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Revision of Precautions

Eliglustat tartrate

February 12, 2019

Non-proprietary name

Eliglustat tartrate

Safety measure

Precautions should be revised in the package insert.

The language concerning patients listed in the Contraindications section should be revised as follows (revised language is underlined):

Patients at risk of experiencing marked elevation in the plasma concentration of this drug depending on their status as a CYP2D6 metabolizer:

1) Patients who are extensive metabolizers (EMs) of CYP2D6 and who meet any of the following criteria:
   - Patients with moderate or severe hepatic impairment (Child-Pugh class B or C)
   - Patients with mild hepatic impairment (Child-Pugh class A) and who are receiving a moderate or strong CYP2D6 inhibitor
   - Patients with mild hepatic impairment (Child-Pugh class A) and who are receiving a weak CYP2D6 inhibitor concomitantly with a moderate or strong CYP3A inhibitor
   - Patients with normal hepatic function and who are receiving a moderate or strong CYP2D6 inhibitor concomitantly with a moderate or strong CYP3A inhibitor
2) Patients who are intermediate metabolizers (IMs) of CYP2D6 and who meet any of the following criteria:
   - Patients with any degree of hepatic impairment (Child-Pugh class A, B, or C)
   - Patients with normal hepatic function and who are receiving a moderate or strong

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CYP3A inhibitor

3) Patients who are poor metabolizers (PMs) of CYP2D6 and who meet any of the following criteria:

・Patients with any degree of hepatic impairment (Child-Pugh class A, B, or C)

・Patients with normal hepatic function and who are receiving a moderate or strong CYP3A inhibitor

In the Precautions concerning Dosage and Administration section, the language concerning CYP2D6 genotyping and the language concerning adjustment of dosage and administration should be respectively revised as follows (revised language is underlined):

CYP2D6 genotyping:

The CYP2D6 genotype, hepatic function, and concomitant medications of the patient should be confirmed prior to the initiation of this drug. Patient hepatic function and the status of concomitant medications should also be carefully monitored during use of this drug.

Adjustment of dosage and administration:

For EMs of CYP2D6, the dosage and administration of this drug should be adjusted based on the table below, at 100 mg per dose. This drug should not be administered to patients with moderate to severe hepatic impairment (Child-Pugh class B or C).

Patients with normal hepatic function

		Co-administration of a CYP3A inhibitor Note)		
		No co-administration	Weak inhibitor	Moderate or strong inhibitor
Co-administration of a CYP2D6	No co-administration	Twice daily	Twice daily	Once daily
	Weak inhibitor	Twice daily	Twice daily	Once daily

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inhibitor Note)	Moderate or strong inhibitor	Once daily	Once daily	Contraindicated

Patients with mild hepatic impairment (Child-Pugh class A)

		Co-administration of a CYP3A inhibitor Note)		
		No co-administration	Weak inhibitor	Moderate or strong inhibitor
Co-administration of a CYP2D6 inhibitor Note)	No co-administration	Twice daily	Once daily	Once daily
	Weak inhibitor	Once daily	Once daily	Contraindicated
	Moderate or strong inhibitor	Contraindicated	Contraindicated	Contraindicated

For IMs of CYP2D6, the dosage and administration of this drug should be adjusted based on the table below, at 100 mg per dose. This drug should not be administered to patients with hepatic impairment (Child-Pugh class A, B, or C).

Patients with normal hepatic function

		Co-administration of a CYP3A inhibitor Note)		
		No co-administration	Weak inhibitor	Moderate or strong inhibitor
Co-administration of a CYP2D6 inhibitor Note)	No co-administration	Twice daily	Twice daily	Contraindicated
	Weak inhibitor	Twice daily	Twice daily	Contraindicated
	Moderate or strong inhibitor	Once daily	Once daily	Contraindicated

Administration of this drug should ideally be avoided in PMs of CYP2D6, due to the risk

of elevation of the plasma concentration of eliglustat. When determined to be absolutely necessary, this drug should be administered carefully, and generally at a dosage of 100 mg once daily. This drug should not be given to any patient with hepatic impairment (Child-Pugh class A, B, or C) or any patient receiving a moderate or strong CYP3A inhibitor.

Note: Refer to the Interactions section regarding CYP2D6 and CYP3A inhibitors and confirm the applicability of any contraindicated drugs or drugs requiring adjustment of dosage and administration.

The following language should be added to the Contraindication for Co-administration subsection of the Interactions section (revised language is underlined):

Patients who are EMs of CYP2D6 with mild hepatic impairment (Child-Pugh class A): Moderate or strong CYP2D6 inhibitors
Co-administration of a weak CYP2D6 inhibitor and a moderate or strong CYP3A inhibitor
Class IA antiarrhythmic agents (quinidine, procainamide, etc.), Class III antiarrhythmic agents (amiodarone, sotalol, etc.), bepridil hydrochloride