独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

Drugs with GLP-1 agonist activity

July 30, 2025

Non-proprietary name

Semaglutide (genetical recombination)

Tirzepatide

Insulin glargine (genetical recombination)/lixisenatide

Brand name (marketing authorization holder)

See attachment.

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

1. “Patients with a medical history of abdominal surgery or ileus” should be added to the 9.1 Patients with Complication or History of Diseases, etc. section in 9 PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS.
2. “Ileus” should be added to the 11.1 Clinically Significant Adverse Reactions section in 11. ADVERSE REACTIONS.

Investigation results and background of the revision

Cases involving ileus were evaluated. Cases for which a causal relationship between drugs with GLP-1 agonist activity and ileus was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of

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PRECAUTIONS was necessary.

Reference: Number of cases*1 and patient mortalities involving ileus reported in Japan

a.

A total of 25 cases have been reported to date. (A causal relationship between the drug and the event was reasonably possible for 7 cases, including 1 case in which the drug was administered outside the approved indications.)

One instance of patient mortality has been reported to date. (A causal relationship between the drug and the death following the event could not be established for this case.)

b.

A total of 22 cases have been reported to date (including 2 cases for which a causal relationship between the drug and the event was reasonably possible).

No patient mortalities have been reported to date.

c.

A total of 3 cases have been reported to date (including 1 case for which a causal relationship between the drug and the event was reasonably possible).*2

No patient mortalities have been reported to date.

*1 Cases were retrieved from the PMDA's safety database for drugs. Among the cases that fell under SMQ “gastrointestinal obstruction,” those falling under the PTs of “impaired gastric emptying,” “oesophageal obstruction,” “necrotising oesophagitis,” or “gastric volvulus,” in which the site of onset of the adverse event is not intestinal, were excluded.

*2 Cases for Lyxumia S.C. Injection (lixisenatide), for which marketing has been discontinued, were also included.

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the “Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency” (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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Attachment

No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	Indications
a.	Semaglutide (genetical recombination)	Wegovy Subcutaneous Injection 0.25 mg SD, 0.5 mg SD, 1.0 mg SD, 1.7 mg SD, 2.4 mg SD, 0.25 mg pen 1.0 MD, 0.5 mg pen 2.0 MD, 1.0 mg pen 4.0 MD, 1.7 mg pen 6.8 MD, 2.4 mg pen 9.6 MD Ozempic Subcutaneous Injection 2 mg Rybelsus tablets 3 mg, 7 mg, 14 mg	Novo Nordisk Pharma Ltd.	Wegovy Subcutaneous Injection SD: February 2024 Wegovy Subcutaneous Injection MD: July 2025 Ozempic Subcutaneous Injection: May 2022 Rybelsus tablets: February 2021	•Wegovy Subcutaneous Injection Obesity For use only in patients with any of hypertension, hyperlipidemia or type 2 diabetes mellitus who have not responded sufficiently to diet therapy and exercise therapy, and who meet the following conditions: ·BMI of 27 kg/m^2 or greater in the presence of at least two obesity-related comorbidities ·BMI of 35 kg/m^2 or greater •Ozempic Subcutaneous Injection, Rybelsus tablets Type 2 diabetes mellitus
b.	Tirzepatide	Zepbound Subcutaneous Injection 2.5 mg Ateos, 5 mg Ateos, 7.5 mg Ateos, 10 mg Ateos, 12.5 mg Ateos, 15 mg Ateos Mounjaro Subcutaneous Injection 2.5 mg Ateos, 5 mg Ateos, 7.5 mg Ateos, 10 mg Ateos, 12.5 mg Ateos, 15 mg Ateos	Eli Lilly Japan K.K.	Zepbound Subcutaneous Injection: April 2025 Mounjaro Subcutaneous Injection 2.5 mg, 5 mg: April 2023 Mounjaro Subcutaneous Injection 7.5 mg, 10 mg, 12.5 mg, 15 mg: June 2023	•Zepbound Subcutaneous Injection Obesity For use only in patients with any of hypertension, hyperlipidemia or type 2 diabetes mellitus who have not responded sufficiently to diet therapy and exercise therapy, and who meet the following conditions: ·BMI of 27 kg/m^2 or greater in the presence of at least two obesity-related comorbidities ·BMI of 35 kg/m^2 or greater •Mounjaro Subcutaneous Injection Type 2 diabetes mellitus
c.	Insulin glargine (genetical recombination)/ lixisenatide	Soliqua Injection SoloStar	Sanofi K.K.	June 2020	Type 2 diabetes mellitus for which insulin therapy is indicated