



News Release

New data analysis of EXAMINE cardiovascular safety outcomes trial of Takeda type 2 diabetes treatment alogliptin published in *The Lancet*

Data show no increased risk of heart failure outcomes with alogliptin versus placebo in type 2 diabetes patients with recent acute coronary syndrome

OAKVILLE, Ontario – May 26, 2015 – Patients with type 2 diabetes and at high cardiovascular risk due to recent acute coronary syndrome (ACS) who were given the Takeda treatment alogliptin were at no increased risk for heart failure outcomes than those given placebo, according to results of a new post hoc analysis of data from the EXAMINE cardiovascular safety trial published recently in *The Lancet*.

The study results are the first time a type 2 diabetes dipeptidyl peptidase 4 (DPP-4) inhibitor has demonstrated such cardiovascular safety outcomes in patients who are at high risk due to recent ACS. Heart or cardiovascular disease is the leading cause of morbidity and mortality in patients with type 2 diabetes and is responsible for more than half of deaths in people with diabetes.

“When treating type 2 diabetes patients we are always alert to the risk of cardiovascular disease and ways to minimize that risk, particularly when it is already high,” said Dr. Jean-François Yale, an endocrinologist in Montreal. “The EXAMINE study and these new data provide important new information to support our efforts to treat these high risk patients.”

About EXAMINE and the new data analysis

The EXAMINE (EXamination of CArdiovascular OutcoMes: AlogliptiN vs. Standard of CarE in Patients with Type 2 Diabetes Mellitus and Acute Coronary Syndrome) cardiovascular (CV) safety outcomes trial was designed to evaluate CV safety following treatment with alogliptin in addition to standard of care, versus placebo in addition to standard of care, in patients with type 2 diabetes and a recent ACS. The trial randomized 5,380 patients in 49 countries who had type 2 diabetes and who had had an ACS within the previous 15-90 days. The EXAMINE trial’s primary composite endpoint (CV death, nonfatal myocardial infarction and nonfatal stroke) established non-inferiority of alogliptin compared to placebo in addition to standard of care, showing no increase in CV risk in a type 2 diabetes patient population at high risk for CV events.

The new analysis of data from the study published in *The Lancet* showed that in patients with type 2 diabetes and recent acute coronary syndrome (ACS), alogliptin compared to placebo did not increase the risk of heart failure (HF) outcomes. Alogliptin (n=201, 7.4%) compared with placebo (n=201, 7.5%) had no effect on the extended exploratory post hoc composite endpoint of CV death and hospitalized heart failure (HHF) (HR=1.00, 95% CI, 0.82, 1.21). Patients with a history of HF prior to randomization had a higher risk of HF outcomes in EXAMINE. The sub-analysis showed that the risk of the composite of CV death and HHF was not increased with alogliptin (n=107, 13.9%) compared with placebo (n=120, 15.7%) (HR=0.90, 95% CI, 0.70, 1.17). In patients without a history of HF at baseline, there was also no increased risk of the composite

endpoint of CV death and HHF for alogliptin (HR=1.14 [95% CI 0.85-1.54], p=0.337) versus placebo, although there was in this sub-group of patients a small absolute increase in HHF for alogliptin versus placebo (0.9%).

About NESINA and KAZANO

NESINA[®] (alogliptin) and KAZANO[™] (alogliptin and metformin hydrochloride) are two forms of alogliptin treatments that are approved and available in Canada from Takeda Canada. These two products recently became available to patients on the Quebec public drug plan, reimbursable under the exceptional drug program.

In addition to diet and exercise, both NESINA and KAZANO are indicated to improve glycemic control in adult patients with type 2 diabetes mellitus, either on their own or in combination with various other diabetes treatments, including insulin, as appropriate. NESINA is a dipeptidyl peptidase-4 inhibitor (DPP-4i) that is designed to slow the inactivation of incretin hormones GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic peptide). It is available in doses of 6.25, 12.5 and 25 mg and is taken once daily, with or without food. KAZANO, a widely used anti-diabetes medication, is a single tablet. It is available in doses of 12.5 mg/500 mg, 12.5 mg/850 mg, 12.5 mg/1000 mg of alogliptin and metformin hydrochloride respectively. Because of its metformin content, KAZANO is taken twice daily with food.

About Takeda's diabetes business

Takeda's heritage in diabetes globally includes significant contributions towards scientific discovery and exchange, starting with the discovery of the TZD pioglitazone, the more recent developments of alogliptin and FDCS alogliptin and pioglitazone, and alogliptin and metformin HCl. The company's strong, diverse diabetes portfolio and available medications mark important milestones in Takeda's ongoing commitment to advancing patient care and helping to meet the individual needs of this growing patient population. Additional information about Takeda is available through its corporate website, www.takeda.com.

About Takeda Canada

Takeda Canada, located in Oakville, Ontario, is the Canadian sales and marketing organization of Takeda Pharmaceutical Company Limited, Osaka, Japan. The company has a commercial presence covering more than 70 countries, with particular strength in Asia, North America, Europe and fast-growing emerging markets including Latin America, Russia-CIS and China. Areas of focus include cardiovascular and metabolic, oncology, respiratory and immunology, central nervous system, general medicine, and vaccines. Takeda is a research-based global company with its main focus on pharmaceuticals. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda is committed to strive towards better health for people worldwide through leading innovation in medicine. Through strategic acquisitions, Takeda has been transforming itself, broadening its therapeutic expertise and geographic outreach. www.takedacanada.com.

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