This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Summary of Investigation Results

Venetoclax

Posaconazole

December 8, 2020

Non-proprietary name

a. Venetoclax

b. Posaconazole

Branded name (Marketing authorization holder)

a. Venclexta Tablets 10 mg, 50 mg, 100 mg (AbbVie GK)

b. Noxafil Tablets 100 mg, Noxafil for Intravenous Infusion 300 mg (MSD K.K.)

Indications

a. Relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)

b. · Prophylaxis of deep mycosis in haematopoietic stem cell transplant patients or patients with haematological malignancy who are expected to have neutropenia
· Treatment of the following fungal infections
Fusariosis, mucormycosis, coccidioidomycosis, chromoblastomycosis, mycetoma

Summary of revisions

a.

1. “Posaconazole” should be added to the “Potent CYP3A inhibitors during the dose escalation phase of this drug” in the CONTRAINDICATIONS section
2. “Posaconazole” should be added to the “Potent CYP3A inhibitors during the dose escalation phase of this drug” in the Contraindications for Co-administration section.
3. “Posaconazole” should be added to the “Potent CYP3A inhibitors during the

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maintenance phase of this drug" in the Precautions for Co-administration section.

b.

1. "Patients receiving venetoclax (during its dose escalation phase)" should be added to the CONTRAINDICATIONS section.
2. "Venetoclax (during its dose escalation phase)" should be added to the Contraindications for Co-administration section.
3. "Venetoclax (during its maintenance phase)" should be added to the Precautions for Co-administration section.

Investigation results and background of the revision

As a result of the co-administration study of venetoclax and posaconazole, increased blood concentrations of venetoclax were observed when co-administered with posaconazole compared to when venetoclax is administered alone. Considering the possibility of the risk of an adverse drug reaction such as tumor lysis syndrome increased by elevated blood concentrations of venetoclax, MHLW/PMDA in consultation with expert advisors concluded that revision of the package insert was necessary.

Number of cases and patient mortalities reported in Japan during the previous 3 fiscal years

No cases of co-administration of venetoclax and posaconazole have been reported to date.
(Japanese market launch: a: November 2019, b: April 2020)

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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