Summary of Investigation Results

Rivaroxaban
Posaconazole

May 8, 2024

Non-proprietary name

a. Rivaroxaban

b. Posaconazole

Brand name (marketing authorization holder)

a. Xarelto tablets 2.5 mg, 10 mg, 15 mg, Xarelto OD tablets 10 mg, 15 mg, Xarelto fine granules 10 mg, 15 mg, Xarelto dry syrup for pediatric 51.7 mg, 103.4 mg (Bayer Yakuhin Ltd.)

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

Japanese market launch

a. Xarelto tablets 2.5 mg: October 2022
Xarelto tablets 10 mg, 15 mg: April 2012
Xarelto OD tablets 10 mg, 15 mg: January 2021
Xarelto fine granules 10 mg, 15 mg: December 2015
Xarelto dry syrup for pediatric 51.7 mg, 103.4 mg: July 2021

b. Noxafil Tablets 100 mg: April 2020
Noxafil for Intravenous Infusion 300 mg: July 2020

Indications

a. <Xarelto Tablets 2.5 mg>
Adults
•Prevention of thrombus/embolization formation in patients with peripheral arterial

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

disease after lower limb revascularization surgery

Children

•Prevention of thrombus/embolus formation after Fontan surgery

<Xarelto tablets 10 mg, 15 mg, Xarelto OD tablets 10 mg, 15 mg, Xarelto fine granules 10 mg, 15 mg>

Adults

•Prevention of ischaemic stroke and systemic embolism in patients with non-valvular atrial fibrillation

•Treatment and prevention of the relapse of venous thromboembolism (deep vein thrombosis and pulmonary thromboembolism)

Children

•Treatment and prevention of the relapse of venous thromboembolism

•Prevention of thrombus/embolus formation after Fontan surgery

<Xarelto dry syrup for pediatric 51.7 mg, 103.4 mg>

•Treatment and prevention of the relapse of venous thromboembolism

•Prevention of thrombus/embolus formation after Fontan surgery

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

Invasive aspergillosis, fusarium infection, mucormycosis, coccidioidomycosis, chromoblastomycosis, mycetoma

Summary of revisions

a.

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.

b.

1. “Patients receiving rivaroxaban” should be added to the 2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.) section.

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

2. “Rivaroxaban” 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

The degree of increased exposure to rivaroxaban when co-administered with posaconazole was evaluated based on the published literature*, etc. As a result of consultation with expert advisors, it was considered that the blood concentration of rivaroxaban may rise due to the potent inhibition of CYP3A4 by posaconazole, as well as the inhibition of P-glycoprotein, resulting in the enhancement of the anticoagulant effect of rivaroxaban and concerns about haemorrhage. Therefore, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

*: Clin Pharmacokinet. 2022 ;61:97-109, Antimicrob Agents Chemother. 2016 ;60:3372-9

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).

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp