

FOR IMMEDIATE RELEASE



**SHIONOGI ANNOUNCES COMMERCIAL AVAILABILITY OF CUVPOSA™  
(glycopyrrolate) ORAL SOLUTION FOR PEDIATRIC CHRONIC SEVERE DROOLING  
ASSOCIATED WITH NEUROLOGIC CONDITIONS**

**FLORHAM PARK, NJ (April 7, 2011)** – Shionogi Inc., the U.S.-based group company of Shionogi & Co., Ltd., today announced the U.S. commercial availability of CUVPOSA™ (glycopyrrolate) oral solution, the first and only FDA-approved treatment to reduce chronic severe drooling in patients aged 3 to 16 with neurologic conditions associated with problem drooling, such as cerebral palsy.

“Shionogi is proud to expand its mission of helping to bring high quality care to pediatric patients by introducing CUVPOSA™ to the U.S. market,” said Donald C. Manning, MD, PhD, Chief Medical Officer of Shionogi Inc. “Unlike tablet formulations, liquid CUVPOSA™ does not require compounding by a pharmacist before it is administered by caregivers, providing families with a new approach to treating chronic severe drooling in children and adolescents with neurologic conditions.”

Shionogi Inc. is partnering with Diplomat Specialty Pharmacy to grant caregivers convenient access to the newly-available treatment via a patient’s physician. Once the physician places the order by calling 877.830.3797, Diplomat will verify the information, fill the prescription and ship to the patient. CUVPOSA™ is readily available as a clear, cherry flavored oral solution.

“Chronic severe drooling is an often overlooked condition affecting 10 to 30 percent of pediatric patients suffering from neurologic disorders,” explained Dr. Robert Zeller, Director, Blue Bird Circle Clinic for Pediatric Neurology at Texas Children’s Hospital and Professor, Baylor College of Medicine. “For these children and adolescents who exhibit excessive drooling, the availability of CUVPOSA™ offers an important advancement in therapy.”

CUVPOSA™ has been classified by the FDA as an “Orphan Drug” that was developed to treat a rare disease or condition (chronic severe drooling). Clinical studies of orphan drugs do not typically contain high numbers of study subjects. The FDA approval of CUVPOSA™ in July 2010 was based on the results of a 8-week randomized, double-blind, placebo-controlled Phase III study of 38 subjects which showed that 75% of children and adolescents treated with CUVPOSA™ experienced an improvement in symptoms, versus 11% who received placebo. CUVPOSA™ was also evaluated in a long-term, open-label, 24-week safety study in 137 patient subjects. Dry mouth, vomiting, constipation, flushing and nasal congestion were the most commonly reported adverse reactions.

**About CUVPOSA™**

CUVPOSA™ is an anticholinergic indicated to reduce chronic severe drooling in patients ages 3-16 with neurologic conditions associated with problem drooling (e.g., CP). CUVPOSA™ indirectly reduces the rate of salivation by preventing stimulation of acetylcholine receptors that are located on certain peripheral tissues such as salivary glands. CUVPOSA™ is dosed on a titration schedule based on weight, therapeutic response and adverse reactions. It must be administered to patients by caregivers using an accurate measuring device. Please see the full prescribing information at [www.CUVPOSA.com](http://www.CUVPOSA.com) for administration and dosing instructions.

### **Important Safety Information**

CUVPOSA™ is contraindicated in conditions that preclude anticholinergic therapy (e.g., glaucoma, paralytic ileus, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis). CUVPOSA™ is contraindicated in patients taking solid oral dosage forms of potassium chloride. The passage of potassium chloride tablets through the GI tract may be arrested or delayed with coadministration of CUVPOSA™.

Constipation or intestinal pseudo-obstruction may occur when taking CUVPOSA™. Constipation is a common dose-limiting adverse reaction and may lead to discontinuation of CUVPOSA™. CUVPOSA™ may present abdominal distention, pain, nausea, or vomiting. It is important for physicians to assess patients for constipation, particularly within four to five days of initial dosing or after a dose increase. Diarrhea associated with CUVPOSA™ may be an early symptom of incomplete mechanical intestinal obstruction especially in patients with ileostomy or colostomy. If obstruction is suspected, discontinue CUVPOSA™.

Avoid patient exposure to high ambient temperatures. Heat prostration (fever and heat stroke due to decreased sweating) can occur with use of anticholinergic drugs such as CUVPOSA™.

Patients should not engage in age-appropriate activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work, as CUVPOSA™ may cause drowsiness or blurred vision.

Use CUVPOSA™ with caution in patients with conditions that are exacerbated by anticholinergic drug effects including:

- Autonomic neuropathy, renal disease and ulcerative colitis. (Large doses may suppress intestinal motility to the point of producing a paralytic ileus and for this reason, may precipitate or aggravate “toxic megacolon,” a serious complication of the disease.)
- Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac tachyarrhythmias, tachycardia, hypertension, and hiatal hernia associated with reflux esophagitis.

Glycopyrrolate reduces GI transit time which may result in altered release of certain drugs when formulated in delayed or controlled-release forms. CUVPOSA™ can increase serum levels of atenolol, metformin and digoxin (slow dissolution tablets; consider other dosage forms of digoxin). Dose reductions of atenolol or metformin may be needed.

CUVPOSA™ may decrease serum levels of haloperidol or levodopa. Consider dose increase of levodopa and monitor haloperidol patients for worsening of schizophrenic symptoms and development of dyskinesia.

The anticholinergic effects of CUVPOSA™ may be increased with concomitant administration of amantadine. CUVPOSA™ dose reduction should be considered.

Use with caution in patients with renal impairment.

The most common adverse reactions (incidence  $\geq 30\%$ ) are dry mouth (40%), vomiting (40%) constipation (35%), flushing (30%), and nasal congestion (30%).

For full prescribing information, please visit [www.CUVPOSA.com](http://www.CUVPOSA.com).

To report SUSPECTED ADVERSE REACTIONS, contact Shionogi Pharma, Inc. at 1-800-849-9707 ext. 1454 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### **About Shionogi & Co., Ltd.**

Headquartered in Osaka, Japan, Shionogi & Co., Ltd. is a major research-driven pharmaceutical company dedicated to placing the highest value on patients. Shionogi's Research and Development currently targets three therapeutic areas: Infectious Diseases, Pain, and Metabolic Syndrome. The Company has provided such innovative medicines as Crestor and Doripenem, which have been successfully delivered to millions of patients. In addition, Shionogi is engaged in new research areas such as allergy and cancer. Contributing to the health of patients around the world through development in these therapeutic areas is Shionogi's primary goal. For more details, please visit [www.shionogi.co.jp](http://www.shionogi.co.jp). For more information on Shionogi Inc., headquartered in Florham Park, NJ, please visit [www.shionogi-inc.com](http://www.shionogi-inc.com).

### **Forward Looking Statements**

*This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.*

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