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Revision of Precautions

Ipragliflozin L-proline, Luseogliflozin hydrate, and Tofogliflozin hydrate

September 15, 2015

Non-proprietary name

a. Ipragliflozin L-proline

b. Luseogliflozin hydrate

c. Tofogliflozin hydrate

Safety measure

Precautions should be revised in the package insert.

In the Important Precautions section regarding urinary tract infection and genital infection, the following text should be revised (underlined parts are revised):

> Urinary tract infection may occur, which may lead to severe infections such as pyelonephritis and sepsis. Genital infections such as vaginal candidiasis may also occur. Patients should be carefully monitored for urinary tract infection and genital infection. If infection occurs, appropriate measures should be adopted, and measures such as temporary discontinuation of this drug should be taken into consideration based on the patient's condition. Symptoms and management of urinary tract infection and genital infection should be explained to patients.

In the Important Precautions section regarding ketone bodies increase and diabetic ketoacidosis, the following text should be revised (underlined parts are revised):

> Due to the mechanism of action which accelerates secretion of urinary glucose, metabolism of fatty acids may increase and cause ketosis, which can then lead to ketoacidosis even if blood glucose is controlled. Significant increase in blood glucose level may not occur in such cases; therefore, caution should be exercised for the following points.

Pharmaceuticals and Medical Devices Agency
Office of Safety I
3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

1. If symptoms such as nausea/vomiting, decreased appetite, abdominal pain, excessive thirst, malaise, dyspnoea, and/or disturbed consciousness are observed, laboratory tests including those that measure blood and urinary ketone bodies should be conducted. If any abnormalities are observed, administration of this drug should be discontinued, and appropriate measures should be adopted.
2. The following patients are especially susceptible to developing ketoacidosis and should be carefully monitored: patients who experienced decreased insulin secretion function, dosage reduction or discontinuation of administration of insulin products, excessively restrict sugar intake, poor feeding habits, infection, or dehydration.
3. Inform patients about the symptoms of ketoacidosis (such as nausea/vomiting, decreased appetite, abdominal pain, excessive thirst, malaise, dyspnoea, and/or disturbed consciousness), and instruct them to seek medical attention immediately, if they experience such symptoms.

In the Clinically significant adverse reaction subsection regarding pyelonephritis of the Adverse Reaction section, the following text should be revised (underlined parts are revised):

Pyelonephritis and sepsis:
Pyelonephritis may occur, which may lead to sepsis (including septic shock). Patients should be carefully monitored. If any abnormalities are observed, administration of this drug should be discontinued, and appropriate measures should be adopted.

In the Clinically significant adverse reaction subsection of the Adverse Reaction section, the following text should be added (underlined parts are revised):

Ketoacidosis:
Ketoacidosis (including diabetic ketoacidosis) may occur. Patients should be carefully monitored. If any abnormalities are observed, administration of this drug should be discontinued, and appropriate measures should be adopted.

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