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

Dulaglutide (genetical recombination)

March 5, 2025

Non-proprietary name

Dulaglutide (genetical recombination)

Brand name (marketing authorization holder)

Trulicity Subcutaneous Injection 0.75 mg Ateos, 1.5 mg Ateos (Eli Lilly Japan K.K.)

Japanese market launch

Trulicity Subcutaneous Injection 0.75 mg Ateos: September 2015

Trulicity Subcutaneous Injection 1.5 mg Ateos: Before market launch

Indications

Type 2 diabetes mellitus

Summary of revisions

“Hepatic impairment” 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 hepatic impairment as well as the results of a study*[1] were evaluated. Cases for which a causal relationship between dulaglutide (genetical recombination) and hepatic impairment was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of these cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases and patient mortalities involving hepatic impairment

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reported in Japan*2 and overseas*3

A total of 19 cases have been reported in Japan to date (including 4 cases for which a causal relationship between the drug and the event was reasonably possible).
One instance of patient mortality has been reported in Japan to date. (A causal relationship between the drug and the death subsequent to the event could not be established for this case.)

A total of 3 cases have been reported overseas to date (including 1 case for which a causal relationship between the drug and the event was reasonably possible).
No patient mortalities have been reported overseas to date.

*1 In association with this investigation, a MID-NET® study (appendix) was performed.
*2 Cases meeting both of the following conditions were retrieved from those collected in the PMDA's database for adverse drug reactions, etc. reports:
•Cases that fell under MedDRA ver.27.0 SMQ "Hepatic disorders (broad)"
•Cases in which the hepatic function test value (either of ALT, AST, ALP, γ-GTP, or T-Bil) was classified as grade 3 or higher according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0
*3 Cases meeting all of the following conditions were retrieved from those collected in the PMDA's database for adverse drug reactions, etc. reports:
•Cases that fell under MedDRA ver.27.0 SMQ "Hepatic disorders (broad)"
•Cases in which the hepatic function test value (either of ALT, AST, ALP, γ-GTP, or T-Bil) was classified as grade 3 or higher according to CTCAE version 5.0
•Cases that included descriptions of hepatic function-related test values at 3 time points (before administration and after discontinuation of dulaglutide (genetical recombination), and at the onset of the event)

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).