



Summary of Investigation Results

Preparations containing azelnidipine

Posaconazole

Fosravuconazole L-lysine ethanolate

August 27, 2024

Non-proprietary name

- a. Azelnidipine
- b. Olmesartan medoxomil/azelnidipine
- c. Posaconazole
- d. Fosravuconazole L-lysine ethanolate

Brand name (marketing authorization holder)

- a. Calblock Tablets 8 mg, 16 mg (Daiichi Sankyo Co., Ltd.), and the others
- b. Rezaltas Combination Tablets LD, HD (Daiichi Sankyo Co., Ltd.)
- c. Noxafil Tablets 100 mg, Noxafil for Intravenous Infusion 300 mg (MSD K.K.)
- d. Nailin Capsules 100 mg (Sato Pharmaceutical Co., Ltd.)

Japanese market launch

- a. May 2003
- b. April 2010
- c. Tablets 100 mg: April 2020
Intravenous Infusion 300 mg: July 2020
- d. July 2018

Indications

- a. Hypertension
- b. Hypertension
- c. •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
Invasive aspergillosis, fusarium infection, mucormycosis, coccidioidomycosis, chromoblastomycosis, mycetoma
- d. <Applicable microorganisms>
Dermatophyte (genus *Trichophyton*)
<Applicable conditions>
Nail tinea

Summary of revisions

a., b.

1. “Patients receiving posaconazole” should be added to the 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.) section.
2. “Posaconazole” should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.
3. “Azoles (excluding drugs which are contraindicated for co-administration) such as fosravuconazole” should be added to the 10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.) in 10. INTERACTIONS.

c.

1. “Patients receiving azelnidipine, olmesartan medoxomil/azelnidipine” should be added to the 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.) section.
2. “Azelnidipine, olmesartan medoxomil/azelnidipine” should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.

d.

“Azelnidipine” should be added to the 10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.) in 10. INTERACTIONS.

Investigation results and background of the revision

<Co-administration of posaconazole and preparations containing azelnidipine >

The pharmacokinetic effects and post-marketing safety information concerning co-

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administration of posaconazole and azelnidipine were evaluated. As a result of consultation with expert advisors, the MHLW/PMDA concluded that revising PRECAUTIONS to list the co-administration of these drugs in the Contraindications for Co-administration section was necessary for the following reason:

- Based on the analysis of physiological pharmacokinetic models, when posaconazole, a potent CYP3A inhibitor, is co-administered with azelnidipine, it is expected that the AUC of azelnidipine increases approximately 5-fold, raising concerns about the occurrence of adverse reactions.

Of note, opinions from relevant academic societies were solicited regarding the influence on clinical settings of contraindicating co-administration of posaconazole and preparations containing azelnidipine, revealing no specific concerns.

<Co-administration of fosravuconazole and preparations containing azelnidipine>

The pharmacokinetic effects and post-marketing safety information concerning co-administration of fosravuconazole and azelnidipine were evaluated. As a result of consultation with expert advisors, the MHLW/PMDA concluded that revising PRECAUTIONS to list the co-administration of these drugs in the Precautions for Co-administration section was necessary for the following reason.

- Since azelnidipine is metabolized mainly by CYP3A4, when fosravuconazole, which is a moderate CYP3A inhibitor, is co-administered with azelnidipine, the increase in the AUC of azelnidipine is assumed to be comparable to that of midazolam (approximately 3-fold)*, which is the representative substrate of CYP3A. However, considering the dose adjustment range of azelnidipine, fosravuconazole and azelnidipine may be co-administered in some cases if risk minimization measures such as dose adjustment are taken.

*Electronic package of Nailin Capsules 100 mg