Published by
Ministry of Health, Labour and Welfare

Translated by
Pharmaceuticals and Medical Devices Agency

Revision of Precautions

Riociguat

September 13, 2022

Therapeutic category

Other cardiovascular agents

Non-proprietary name

Riociguat

Safety measure

Precautions should be revised.

Pharmaceuticals and Medical Devices Agency

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

Revision in line with the Instructions for Electronic Package Inserts of Prescription Drugs, etc. PSEHB Notification No. 0611-1 by the Director of Pharmaceutical Safety and Environmental Health Bureau, MHLW, dated June 11, 2021 (New instructions):

Revised language is underlined.

<table>
<tr><th>Current</th><th>Revision</th></tr>
<tr><td>
2. CONTRAINDICATIONS
Patients receiving azoles (itraconazole, voriconazole), HIV protease inhibitors (ritonavir, lopinavir/ritonavir, indinavir, atazanavir, saquinavir), or ombitasvir/paritaprevir/ritonavir

10. INTERACTIONS
10.1 Contraindications for Co-administration
<table>
<tr><th>Drugs</th><th>Signs, Symptoms, and Treatment</th><th>Mechanism and Risk Factors</th></tr>
<tr><td>HIV protease inhibitors (ritonavir, lopinavir/ritonavir, indinavir, atazanavir, saquinavir)</td><td>When co-administered with ketoconazole (oral dosage form, not marketed in Japan), the AUC and C_{max} of riociguat were increased by 150% and 46%, respectively. In addition, the</td><td>The clearance of riociguat is decreased by the inhibition of multiple CYP isoforms (CYP1A1, CYP3A, etc.) and P-gp/BCRP.</td></tr>
</table>
</td><td>
2. CONTRAINDICATIONS
Patients receiving azoles (itraconazole, voriconazole), HIV protease inhibitors (indinavir, saquinavir), or ombitasvir/paritaprevir/ritonavir

10. INTERACTIONS
10.1 Contraindications for Co-administration
<table>
<tr><th>Drugs</th><th>Signs, Symptoms, and Treatment</th><th>Mechanism and Risk Factors</th></tr>
<tr><td>HIV protease inhibitors (indinavir, saquinavir)</td><td>When co-administered with ketoconazole (oral dosage form, not marketed in Japan), the AUC and C_{max} of riociguat were increased by 150% and 46%, respectively. In addition, the</td><td>The clearance of riociguat is decreased by the inhibition of multiple CYP isoforms (CYP1A1, CYP3A, etc.) and P-gp/BCRP.</td></tr>
</table>
</td></tr>
</table>

Pharmaceuticals and Medical Devices Agency

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

	elimination half-life was prolonged, and the clearance was decreased.	

10.2 Precautions for Co-administration

(N/A)

	elimination half-life was prolonged, and the clearance was decreased.	

10.2 Precautions for Co-administration

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Preparations containing ritonavir, atazanavir	The blood concentration of riociguat may increase. If administration of riociguat is started in patients being treated with these drugs, starting at a dose of 0.5 mg 3 times a day should also be considered.	The clearance of riociguat is decreased by the inhibition of CYP1A1 and/or CYP3A by these drugs.

(Reference) DeJesus,E.,et al.:Pulm.Circ. 2019;9:1-10

N/A: Not Applicable. No corresponding language is included in the current Precautions.