

Contact: Maribeth Landwehr
Astellas US LLC
(847) 317-8988

Katherine Williams
For Astellas
(312) 397-6613

For Immediate Release

FDA APPROVES ASTELLAS' VAPRISOL® (CONIVAPTAN HYDROCHLORIDE INJECTION) PREMIXED IN 5% DEXTROSE FOR THE TREATMENT OF HYPONATREMIA

Arginine vasopressin (AVP) receptor antagonist now approved in single-use premixed formulation

DEERFIELD, Illinois, October 22, 2008 — Astellas Pharma US, Inc. today announced that the U.S. Food and Drug Administration (FDA) has approved a new premixed formulation of Vaprisol: Vaprisol® (conivaptan hydrochloride injection) Premixed in 5% Dextrose. Discovered and developed by Astellas, Vaprisol, an arginine vasopressin (AVP) receptor antagonist, is the first and only approved drug indicated for the treatment of both euvolemic and hypervolemic hyponatremia in hospitalized patients. Hyponatremia is a potentially life-threatening condition that occurs when the body's blood sodium level falls significantly below normal. Vaprisol was originally approved by the FDA in an ampule formulation for the treatment of euvolemic hyponatremia in December 2005 and hypervolemic hyponatremia in February 2007. ¹

The 100mL, single-use premixed formulation of Vaprisol comes in an INTRAVIA® Container, a product of Baxter Healthcare Corporation, containing 20 mg of conivaptan hydrochloride in 5% Dextrose solution. Lactic acid, USP is added for pH adjustment to pH 3.4 to 3.8. The new formulation will make preparation easier for health care providers as it requires no measuring or mixing. Additionally, it has an expiration date of 24 months, six months longer than the original ampule formulation.

“Vaprisol Premixed in 5% Dextrose will be helpful in quickly preparing treatment for hyponatremia patients,” said Dr. Joseph Verbalis, M.D., Professor of Medicine and Physiology at Georgetown University. “This ready-to-use product will be useful for hospitals and emergency rooms.”

Hyponatremia is present in approximately 28 percent of patients upon admission into acute hospital care and another 14 percent acquire the condition while in acute care.² Severe cases are medical emergencies that can result in swelling of the brain, respiratory arrest, catastrophic brain damage and death.³

In the treatment of hyponatremia associated with congestive heart failure, Vaprisol is indicated only for those patients for whom the expected benefit of raising serum sodium outweighs the increased risk of adverse events. Vaprisol is contraindicated in patients with hypovolemic hyponatremia.¹

About Hyponatremia

Hyponatremia, a condition of low serum sodium concentration, 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 clinical medicine and one of the most difficult to treat. Syndrome of inappropriate antidiuretic hormone (SIADH), advanced kidney failure, hypothyroidism and cancer are common causes of hyponatremia. Dilutional hyponatremia, which includes euvolemic and hypervolemic hyponatremia, is the most common form of the condition, and occurs when retained water dilutes serum sodium content. Patients with hyponatremia are classified as *hypervolemic* if swelling of body tissues (edema) is present or *euvolemic* if there is an increase in total body water content without edema.³

About Vaprisol

Discovered and developed by Astellas Pharma Inc. headquartered in Tokyo, Japan, Vaprisol is a 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 increase serum sodium levels in patients with hyponatremia. Vaprisol is the first AVP receptor antagonist with a demonstrated safety profile and that effectively promotes aquaresis in order to help restore salt and water balance in patients with euvolemic and hypervolemic hyponatremia.¹

Vaprisol is indicated for the treatment of euvolemic and hypervolemic hyponatremia in hospitalized patients. Vaprisol is not indicated for the treatment of congestive heart failure. It should only be used for the treatment of hyponatremia in patients with underlying heart failure when the expected benefit of raising

serum sodium outweighs the increased risk of adverse events. Vaprisol is contraindicated in patients with hypovolemic hyponatremia. In addition, coadministration of Vaprisol with potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, clarithromycin, ritanovir, and indinavir, is contraindicated. Solutions containing dextrose may be contraindicated in patients with known allergy to corn or corn products. Serum sodium, volume, and neurological status must be monitored frequently because Vaprisol potentially can cause overly rapid correction of 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. Use caution when administering Vaprisol to these patients. The most common adverse reactions reported were infusion site reactions (incidence of 73% and 63% for 20 mg/day and 40 mg/day respectively) which were also the most common type of adverse reaction leading to discontinuation of Vaprisol. Discontinuations from treatment due to infusion site reactions were more common among Vaprisol-treated patients (3%) than among placebo-treated patients (0%). Other common adverse reactions were headaches (8%, 10%), hypokalemia (22%, 10%), orthostatic hypotension (14%, 6%), and pyrexia (11%, 5%) for Vaprisol 20mg/day and 40mg/day, respectively.¹ For full prescribing information, please visit www.Vaprisol.com.

About Astellas

Astellas Pharma US, Inc., located in Deerfield, Illinois, is a US affiliate of Tokyo-based Astellas Pharma Inc., Astellas is a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. The organization is committed to becoming a global pharmaceutical company by combining outstanding R&D and marketing capabilities and continuing to grow in the world pharmaceutical market. For more information about Astellas Pharma US, Inc., please visit our website at www.astellas.com/us.

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1. Vaprisol [package insert]. Deerfield, IL: Astellas Pharma US, Inc.; 2008.

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2. Upadhyay A, Jaber BL, Madias NE. Incidence and Prevalence of Hyponatremia. *Am J Med.* 2006; 119 (7A): S31-S35.
3. Ghali JK. Mechanisms, Risks and New Treatment Options for Hyponatremia. *Cardiology.* 2008;111:147-157.