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Summary of Investigation Results

Preparations containing SGLT2 inhibitors

December 17, 2024

Non-proprietary name

a. Ipragliflozin L-proline

b. Sitagliptin phosphate hydrate/ipragliflozin L-proline

c. Empagliflozin

d. Empagliflozin/linagliptin

e. Canagliflozin hydrate

f. Teneligliptin hydrobromide hydrate/canagliflozin hydrate

g. Dapagliflozin propylene glycolate hydrate

h. Tofogliflozin hydrate

i. Luseogliflozin hydrate

Brand name (marketing authorization holder)

See attachment.

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

A cautionary statement should be added to the 8. IMPORTANT PRECAUTIONS section regarding the prolongation of urinary glucose excretion and ketoacidosis after discontinuing administration.

Investigation results and background of the revision

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Currently, cautionary statements related to ketoacidosis are included in PRECAUTIONS for all SGLT2 inhibitors. Cases involving prolongation of urinary glucose excretion and ketoacidosis after discontinuing administration had been reported post-marketing, and those events were considered to be unexpected from the current cautionary statements. Therefore, the necessity of revision of PRECAUTIONS was evaluated and, as a result of consultation with expert advisors, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases*† and patient mortalities involving prolonged ketoacidosis reported in Japan

a.
A total of 30 cases have been reported to date.
No patient mortalities have been reported to date.

b.
No cases have been reported to date.

c.
A total of 44 cases have been reported to date.
One instance of patient mortality has been reported to date.

d.
A total of 3 cases have been reported to date.
No patient mortalities have been reported to date.

e.
A total of 21 cases have been reported to date.
No patient mortalities have been reported to date.

f.
A total of 5 cases have been reported to date.
No patient mortalities have been reported to date.

g.
A total of 64 cases have been reported to date.
No patient mortalities have been reported to date.

h.
A total of 7 cases have been reported to date.
No patient mortalities have been reported to date.

i.

A total of 21 cases have been reported to date.

No patient mortalities have been reported to date.

* Cases collected in the PMDA's database for adverse drug reactions, etc. reports

† Cases retrieved by the MAHs based on the criteria of each MAH as those involving ketoacidosis persisting for 3 days or more after discontinuing administration. Of note, the possibility of a causal relationship between the drugs and the events was not evaluated.

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.	Ipragliflozin L-proline	Suglat Tablets 25 mg, 50 mg	Astellas Pharma Inc.	April 2014	•Type 2 diabetes mellitus •Type 1 diabetes mellitus
b.	Sitagliptin phosphate hydrate/ ipragliflozin L-proline	Sujanu Combination Tablets	MSD K.K.	May 2018	Type 2 diabetes mellitus (only when a concomitant use of sitagliptin phosphate hydrate with ipragliflozin L-proline is deemed appropriate)
c.	Empagliflozin	Jardiance Tablets 10 mg, 25 mg	Nippon Boehringer Ingelheim Co., Ltd.	February, 2015	<Jardiance Tablets 10 mg, 25 mg> •Type 2 diabetes mellitus <Jardiance Tablets 10 mg> •Chronic cardiac failure (for use only in patients receiving standard treatment of chronic heart failure) •Chronic kidney disease (excluding patients who have end-stage renal failure or are undergoing dialysis)
d.	Empagliflozin/linagliptin	Tradiance Combination Tablets AP, BP	Nippon Boehringer Ingelheim Co., Ltd.	November, 2018	Type 2 diabetes mellitus (only when a concomitant treatment with empagliflozin and linagliptin is deemed appropriate)

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No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	Indications
e.	Canagliflozin hydrate	Canaglu Tablets 100 mg, Canaglu OD Tablets 100 mg	Mitsubishi Tanabe Pharma Corporation	Tablets 100 mg: September 2014 OD Tablets 100 mg: May 2024	•Type 2 diabetes mellitus •Chronic kidney disease associated with type 2 diabetes mellitus (excluding patients who have end-stage renal failure or are undergoing dialysis)
f.	Teneligliptin hydrobromide hydrate/canagliflozin hydrate	Canalia Combination Tablets	Mitsubishi Tanabe Pharma Corporation	September, 2017	•Type 2 diabetes mellitus (only when a concomitant treatment with teneligliptin hydrobromide hydrate and canagliflozin hydrate is deemed appropriate)
g.	Dapagliflozin propylene glycolate hydrate	Forxiga tablets 5 mg, 10 mg	AstraZeneca K.K.	May 2014	•Type 2 diabetes mellitus •Type 1 diabetes mellitus Chronic cardiac failure (for use only in patients receiving standard treatment of chronic heart failure) •Chronic kidney disease (excluding patients who have end-stage renal failure or are undergoing dialysis)
h.	Tofogliflozin hydrate	Deberza Tablets 20 mg	Kowa Company, Ltd.	May 2014	Type 2 diabetes mellitus
i.	Luseogliflozin hydrate	Lusefi tablets 2.5 mg, 5 mg, Lusefi OD film 2.5 mg	Taisho Pharmaceutical Co., Ltd.	Tablets 2.5mg, 5 mg: May 2014 OD film 2.5 mg: June 2022	Type 2 diabetes mellitus

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