



ADA Scientific Sessions Poster # 484
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NEW STUDY DEMONSTRATES COLESEVELAM HCl LOWERS BOTH A1C AND LDL CHOLESTEROL IN PATIENTS WITH UNCONTROLLED TYPE 2 DIABETES MELLITUS ON METFORMIN-BASED REGIMEN

Parsippany, NJ (June 23, 2007) – Data to be presented at the American Diabetes Association’s (ADA) 67th Annual Scientific Sessions in Chicago demonstrate that colesevelam HCl can lower both A1C and LDL cholesterol levels in patients with type 2 diabetes mellitus who were uncontrolled on a metformin-based regimen. The new colesevelam HCl clinical data findings from the pivotal studies are consistent with the pilot study findings. The data was included in Daiichi Sankyo’s supplemental New Drug Application filed with the U.S. Food and Drug Administration (FDA) in December 2006. If approved, colesevelam HCl will be the first LDL cholesterol lowering medication also indicated for improving glycemic control in patients with type 2 diabetes mellitus (DM).

The 26-week study of colesevelam HCl included patients with type 2 DM who had previously failed to reach glycemic control (ADA target of A1C<7%) with metformin, a common oral medication for type 2 diabetes mellitus. Patients in the study were randomly assigned to two groups. The addition of colesevelam HCl tablets was compared to the addition of placebo in patients on a metformin-based regimen.

Two separate presentations of the study will be made at the ADA poster session on Sunday, June 24th. Dr. Harold Bays, MD, study investigator and Medical Director of the Louisville Metabolic and Atherosclerosis Research Center in Kentucky, will describe colesevelam HCl’s effect on A1C and glycemic control in a poster presentation titled “Effect of Colesevelam HCl on Glycemic Control in Type 2 Diabetic Subjects Receiving Metformin Monotherapy.” The study demonstrated that the colesevelam HCl treatment group with metformin monotherapy cohort achieved significantly greater reductions in A1C levels compared to the placebo group (mean=0.47%, p<0.0024). Further, the colesevelam HCl total treatment group (metformin monotherapy and combination therapy) achieved significantly greater reductions in A1C levels compared to placebo (mean=0.54%, p<0.001). Fructosamine, another indicator of glycemic control, was also significantly reduced in the patients receiving colesevelam HCl (mean=17.8 µmol/L, p<0.05).

“Diabetes mellitus and hypercholesterolemia often coexist in patients,” said Dr. Bays. “This study provides evidence that colesevelam HCl is not only safe and effective in improving cholesterol levels in patients with type 2 diabetes mellitus, but may also lower glucose levels as well.”

The second presentation demonstrates colesevelam HCl’s effect on LDL cholesterol and other lipid parameters. The poster presentation titled “Colesevelam HCl Improves the Lipid Profile in Type 2 Diabetic Subjects with Inadequate Glycemic Control on Metformin,” notes that the colesevelam HCl treatment group achieved significantly lower LDL cholesterol levels compared to the placebo group (mean=15.9%, $p<0.001$). The colesevelam HCl group also achieved significant reductions in apolipoprotein B levels and C-reactive protein, two known cardiovascular risk factors. Significant weight gain, a common side effect of some oral anti-diabetic agents, was not observed in the colesevelam HCl group. In this study, colesevelam HCl had no significant effect on triglycerides compared to placebo (median percent change=11.8% vs. 6.6%, $p=0.221$).

“Given the prevalence of diabetes and high LDL cholesterol, a medication that can help lower both A1C and LDL cholesterol can be beneficial for many patients,” said Ronald B. Goldberg, MD, a lead investigator in the study and Professor of Medicine at the Division of Diabetes and Metabolism and Associate Director of the Diabetes Research Institute at the University of Miami, Miller School of Medicine in Florida. “A new therapeutic option that would address these two chronic health conditions would provide physicians with a different therapeutic approach for treating patients with type 2 diabetes.”

The ADA estimates that there are 20.8 million people in the United States with diabetes; 90-95% of this population are diagnosed as type 2.¹ The ADA recommends that patients with type 2 diabetes achieve an A1C level of $<7\%$.¹ A1C is a common test for persistent hyperglycemia (“too much glucose in the blood”).

People with diabetes face significantly higher risk of heart attacks and developing other forms of cardiovascular disease.² Accordingly, the National Cholesterol Education Program (NCEP) recommends that patients with type 2 diabetes adhere to a more stringent LDL cholesterol (“bad cholesterol”) goal of <100 mg/dL.³

It is estimated that approximately half of all Americans have elevated blood cholesterol levels that can negatively impact their health and quality of life.⁴ According to a recent Harris Interactive Survey, approximately 29% of adults previously diagnosed with hypercholesterolemia have also been diagnosed with diabetes.⁵

About the Study

The study was designed as a 26-week, prospective, randomized, double-blind, placebo-controlled, parallel-group, multi-center study. Three hundred and sixteen patients were randomized, with 222 patients completing the study. The sample consisted of subjects aged 18 to 75 years of age with type 2 diabetes (per ADA criteria) and A1C levels between 7.5%-9.5% (inclusive). Subjects were maintained on a stable dose of metformin. Following a 2-week placebo run-in period, subjects were randomized to receive either colesevelam HCl (3.75 g/day in 6 tablets/day) or matching placebo (6 tablets/day) for 26 weeks. The primary objective of the study was to evaluate the effect of

colesevelam HCl on glycemic control in subjects with type 2 diabetes, measured by change in A1C from baseline to week 26 for the intent-to-treat population with last observation carried forward. Primary and secondary endpoints were presented in two separate posters at the ADA Scientific Sessions:

Poster #484 – “Colesevelam HCl Improves the Lipid Profile in Type 2 Diabetic Subjects with Inadequate Glycemic Control on Metformin”: Examines colesevelam HCl’s effect on lipid parameters, including LDL cholesterol, total cholesterol, non-HDL cholesterol, apolipoprotein B, apolipoprotein A-1 and triglycerides in patients that have uncontrolled type 2 diabetes and are taking metformin.

Poster #485 – “Effect of Colesevelam HCl on Glycemic Control in Type 2 Diabetic Subjects Receiving Metformin Monotherapy”: Examines colesevelam HCl’s effect on glycemic control parameters including A1C, fasting plasma glucose and fructosamine in patients that have uncontrolled type 2 diabetes and are taking metformin.

About WelChol®

WelChol (colesevelam HCl) is indicated for LDL-C lowering and was approved by the U.S. Food and Drug Administration (FDA) for marketing in May 2000. WelChol is the top-selling branded drug in the bile acid sequestrants (BAS) class. WelChol is different from most other cholesterol-lowering drugs on the market because it is non-systemic, meaning that the body does not absorb it and it is eliminated without traveling to the liver or kidneys. Therefore, WelChol is not expected to have drug-drug interactions via the cytochrome P-450 pathway. Systemic medications, which include statins, fibrates, and cholesterol absorption inhibitors, are those that are absorbed from the intestine into the bloodstream and travel throughout the body, specifically to the liver and/or kidneys.

WelChol is a prescription drug indicated alone or in combination with a statin, as an adjunct to diet and exercise for the reduction of elevated LDL cholesterol in patients with primary hypercholesterolemia (Fredrickson Type IIa) when the response to diet and exercise has been inadequate. Liver-function monitoring is not required with WelChol when used as monotherapy, and in combination with a statin, no additional liver-function monitoring is required beyond that for the prescribed statin alone.

In clinical trials with patients with primary hypercholesterolemia, when WelChol was given alone in addition to a low-fat diet and exercise, it was shown to reduce LDL cholesterol by an average of 15% to 18%.

When WelChol is given in combination with a statin, the combination can lower cholesterol levels more effectively than using either therapy alone. In pivotal studies where WelChol was taken with a statin, WelChol 3.8g provided up to an additional mean 16% (32 mg/dL) reduction in LDL cholesterol. WelChol is the only non-systemic cholesterol-lowering agent approved by the FDA for combination with a statin. WelChol can be used in combination with any dose of any statin.

WelChol is engineered for affinity and high capacity bile acid binding. It has been studied with four commonly prescribed statins – Lipitor® (atorvastatin calcium), Zocor® (simvastatin), Pravachol®

(pravastatin sodium) and Mevacor® (lovastatin). Additionally, WelChol has been studied with fenofibrate and had no significant effect on the bioavailability of fenofibrate. Like most prescription drugs, WelChol has not been studied in combination with all medications or supplements. Patients should always tell their doctor about all medications and supplements they are taking before starting any new therapy, including WelChol.

WelChol is not for everyone, especially those with bowel blockage. Caution should be exercised when treating patients who have trouble swallowing or severe stomach or intestinal problems. Side effects may include constipation, indigestion and gas. WelChol, either alone or in combination with a statin or fenofibrate, has not been shown to prevent heart disease or heart attacks.

WelChol is only indicated for the reduction of LDL-C either alone or in combination with a statin in patients with primary hypercholesterolemia. Additionally, WelChol has demonstrated beneficial effects on other lipid parameters such as HDL-C and APO-B. WelChol has also been studied in combination with fenofibrate in patients with mixed dyslipidemia (Fredrickson Type II B), and provided additional LDL-C reductions in these patients when added to a stable fenofibrate regimen. WelChol is not indicated for use in the treatment of mixed dyslipidemia or lipid parameters other than LDL-C.

For more information on WelChol, call 877-4-DSPROD (877-431-7763), or go to the WelChol web site at www.WelChol.com.

About Daiichi Sankyo, Inc.

Daiichi Sankyo, Inc., headquartered in Parsippany, New Jersey, is the U.S. subsidiary of Daiichi Sankyo Co., Ltd., Japan's second largest pharmaceutical company and a global leader in pharmaceutical innovation since 1899. The company is dedicated to the discovery, development and commercialization of innovative medicines that improve the lives of patients throughout the world.

The primary focus of Daiichi Sankyo's research and development is cardiovascular disease, including therapies for dyslipidemia, hypertension, diabetes, and acute coronary syndrome. The company is also pursuing the discovery of new medicines in the areas of glucose metabolic disorders, infectious diseases, cancer, bone and joint diseases, and immune disorders.

For more information, please visit www.dsus.com.

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¹ American Diabetes Association. Standards of medical care in diabetes -- 2006. *Diabetes Care*. 2006;29(Suppl 1):S4--S42

² Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics--2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. Feb 6, 2007;115(5):e69-171

³ Grundy S, Cleeman J, Merz C, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *Circulation*. 2004;110:227-239

⁴ Rosamond W, Flegal K, Friday G, et al. Heart disease and stroke statistics--2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. Feb 6, 2007;115(5):e69-171

⁵ Harris Interactive. *Cholesterol Survey*. New York, NY. February 2007