Patients with diabetes achieve greater LDL cholesterol lowering and goal attainment on EZETROL

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EZETROL® Co-Administration with Statin Therapy Results in Greater LDL Cholesterol Lowering and Goal Attainment for Patients with Diabetes and Metabolic Syndrome, Studies Reveal

MUNICH, GERMANY, Monday, 6 September, 2004 – Results from two new clinical trials show that patients with diabetes and metabolic syndrome who are treated with ezetimibe (EZETROL®) co-administered with a statin experience greater reductions in LDL ("bad") cholesterol, compared to patients taking a statin alone. The new data also demonstrates that patients with diabetes and metabolic syndrome taking ezetimibe co-administered with a statin show greater LDL-C goal attainment compared to those patients taking a statin alone.

The findings of these studies confirm that, through Dual Inhibition of two sources of cholesterol, greater LDL efficacy can be achieved in patients with diabetes and metabolic syndrome when ezetimibe is co-administered with a statin compared with statin alone. Dual Inhibition is the co-administration of the cholesterol absorption inhibitor ezetimibe, which blocks absorption of cholesterol in the intestine, with a statin, which reduces production of cholesterol in the liver; thereby resulting in greater efficacy.
The studies are being presented here today at the 40th Annual Meeting of the European Association for the Study of Diabetes (EASD).

Greater goal attainment and reduction in LDL cholesterol levels for patients with diabetes and metabolic syndrome

High LDL-C levels are a common problem in people with diabetes. There is a very high risk of cardiovascular disease (CVD) in these patients and more than 65% of deaths in patients with diabetes are attributed to heart and vascular disease1.

The McKenny et al study assessed as the primary endpoint how many patients could reach their LDL cholesterol goal. This study was a post-hoc subgroup analysis of data from a 23 week double blind,

randomized study involved patients with diabetes who met United States National Cholesterol Education program (NCEP ATP III) criteria for coronary heart disease (CHD) risk equivalent. Patients were randomized to one of four daily treatment groups: simvastatin 20 mg (n=113), ezetimibe and simvastatin 10/10mg (n=128), ezetimibe and simvastatin 10/20mg (n=60) or ezetimibe and simvastatin 10/40mg (n=41). Patients not at NCEP LDL cholesterol goal at 5 weeks had the simvastatin dose doubled, and the dose of simvastatin could be subsequently doubled again at weeks 12 and 18 up to a maximum of 80mg if still not at LDL cholesterol goal. The study2 evaluated whether ezetimibe with simvastatin would be more effective than simvastatin alone in helping diabetic patients achieve an LDL-C goal of <2.6 mmol/L. At just five weeks, significantly more patients taking ezetimibe coadministered with simvastatin patients achieved goal (83.7% for ezetimibe/simvastatin 10/10 mg/mg, 86.4% for ezetimibe/simvastatin 10/20 mg/mg and 92.7% for ezetimibe/simvastatin 10/40 mg/mg) than patients on simvastatin alone (53.6%) ($p<0.001$). This superiority was sustained throughout the trial to week 23, across all doses. Goal attainment at week 23 for ezetimibe/simvastatin 10/10 mg group was 82%, ezetimibe/simvastatin 10/20 mg/mg was 87%, and ezetimibe/simvastatin 10/40 mg/mg was 85%, compared to 69% for simvastatin 20 mg alone ($p<0.001$).

The McKenney et al study2 also found that ezetimibe co-administered with simvastatin produced greater percentage reductions of LDL cholesterol in patients with diabetes than simvastatin alone. Those in the ezetimibe/simvastatin 10/40 mg/mg group saw a mean percentage LDL cholesterol reduction at 5 weeks of 59.2%, compared to 38.7% in the simvastatin 20mg group.

Superior LDL-C lowering efficacy and goal attainment when using Dual Inhibition therapy was also noted in the McBride et al study3 which was another subgroup analysis of patients with diabetes (38.5%), patients with metabolic syndrome (26.9), and patients with metabolic dyslipidemia (24.6%). The study concluded that the addition of ezetimibe 10mg/day to ongoing statin therapy, compared with the addition of placebo resulted in substantial improvements in NCEP ATP III LDL-C goal attainment, reductions in LDL-C from statin baseline, and improvements in other key lipid abnormalities (TG, HDL-C, non-HDL-C, TC, and apolipoprotein B) after 6 weeks of treatment.

Greater reduction of LDL cholesterol levels for patients taking ezetimibe with fenofibrate

A study4, authored by Farnier et al, examined the efficacy and safety of co-administration of ezetimibe together with fenofibrate in patients with mixed hyperlipidemia, a metabolic disorder characterized by elevated LDL-C, triglycerides, non-HDL-C and reduced HDL-C. Patients with mixed hyperlipidemia are at increased risk for cardiovascular disease. The study concluded that the coadministration of ezetimibe with fenofibrate significantly reduced LDL-C levels by 20.4% compared to a 5.5% reduction in fenofibrate patients alone ($p<0.001$). HDL-C levels were also increased, a 19% increase in patients taking ezetimibe with fenofibrate, compared to an increase of 18.8% in patients taking fenofibrate alone. The study concluded that the co-administration of ezetimibe and fenofibrate provides a therapy with complementary effects to improve the atherogenic lipid profile of patients with mixed hyperlipidemia.

Ezetimibe was well tolerated within all three trials.

About EZETROL

EZETROL (ezetimibe), a cholesterol absorption inhibitor, has been developed and is being marketed by Merck & Co., Inc. (NYSE:MRK) and Schering-Plough Corporation (NYSE:SGP) in connection with a partnership formed by both companies to develop and market worldwide (excluding Japan) new prescription medicines in cholesterol management. EZETROL has now been launched in many European countries including, Germany, the United Kingdom, Spain, Belgium, Switzerland, Sweden, Ireland, and Holland.

About Merck

Merck & Co., Inc., which operates in many countries as Merck Sharp & Dohme, is a global research-driven pharmaceutical products company. Merck discovers, develops, manufactures and markets a broad range of innovative products to improve human health, directly or through its joint ventures.

About Schering-Plough

Schering-Plough Corporation is a global science-based health care company with leading prescription, consumer and animal health products. Through internal research and collaborations with partners, Schering-Plough discovers, develops, manufactures and markets advanced drug therapies to meet important medical needs. Schering-Plough's vision is to earn the trust of the physicians, patients and customers served by its more than 30,000 people around the world.

Notes to Editors

Ezetimibe is indicated as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolemia who are not appropriately controlled with a statin alone and as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolemia in whom a statin is considered inappropriate or is not tolerated. Ezetrol is indicated as adjunctive therapy to diet for use in patients with HoFH and in patients with homozygous familial sitosterolemia. Ezetimibe is not indicated as adjunctive therapy with fenofibrate.

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References

1 American Diabetes Association 'Diabetes.Org' factsheets: accessed 03 August 2004 from www.diabetes.org

2 McKenney et al. Low-density lipoprotein cholesterol goal attainment among patients with diabetes mellitus treated with ezetimibe plus simvastatin coadministered versus simvastatin alone. Presentation at European Association for the Study of Diabetes annual meeting 2004.

3 McBride et al. Ezetimibe added to statin therapy reduces LDL-C and improves goal attainment in patients with diabetes, metabolic syndrome, or metabolic dyslipidemia. Presentation at European Association for the Study of Diabetes annual meeting 2004

4 Farnier et al. Efficacy and safety of coadministration of ezetimibe with fenofibrate in patients with mixed hyperlipidemia. Presentation at European Association for the Study of Diabetes annual meeting 2004

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