



独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

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Summary of Investigation Results

Eplerenone Voriconazole Posaconazole

May 20, 2025

Non-proprietary name

- a. Eplerenone
- b. Voriconazole
- c. Posaconazole

Brand name (marketing authorization holder)

- a. Selara Tablets 25 mg, 50 mg, 100 mg (Viatris Pharmaceuticals Japan G.K.), and the others
- b. Vfend Tablets 50 mg, 200 mg, Vfend for Intravenous Use 200 mg, Vfend Dry Syrup 2800 mg (Pfizer Japan Inc.), and the others
- c. Noxafil Tablets 100 mg, Noxafil for Intravenous Infusion 300 mg (MSD K.K.)

Japanese market launch

- a. November 2007
- b. June 2005 (tablets, intravenous infusion), December 2014 (dry syrup)
- c. April 2020 (tablets), July 2020 (intravenous infusion)

Indications

See attachment.

Summary of revisions

- a.
- 1. "Voriconazole, posaconazole" should be added to 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.).

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2. "Voriconazole, posaconazole" should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.

b., c.

1. "Eplerenone" should be added to 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.).
2. "Eplerenone" should be added to the 10.1 Contraindications for Co-administration (Do not co-administer with the following.) section in 10. INTERACTIONS.

Investigation results and background of the revision

Pharmacokinetic effects and post-marketing safety information regarding the co-administration of eplerenone with voriconazole or posaconazole were evaluated. As a result of consultation with expert advisors, the MHLW/PMDA concluded that revising PRECAUTIONS to contraindicate the co-administration of these drugs was necessary for the following reasons:

- In the clinical drug-drug interaction studies in which ketoconazole, a strong CYP3A4 inhibitor, was co-administered, the exposure of eplerenone (AUC) increased by approximately 5.4-fold. Taking into account the fact, drugs with a strong CYP3A inhibitory activity comparable to that of ketoconazole (such as itraconazole) have been contraindicated for co-administration since the marketing approval of eplerenone.
- There are no results of clinical drug-drug interaction studies of eplerenone with voriconazole or posaconazole. However, it is known that voriconazole and posaconazole strongly inhibit CYP3A*. When eplerenone is co-administered with these drugs, there is a concern that the plasma concentration of eplerenone increases markedly, and the risk of adverse reactions increases.

Of note, opinions regarding the impacts of contraindicating co-administration of eplerenone with voriconazole or posaconazole in clinical settings were sought from relevant academic societies, confirming that there were no specific problems.

*Electronic package insert of voriconazole or that of posaconazole

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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Attachment

	Non-proprietary name	Indications
a.	Eplerenone	<Selara Tablets 25 mg, 50 mg, and 100 mg> Hypertension < Selara Tablets 25, 50 mg> Patients with the following disease who are receiving basic treatment with angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists, β -blockers, diuretics, etc.: Chronic heart failure
b.	Voriconazole	<Vfend Tablets 50 mg, 200 mg, Vfend Dry Syrup 2800> •The following severe or refractory fungal infections ·Invasive aspergillosis, pulmonary aspergilloma, chronic necrotic pulmonary aspergillosis ·Candidaemia, oesophageal candidiasis, candida peritonitis, bronchial/pulmonary candidiasis ·Cryptococcal meningitis, pulmonary cryptococcosis ·Fusariosis ·Scedosporiosis •Prophylaxis of deep mycosis in haematopoietic stem cell transplant patients <Vfend for Intravenous Use 200 mg> •The following severe or refractory fungal infections ·Invasive aspergillosis, pulmonary aspergilloma, chronic necrotic pulmonary aspergillosis



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		<ul style="list-style-type: none">·Candidaemia, candida peritonitis, bronchial/pulmonary candidiasis·Cryptococcal meningitis, pulmonary cryptococcosis·Fusariosis·Scedosporiosis•Prophylaxis of deep mycosis in haematopoietic stem cell transplant patients
c.	Posaconazole	<p><Noxafil Tablets 100 mg, Noxafil for Intravenous Infusion 300 mg></p> <ul style="list-style-type: none">•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 <p>Invasive aspergillosis, fusarium infection, mucormycosis, coccidioidomycosis, chromoblastomycosis, mycetoma</p>