Revision of Precautions
Alogliptin benzoate/metformin hydrochloride

June 18, 2019

Therapeutic category
Antidiabetic agents

Non-proprietary name
Alogliptin benzoate/metformin hydrochloride

Safety measure
Precautions should be revised in the package insert.
### Contraindications

Current

Patients under the following conditions:

1. History of lactic acidosis
2. Moderate or severe renal impairment
3. Dialysis patients (including peritoneal dialysis)
4. Severe hepatic impairment
5. Patients with a severe disorder in the cardiovascular system and/or pulmonary function such as shock, cardiac failure, myocardial infarction and pulmonary embolism, or other conditions likely to be accompanied by hypoxemia
6. Patients with excessive alcohol consumption
7. Patients with dehydration or gastrointestinal disorders such as diarrhoea and vomiting which are signs of a state of dehydration.

Revision

Patients under the following conditions:

1. Patients with a history of lactic acidosis
2. Patients with severe renal impairment (eGFR <30 mL/min/1.73 m²) or dialysis patients (including peritoneal dialysis)
3. Patients with severe hepatic impairment
4. Patients with a severe disorder in the cardiovascular system and/or pulmonary function (such as shock, cardiac failure, myocardial infarction and pulmonary embolism), or patients with other conditions likely to be accompanied by hypoxemia
5. Patients with dehydration or with signs of a state of dehydration (patients with gastrointestinal disorders such as diarrhoea and vomiting, patients with difficulty ingesting, etc.)
6. Patients with excessive alcohol consumption

### Precautions concerning Indications

Current

(N/A)

Revision

Careful administration is required with this drug in patients with moderate renal impairment (eGFR ≥30 mL/min/1.73 m² and <60 mL/min/1.73 m²) through tapering alogliptin benzoate as well as metformin hydrochloride depending on the level of renal function. This drug should not be used and co-administration of individual preparations should be considered in patients with moderate renal impairment.

### Important Precautions

Current

The patient and their family should be fully instructed on the following because metformin contained in this drug may rarely induce serious lactic acidosis.

1. Excessive alcohol consumption should be avoided.
2. If there is a concern about a state of dehydration due to pyrexia, diarrhea, vomiting, poor meal ingestion, etc., patients should temporarily discontinue this drug and consult the physician.
3. If any initial symptoms of lactic acidosis are observed, patients should seek immediate medical attention.

Revision

Metformin contained in this drug may rarely induce serious lactic acidosis. Known risk factors include renal impairment, hepatic impairment, conditions likely to be accompanied by hypoxemia, dehydration (including co-administration of drugs with diuretic effect), excessive alcohol consumption, infections, and the elderly. Especially, dehydration, excessive alcohol consumption, etc. may suddenly worsen patient’s conditions. Attention should be paid to the following:

1. The patient should be assessed prior to and regularly during treatment with this drug for renal function (eGFR, etc.) and hepatic
Lactic acidosis may occur in patients who undergo a test using an iodinated contrast medium due to co-administration of this drug. This drug should be temporarily suspended before the test (except when the test needs to be urgently performed). This drug should not be resumed until 48 hours after an iodinated contrast medium is administered. Attention should be paid to the patient's condition when this drug is resumed.

Dehydration may lead to lactic acidosis. When a symptom of dehydration is observed, this drug should be discontinued and appropriate measures be taken. When co-administered with a drug with diuretic action (diuretics, SGLT2 inhibitors, etc.), particularly careful attention should be paid for dehydration.

The renal excretion of metformin decreases in patients with renal impairment, leading to increased blood concentration of metformin. Attention should be paid to the following prior to and during treatment.

1) Careful attention should be paid to the renal function and other condition of the patient, and the necessity of administration should be considered. Refer to eGFR, serum creatinine level, etc. to assess the renal function.

2) During treatment with this drug, renal function (eGFR, serum creatinine, etc.) should be monitored regularly, and more frequently when careful follow-up is required for elderly patients, etc. If deterioration of the renal function is observed, discontinuation of this drug should be considered.

Hepatic metabolism of lactic acid may decrease in patients with hepatic impairment. Patients should be regularly monitored for the liver function during treatment with this drug.

Drug Interactions (N/A)

Drug Interactions
Contraindications for Co-administration
Alcohol (excessive consumption)

N/A: Not Applicable, because the section is not included in the current package insert.