Press Release

Sep 26, 2022

Eli Lilly Japan K.K.
Mitsubishi Tanabe Pharma Corporation

Approval of Mounjaro, the world's first sustained release GIP/GLP-1 receptor agonist for the treatment of type 2 diabetes in Japan

September 26, 2022 - Eli Lilly Japan K.K. (Head Office: Kobe, Japan, Representative Director and President: Simone Thomsen, hereinafter called "Eli Lilly Japan") and Mitsubishi Tanabe Pharma Corporation (Head Office: Osaka, Japan, Representative Director: Hiroaki Ueno, hereinafter called "MTPC") announced that Ministry of Health, Labour and Welfare (MHLW) approved the manufacturing and marketing of the following sustained release GIP/GLP-1 receptor agonists: "Mounjaro® subcutaneous injection 2.5 mg / 5 mg / 7.5 mg / 10 mg / 12.5 mg / 15 mg ATEOS®" (Non-proprietary name: Tirzepatide, hereinafter referred called "Mounjaro") indicated for "type 2 diabetes" in Japan.

As the world's first sustained release GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) receptor agonist, Mounjaro is a single molecule that activates two receptors: GIP and GLP-1. Although the structure of Mounjaro is a single molecule based on the natural GIP peptide sequence, it has been modified to also bind to the GLP-1 receptor, and selectively acts for a long time to improve fasting and postprandial blood glucose. Mounjaro is administered once weekly by subcutaneous injection with a single-use autoinjector device (ATEOS).

Approval of Mounjaro is based primarily on the efficacy and safety results of two Japanese phase 3 clinical studies (SURPASS J-mono[i] and SURPASS J-combo[ii]) and two global studies (SURPASS-1[iii] and SURPASS-5[iv]). A Japanese monotherapy study (SURPASS J-mono[i]) demonstrated the superiority of Tirzepatide 5 mg, 10 mg, and 15 mg over Dulaglutide 0.75 mg in terms of the mean change from baseline in HbA1c at Week 52, the primary endpoint. In addition, a Japanese combination therapy study (SURPASS J-combo[ii]) evaluated the safety and efficacy of Tirzepatide 5 mg, 10 mg, and 15 mg in combination with an oral hypoglycemic monotherapy.

Eli Lilly and Company obtained an approval of Mounjaro in the United States on May 13 as the world's first sustained release GIP/GLP-1 receptor agonist, and launched it on June 7. Mounjaro was also approved in the European Union on September 15. Prior to this approval, Eli Lilly Japan and MTPC concluded a sales collaboration agreement for Mounjaro in Japan in July. MTPC will distribute and sell Mounjaro, and Eli Lilly Japan and MTPC will jointly provide information.

"We are very pleased to receive approval for Mounjaro to be able to bring a new class of treatment options to people living with type 2 diabetes in Japan. We hope Mounjaro will help them reach their treat-

ment goals. This is an exciting time as Japan has pioneered many advances in GIP and GLP1 research, so we are appreciative of the incredible research accomplishments in Japan and are honored to bring Mounjaro forward to people in Japan with diabetes," said Mary Thomas, Sr Director, Diabetes and Growth Hormone Business unit, Ely Lilly Japan.

"We are very pleased that Mounjaro has been approved in Japan. By providing a new option for Japanese patients facing type 2 diabetes, we will expand the range of treatment and contribute to solving unmet medical needs.," said Yoshihiro Kobayashi, Head of Pharma Business Strategy Division, MTPC.

Product Summary

Product Name	Mounjaro® subcutaneous injection 2.5 mg ATEOS® Mounjaro® subcutaneous injection 5 mg ATEOS® Mounjaro® subcutaneous injection 7.5 mg ATEOS® Mounjaro® subcutaneous injection 10 mg ATEOS® Mounjaro® subcutaneous injection 12.5 mg ATEOS® Mounjaro® subcutaneous injection 15 mg ATEOS®
Non-proprietary Name	Tirzepatide
Indications	Type 2 diabetes
Dosage and Administration	For adults, the usual maintenance dose of Tirzepatide is 5 mg once a week by subcutaneous injection. However, start with 2.5 mg once weekly and increase to 5 mg once weekly after 4 weeks. The dosage may be adjusted according to the patient's condition, but if the effect is insufficient with 5 mg once a week, the dosage can be increased by 2.5 mg at intervals of 4 weeks or longer. However, the maximum dosage should be up to 15 mg once weekly.
Date of acquisition of manufacturing and marketing approval	September 26, 2022

About SURPASS J-mono [i]

This is a Japanese phase 3 study evaluating the superiority of 5 mg, 10 mg, and 15 mg of Tirzepatide once weekly to Dulaglutide 0.75 mg. The study enrolled 636 adults with type 2 diabetes who had inadequate glycemic management with diet and exercise therapy alone, or with oral hypoglycemic agents alone excluding Thiazolidinediones. The primary endpoint was HbA1c reduction from baseline after 52 weeks. The secondary endpoints included body weight and fasting blood glucose.

About SURPASS J-combo [ii]

This is a Japanese phase 3 study evaluating the incidence of adverse events. The study enrolled 443 adults with type 2 diabetes who had inadequate glycemic management despite being on monotherapy with oral hypoglycemic agents other than DPP-4 inhibitors for at least three months. The primary endpoint was the incidence of adverse events with Tirzepatide 5 mg, 10 mg, and 15 mg once weekly for 52 weeks in concomitant oral hypoglycemic agents (Sulfonylureas, Biguanides, Alpha-glucosidase inhibitors, Thiazolidines, fast-acting Insulin secretagogues or SGLT2 inhibitors). A secondary objective was to evaluate the efficacy of Tirzepatide once weekly for 52 weeks in combination with oral hypoglycemic agents.

About SURPASS-1 [iii]

This is a global phase 3 study evaluating the superiority of 5 mg, 10 mg, and 15 mg of Tirzepatide once weekly to placebo. The study enrolled 478 adults (89 Japanese) with type 2 diabetes who had inadequate glycemic management with diet and exercise alone, and naïve to injectable therapy who had not

used any oral antidiabetic medicines within three months.The primary endpoint was HbA1c reduction from baseline after 40 weeks. The secondary endpoints included body weight and fasting blood glucose.

About SURPASS-5[iv]

This is a global phase 3 study evaluating the superiority of 10 mg and 15 mg of Tirezpatide once weekly in combination with placebo. The study enrolled 475 adults (82 Japanese) with type 2 diabetes who had inadequate glycemic management on once-daily Insulin Glargine with or without metformin. The primary endpoint was HbA1c reduction from baseline after 40 weeks. The secondary endpoints included body weight and fasting blood glucose.

About Tirzepatide

Tirzepatide is a once-weekly glucose-dependent insulinotropic polypeptide (GIP) and glucagon like peptide-1 (GLP-1) receptor agonist that integrates the actions of both incretins into a single novel molecule. GIP is a hormone that may complement the effects of GLP-1. In preclinical models, GIP has been shown to decrease food intake and increase energy expenditure therefore resulting in weight reductions, and when combined with a GLP-1 receptor agonist, may result in greater effects on glucose and body weight. Tirzepatide is in phase 3 development for blood glucose management in adults with type 2 diabetes, for chronic weight management and heart failure with preserved ejection fraction (HFpEF). It is also being studied as a potential treatment for non-alcoholic steatohepatitis (NASH).

About Eli Lilly Japan

Eli Lilly Japan K.K. is a subsidiary of US-based Eli Lilly and Company. It contributes to medical treatment in Japan through the development, manufacture, import and sale of innovative pharmaceutical products that enable people to live longer, healthier, and more fulfilling lives, focusing on the therapeutic areas such as cancer, diabetes, musculoskeletal diseases, central nervous system diseases, autoimmune diseases, growth disorder, and pain. For more information, visit http://www.lilly.co.jp

About Mitsubishi Tanabe Pharma Corporation

Mitsubishi Tanabe Pharma Corporation (MTPC), the pharma arm of the Mitsubishi Chemical Group, is one of the oldest pharmaceutical companies in the world, founded in 1678, and focusing on ethical pharmaceuticals. The Mitsubishi Chemical Group has positioned Health Care as one of its strategic focus in its management policy, “Forging the future”. MTPC set the MISSION of “Creating hope for all facing illness”. To that end, MTPC is working on R&D in the areas of central nervous system and immuno-inflammation and vaccines for global market, and it is also focusing on the areas of diabetes and kidney disease in Japan. For more information, go to https://www.mt-pharma.co.jp/e/

References

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