potassium > 5 mEq/L and in patients receiving drugs known to increase serum potassium levels

Pregnancy and Nursing Mothers – SAMSCA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in nursing infants from SAMSCA, a decision should be made to discontinue nursing or SAMSCA, taking into consideration the importance of SAMSCA to the mother.

Commonly observed adverse reactions – (SAMSCA incidence ≥ 5% more than placebo, respectively): thirst (16% vs 5%), dry mouth (13% vs 4%), asthenia (9% vs 4%), constipation (7% vs 2%), pollakiuria or polyuria (11% vs 3%) and hyperglycemia (6% vs 1%).

Please see accompanying FULL PRESCRIBING INFORMATION, including **Boxed WARNING**.