



News Release

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For Immediate Release

ASTELLAS LAUNCHES VAPRISOL® FOR THE TREATMENT OF EUVOLEMIC HYPONATREMIA IN HOSPITALIZED PATIENTS

First arginine vasopressin (AVP) antagonist approved for the management of potentially life-threatening sodium and water imbalance

DEERFIELD, Illinois, April 26— Astellas Pharma US, Inc. today announced the launch and commercial availability of Vaprisol® (conivaptan hydrochloride injection), an arginine vasopressin (AVP) receptor antagonist for the intravenous treatment of euvolemic hyponatremia in hospitalized patients. VAPRISOL, discovered and developed by Astellas, is the first drug specifically indicated for the treatment of euvolemic hyponatremia, a potentially life-threatening condition that occurs when the body's blood sodium level falls below normal.

“As the first AVP receptor antagonist approved for the management of a potentially life threatening sodium and water imbalance, Vaprisol will offer clinicians a new, safe and effective choice for the treatment of their euvolemic hyponatremia patients,” stated Yoshihiko Hatanaka, Chief Executive Officer at Astellas Pharma US, Inc.. “With the launch of Vaprisol, Astellas continues to solidify its presence in the critical care market through the provision of innovative products.”

Hyponatremia is estimated to affect up to 4 percent of hospitalized patients in the United States each year.¹ While many patients with hyponatremia have no symptoms, severe cases are medical emergencies that can result in swelling of the brain, respiratory arrest and death. Euvolemic hyponatremia, which occurs when total body water increases with little increase in sodium, is most often associated with conditions such as the syndrome of inappropriate antidiuretic hormone (SIADH), adrenal insufficiency, pulmonary disorders, hypothyroidism, certain cancers and the use of certain drugs (such as some antidepressants).²

In a randomized, double-blind, placebo-controlled study, intravenous administration of a 20mg loading dose over 30 minutes followed by a continuous infusion of VAPRISOL 40 mg/day for four days improved the balance of sodium and water in hospitalized patients with mild to moderate euvolemic hyponatremia. Significant improvements in serum sodium levels were observed within the first day of treatment with VAPRISOL. The most common adverse events associated with VAPRISOL were infusion site reactions, most of which were mild and did not lead to discontinuation of the drug.

About Hyponatremia

Hyponatremia often results from elevated levels of the hormone arginine vasopressin (AVP), which regulates water and salt balance in the body. It is the most common electrolyte disorder in hospitalized patients and one of the most difficult to treat. Syndrome of inappropriate antidiuretic hormone (SIADH), hypothyroidism, adrenal insufficiency and pulmonary disorders are common causes of euvolemic hyponatremia.

About VAPRISOL

Discovered and developed by Astellas Pharma Inc. headquartered in Tokyo, Japan, VAPRISOL is a novel drug that blocks the activity of AVP, resulting in increased urine output without loss of valuable electrolytes such as sodium and potassium. This effect, known as “aquaresis,” helps to correct serum sodium levels in patients with euvolemic hyponatremia. VAPRISOL is the first AVP antagonist that safely and effectively promotes aquaresis for improved management of salt and water imbalance in hospitalized patients with euvolemic hyponatremia.

VAPRISOL is administered as a 20mg IV a loading dose followed by 20 mg administered as a continuous infusion over 24 hours. Following the initial day of treatment, VAPRISOL is to be administered for an

additional 1 to 3 days as a continuous infusion of 20 mg/day. If serum sodium does not rise at the desired rate, VAPRISOL may be titrated upward to a daily dose of 40 mg, again administered in a continuous infusion.

VAPRISOL is indicated for the treatment of euvoletic hyponatremia (e.g., the syndrome of inappropriate secretion of antidiuretic hormone, or in the setting of hypothyroidism, adrenal insufficiency, pulmonary disorders, etc.) in hospitalized patients. VAPRISOL is not indicated for the treatment of patients with congestive heart failure. VAPRISOL is contraindicated in patients who have hypovolemic hyponatremia and in those who have hypersensitivity to any of its components. The co-administration of VAPRISOL with potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, clarithromycin, ritonavir, and indinavir, is also contraindicated. The safety of VAPRISOL in hyponatremic patients with underlying congestive heart failure has not been established. Serum sodium and neurological status should be monitored appropriately because vaprisol potentially can cause overly rapid correction of serum sodium, leading to serious sequelae. The use of VAPRISOL in patients with hepatic impairment (including ascites, cirrhosis or portal hypertension) or renal impairment has not been systematically evaluated. The most common adverse reactions reported with VAPRISOL administration were infusion site reactions (52.5%). The majority of these reactions were mild and did not lead to discontinuation of the drug. Other common adverse reactions included headache (12%), thirst (9.8%), hypokalemia (9.8%), vomiting (6.6%), and pollakiuria (6.0%).

About Astellas

Astellas Pharma US, Inc., a US subsidiary of Tokyo-based Astellas Pharma Inc., is a research-based pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. Established on April 1, 2005, Astellas Pharma Inc. was formed through a merger that combined the outstanding research, development and marketing capabilities of Fujisawa Pharmaceutical Co., Ltd. and Yamanouchi Pharmaceutical Co., Ltd. Astellas ranks among the top 20 pharmaceutical companies in the world and will continue to grow as a competitive company in the world pharmaceutical market. For more information on Astellas Pharma US, Inc., go to www.astellas.com/us.

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2. Goh KP. Management of hyponatremia. *Am Fam Physician.* 2004;69:2387–2394.