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Janssen Submits European Marketing Authorisation Application for Canagliflozin/Metformin Fixed-Dose Combination Therapy to Treat Patients with Type 2 Diabetes

BEERSE, March 7, 2013 - Janssen-Cilag International NV (Janssen) today announced it has submitted a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) seeking approval for a fixed-dose therapy combining canagliflozin and immediate release metformin to treat adult patients with type 2 diabetes.

Canagliflozin is an investigational, oral medication for the treatment of adult patients with type 2 diabetes. The kidneys of people with type 2 diabetes reabsorb greater amounts of glucose back into the body compared to people without diabetes, which may contribute to elevated glucose levels in the blood.[1] Canagliflozin, a selective sodium glucose co-transporter 2 (SGLT2) inhibitor, blocks the reabsorption of glucose by the kidney, increasing glucose excretion and lowering blood glucose levels.[2]

Metformin is a first-line pharmacotherapy that can be used alone or with other medications, including insulin, to treat type 2 diabetes. In people with type 2 diabetes, the liver overproduces glucose, which increases blood glucose levels. Metformin lowers blood glucose levels by decreasing the amount of glucose made by the liver, increasing insulin sensitivity in the muscle and delaying intestinal glucose absorption.[3]

If approved, this canagliflozin/metformin fixed-dose combination therapy could provide convenience for patients who may benefit from two diabetes medications working in one pill.

A significant portion of the clinical data in this MAA are derived from the comprehensive global Phase 3 clinical development programme for canagliflozin, which were included in the MAA for canagliflozin submitted to the EMA on 26 June 2012. The canagliflozin Phase 3 programme represents the largest late-stage development programme for an investigational pharmacologic product for the treatment of patients with type 2 diabetes submitted to health authorities to date.

The Phase 3 programme evaluated the safety and efficacy of canagliflozin across the spectrum of type 2 diabetes and included placebo- and active comparator-controlled studies. The programme also includes a study in patients who have or are at high risk for developing cardiovascular disease, called the **CAN**agliflozin cardio**V**ascular **A**ssessment Study (CANVAS).

Janssen presented data from Phase 3 studies in 2012 at the American Diabetes Association (ADA) in Philadelphia in June, at the European Association for the Study of Diabetes (EASD) in Berlin in October, and at the World Congress on Controversies to Consensus in Diabetes, Obesity, and Hypertension (CODHY) in Barcelona in November.

New Drug Applications (NDA) have also been submitted to the U.S. Food and Drug Administration (FDA) for canagliflozin on May 31, 2012 and for a fixed-dose therapy combining canagliflozin and immediate release metformin on December 12, 2012 for the treatment of adult patients with type 2 diabetes.

Janssen is confident in the value of the comprehensive clinical trial programme of canagliflozin supporting the regulatory submissions to the EMA and the FDA. However, the company cannot speculate on the outcome of these regulatory procedures whilst they are ongoing.

Janssen and its affiliates have rights to canagliflozin through a license agreement with Mitsubishi Tanabe Pharma Corporation. Janssen Pharmaceuticals, Inc. has marketing rights in North America, South America, Europe, the Middle East, Africa, Australia, New Zealand and parts of Asia.

About Type 2 Diabetes
Type 2 diabetes is a chronic condition that affects the body's ability to metabolize sugar, or glucose, and is characterized by the inability of pancreatic beta cell function to keep up with the body's demand for insulin. If left uncontrolled, type 2 diabetes can lead to serious long-term microvascular and macrovascular complications such as coronary heart disease (leading to heart attack) and stroke, nerve disease leading to amputation, retinopathy resulting in blindness and nephropathy causing end-stage renal disease. Improved glycemic control has been demonstrated to reduce the onset and progression of these complications.[4]

About Janssen
The Janssen Pharmaceutical Companies of Johnson & Johnson are dedicated to addressing and solving the most important unmet medical needs of our time, including oncology, immunology, neuroscience, infectious disease, and cardiovascular and

metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world.

More information can be found at www.janssen-emea.com

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[1] Gerich J. *Diabetes Med.* 2010; 27: 136-42

[2] Rosenstock et al. *Diabetes Care.* 2012 Jun; 35(6):1232-8. doi: 10.2337/dc11-1926. Epub 2012 Apr 9

[3] Summary of Product Characteristics last updated on the eMC: 12/10/2010. Available at: http://www.medicines.org.uk/emc/medicine/1043/spc. Last accessed Feb 2013

[4] International Diabetes Federation. About Diabetes. Available http://www.idf.org/about-diabetes. Last Accessed: Feb2013