Once-Daily Welchol® (colesevelam HCl) for Oral Suspension Receives FDA Approval To be Mixed with Fruit Juice or Diet Soft Drinks

Adult patients taking Welchol to lower their blood sugar and/or high LDL cholesterol now have more flexible dosing options

July 25, 2011; Parsippany, NJ – Daiichi Sankyo, Inc., announced that the U.S. Food and Drug Administration (FDA) has approved the supplemental new drug application (sNDA) for Welchol® (colesevelam HCl) for Oral Suspension to be mixed with fruit juice or diet soft drinks, offering a new option for adult patients with primary hyperlipidemia and type 2 diabetes. Welchol for Oral Suspension was first approved in 2009 to be mixed with water.

Welchol is currently the only product approved by the FDA, in addition to diet and exercise, to improve both glycemic control and LDL cholesterol (LDL-C or "bad" cholesterol) in adults with type 2 diabetes and high LDL cholesterol. Originally approved in 2000 for LDL-C lowering and in 2008 for A1C reduction in adults, a once-daily formulation of Welchol, Welchol for Oral Suspension, was approved by the FDA for both these indications in 2009. In addition, Welchol has a pediatric indication, specifically approved to reduce LDL-C levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia. Please see Important Information about Welchol below.

"Since the approval of once-daily Welchol for Oral Suspension, we've seen that patients appreciate the flexible dosing options provided by Welchol, taken as tablets with a meal and liquid, or as a drinkable formulation with a meal, to help them reach their LDL-C and A1C goals," said Oliseyenum M. Nwose, MBBS, MRCPath, Executive Medical Director, Medical Research and Strategy Therapeutic Areas Head, Hypertension and Metabolism at Daiichi Sankyo, Inc. "We are pleased that patients, depending on their preference, can now choose to mix their Welchol for Oral Suspension with fruit juice, diet soft drinks or water. Welchol for Oral Suspension is once-daily, sugar-free*, citrus-flavored and non-systemically absorbed, which means it is not metabolized in the liver or kidneys."

The number of Americans affected by diabetes has swelled past the 25 million mark (90 to 95 percent of all individuals with diabetes are type 2)[1], and according to the American Diabetes Association (ADA), every 21 seconds another person is diagnosed.[2] The ADA and the American College of Cardiology emphasize that it is critical to reduce both A1C and LDL-C levels, as more than 50 percent of adults with type 2 diabetes also have elevated LDL-C.[3,4,5] The ADA recommends that in general, adult patients with type 2 diabetes target an A1C level of less than 7 percent, and an LDL-C goal of less than 100 mg/dL.[6]

* **Phenylketonurics:** Welchol for Oral Suspension contains 48 mg phenylalanine per 3.75 gram dose.

IMPORTANT INFORMATION ABOUT WELCHOL

Indications
Welchol is indicated as an adjunct to diet and exercise to:
- reduce elevated low-density lipoprotein cholesterol (LDL-C) in patients with primary hyperlipidemia (Fredrickson Type IIa) as monotherapy or in combination with an hydroxymethylglutaryl-coenzyme (HMG CoA) reductase inhibitor (statin)
- reduce LDL-C levels in boys and postmenarchal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia, as monotherapy or in combination with a statin after failing an adequate trial of diet therapy
- improve glycemic control in adults with type 2 diabetes mellitus

Important Limitations of Use
- Welchol (colesevelam HCl) should not be used for the treatment of type 1 diabetes or for the treatment of diabetic ketoacidosis
- Welchol has not been studied in type 2 diabetes as monotherapy or in combination with a dipeptidyl peptidase 4 inhibitor and has not been extensively studied in combination with thiazolidinediones
- Welchol has not been studied in Fredrickson Type I, III, IV, and V dyslipidemias
- Welchol has not been studied in children younger than 10 years of age or in premenarchal girls

Contraindications
Welchol is contraindicated in individuals with a history of bowel obstruction, those with serum triglyceride (TG) concentrations of >500 mg/dL, or with a history of hypertriglyceridemia-induced pancreatitis.

Warnings and Precautions
The effect of Welchol on cardiovascular morbidity and mortality has not been determined.

Welchol can increase serum TG concentrations particularly when used in combination with sulfonylureas or insulin. Caution should be exercised when treating patients with TG levels >300 mg/dL.

Welchol may decrease the absorption of fat-soluble vitamins A, D, E, and K. Patients on vitamin supplements should take their vitamins at least 4 hours prior to Welchol. Caution should be exercised when treating patients with a susceptibility to vitamin K or fat-soluble vitamin deficiencies.

Caution should also be exercised when treating patients with gastroparesis, gastrointestinal motility disorders, a history of major gastrointestinal tract surgery, and when treating patients with dysphagia and swallowing disorders.

Welchol reduces gastrointestinal absorption of some drugs. Drugs with a known interaction with colesevelam (cyclosporine, glyburide, levothyroxine, and oral contraceptives [ethinyl estradiol, norethindrone]), should be administered at least 4 hours prior to Welchol. Drugs that have not been tested for interaction with colesevelam, especially those with a narrow therapeutic index, should also be administered at least 4 hours prior to Welchol. Alternatively, the physician should monitor drug levels of the co-administered drug.

To avoid esophageal distress, Welchol for Oral Suspension should not be taken in its dry form.

Due to tablet size, Welchol for Oral Suspension is recommended for, but not limited to, use in the pediatric population as well as in any patient who has difficulty swallowing tablets.

Phenylketonurics: Welchol for Oral Suspension contains 48 mg phenylalanine per 3.75 gram dose.

Adverse Reactions
In clinical trials, the adverse reactions observed in ≥2% of patients, and more commonly with Welchol than placebo, regardless of investigator assessment of causality seen in:

- Adults with Primary Hyperlipidemia were: constipation (11.0% vs 7.0%), dyspepsia (8.3% vs 3.5%), nausea (4.2% vs 3.9%), accidental injury (3.7% vs 2.7%), asthenia (3.6% vs 1.9%), pharyngitis (3.2% vs 1.9%), flu syndrome (3.2% vs 3.1%), rhinitis (3.2% vs 3.1%), and myalgia (2.1% vs 0.4%)
- Pediatric patients with heFH primary hyperlipidemia were: nasopharyngitis (6.2% vs 4.6%), headache (3.9 vs 3.1%), fatigue (3.9% vs 1.5%), creatine phosphokinase increase (2.3% vs 0.0%), rhinitis (2.3% vs 0.0%), and vomiting (2.3% vs 1.5%)
- Adult patients with Type 2 Diabetes were: constipation (8.7% vs 2.0%), nasopharyngitis (4.1% vs 3.6%), dyspepsia (3.9% vs 1.4%), hypoglycemia (3.0% vs 2.3%), nausea (3.0% vs 1.4%), and hypertension (2.8% vs 1.6%)

Post-marketing experience: Due to the voluntary nature of these reports it is not possible to reliably estimate frequency or establish a causal relationship:

- Increased seizure activity or decreased phenytoin levels have been reported in patients receiving phenytoin concomitantly with Welchol (colesevelam HCl)
- Reduced International Normalized Ratio (INR) has been reported in patients receiving warfarin concomitantly with Welchol
- Elevated thyroid-stimulating hormone (TSH) has been reported in patients receiving thyroid hormone replacement therapy

Pregnancy
Welchol is Pregnancy Category B.

Please visit http://www.welchol.com/pdf/Welchol_PI.pdf for full Product Information on Welchol.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

For more information on Welchol, call 877-4-DSPROD (877-437-7763), or go to the Welchol website at www.Welchol.com.

For patients having difficulty affording their Welchol medication, please call the Daiichi Sankyo, Inc., Open Care Patient Assistance Program at 1-866-268-7327 for more information or visit www.dsi.com.

About Welchol (colesevelam HCl)

Welchol, along with diet and exercise, lowers LDL or "bad" cholesterol. It can be taken alone or with other cholesterol-lowering medications known as statins. Welchol, along with diet and

exercise, also lowers blood sugar levels in adult patients with type 2 diabetes mellitus when added to other anti-diabetic medications (metformin, sulfonylureas, or insulin). Welchol was approved by the FDA to lower bad cholesterol in 2000 and to lower blood sugar levels in 2008. Welchol is available in two formulations, Welchol tablets and Welchol for Oral Suspension, which can be mixed with water, diet soft drinks or fruit juice.

Welchol should not be used to treat type 1 diabetes or diabetic ketoacidosis, and it has not been studied with all anti-diabetic medications. Welchol is not approved for use in children with type 2 diabetes mellitus. Welchol is not for everyone, especially those with a history of intestinal blockage, those with blood triglyceride levels of greater than 500 mg/dL, or a history of pancreatitis (inflammation of the pancreas) due to high triglyceride levels.

In clinical studies of adult patients with type 2 diabetes, Welchol lowered A1C, fasting blood sugar and LDL-C, important risk factors for heart disease. In clinical studies of patients with elevated LDL-C, Welchol lowered LDL-C when used alone or when added to other cholesterol-lowering medications known as statins. Welchol has not been shown to prevent heart disease or heart attacks.

About Daiichi Sankyo

In keeping with its vision of becoming a “Global Pharma Innovator,” the Daiichi Sankyo Group is dedicated to the creation and supply of innovative pharmaceutical products to address the diversified, unmet medical needs of customers in both developed and emerging markets. While maintaining its portfolio of marketed pharmaceuticals for hypertension, hyperlipidemia, and bacterial infections, the Group is engaged in the development of treatments for thrombotic disorders and focused on the discovery of novel oncology and cardiovascular-metabolic therapies. Furthermore, the Daiichi Sankyo Group has created a “Hybrid Business Model,” which will respond to market and customer diversity and optimize growth opportunities across the value chain. For more information, please visit www.daiichisankyo.com.

Daiichi Sankyo, Inc., headquartered in Parsippany, New Jersey, is the U.S. subsidiary of Daiichi Sankyo Company, Ltd. For more information on Daiichi Sankyo, Inc., please visit www.dsi.com

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