



Summary of investigation results

Sodium-glucose co-transporter 2 inhibitors

January 9, 2015

Non-proprietary Name

- a. ipragliflozin _L-proline
- b. dapagliflozin propylene glycolate hydrate
- c. tofogliflozin hydrate
- d. luseogliflozin hydrate
- e. canagliflozin hydrate
- f. empagliflozin

Brand Name (Marketing Authorization Holder)

- a. Suglat Tablets 25 mg and 50 mg (Astellas Pharma Inc.)
- b. Forxiga Tablets 5 mg and 10 mg (Bristol-Myers K.K.)
- c. Apleway Tablets 20 mg (Sanofi K.K.) and Deberza Tablets 20 mg (Kowa Company, Ltd.)
- d. Lusefi Tablets 2.5 mg and 5 mg (Taisho Pharmaceutical Co., Ltd.)
- e. Canaglu Tablets 100 mg (Mitsubishi Tanabe Pharma Corporation)
- f. Jardiance Tablets 10 mg and 25 mg (Nippon Boehringer Ingelheim Co., Ltd.) (This product has not been launched in Japan yet.)

Indications

Type 2 diabetes mellitus

Summary of revision

- ‘Patients who are susceptible to dehydration (ex. patients with poor blood glucose control, geriatric patients, and patients who are concomitantly administered diuretics)’ should be added in the Careful administration section.
- ‘Dehydration’ should be added in the Clinically significant adverse reactions section.

Background of the revision and investigation results

Cases of adverse events suggestive of dehydration* have been reported in patients treated with ipragliflozin _L-proline, dapagliflozin propylene glycolate hydrate, or tofogliflozin hydrate in Japan. Following an investigation based on the opinions of expert advisors and available



evidence, the MHLW/PMDA concluded that revision of the package inserts was necessary. Although no case of adverse events suggestive of dehydration* has been reported in patients treated with luseogliflozin hydrate, canagliflozin hydrate, or empagliflozin in Japan, dehydration may occur also with the use of these products because sodium-glucose co-transporter 2 inhibitors have an osmotic diuretic effect. Following an investigation based on the opinions of expert advisors and available evidence, the MHLW/PMDA concluded that revision of the package inserts was necessary.

The number of reported adverse reactions and fatal cases in the last 3 fiscal years in Japan

Dehydration related cases*

a. ipragliflozin L-proline

A total of 26 cases of adverse events suggestive of dehydration have been reported. Of the 26 cases, causality could not be ruled out in 13 cases (including a patient who did not comply with Precautions for indications). No fatalities have not been reported.

b. dapagliflozin propylene glycolate hydrate

A total of 6 cases of adverse events suggestive of dehydration have been reported (including 2 cases in which causality could not be ruled out). A fatality has been reported. No causal relationship with dapagliflozin propylene glycolate hydrate was established in the fatal case.

c. tofogliflozin hydrate

A total of 9 cases of adverse events suggestive of dehydration have been reported (including 3 cases in which causality could not be ruled out). A fatality has been reported. No causal relationship with tofogliflozin hydrate was established in the fatal case.

d. luseogliflozin hydrate

No case of adverse events suggestive of dehydration has been reported.

e. canagliflozin hydrate

No case of adverse events suggestive of dehydration has been reported.

f. empagliflozin

No case of adverse events suggestive of dehydration has been reported. (This product has not been launched in Japan yet.)

*NOTE: Cases of dehydration in which serious events resulting from dehydration (thromboembolism, diabetic ketoacidosis, hyperosmolar hyperglycaemic syndrome, arrhythmia, cardiac failure, renal impairment, mental disorder, and loss of consciousness) were observed.