

This document is an English-translated version of an attachment of a notification for Revision of PRECAUTIONS issued by the Ministry of Health, Labour and Welfare.

This English version is intended to be a reference material to provide convenience for users.

In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Revision of PRECAUTIONS

Riociguat

May 20, 2025

Therapeutic category

Other cardiovascular agents

Non-proprietary name

Riociguat

Safety measure

PRECAUTIONS should be revised.

Revised language is underlined.

Current	Revision												
<p>2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)</p> <p><u>Patients receiving azole antifungal drugs (itraconazole, voriconazole)</u></p> <p>10. INTERACTIONS</p> <p>10.1 Contraindications for Co-administration (Do not co-administer with the following.)</p> <table><tr><th>Drugs</th><th>Signs, symptoms, and treatment</th><th>Mechanism/risk factors</th></tr><tr><td><u>Azole antifungal drugs</u> <u>Itraconazole</u> <u>Voriconazole</u></td><td><u>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 elimination half-life was prolonged, and the clearance was also decreased.</u></td><td><u>The clearance of riociguat is decreased by the inhibition of multiple CYP isoforms (CYP1A1, CYP3A, etc.) and P-gp/BCRP.</u></td></tr></table> <p>10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.)</p> <p>(N/A)</p>	Drugs	Signs, symptoms, and treatment	Mechanism/risk factors	<u>Azole antifungal drugs</u> <u>Itraconazole</u> <u>Voriconazole</u>	<u>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 elimination half-life was prolonged, and the clearance was also decreased.</u>	<u>The clearance of riociguat is decreased by the inhibition of multiple CYP isoforms (CYP1A1, CYP3A, etc.) and P-gp/BCRP.</u>	<p>2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)</p> <p>(deleted)</p> <p>10. INTERACTIONS</p> <p>10.1 Contraindications for Co-administration (Do not co-administer with the following.)</p> <p>(deleted)</p> <p>10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.)</p> <table><tr><th>Drugs</th><th>Signs, symptoms, and treatment</th><th>Mechanism/risk factors</th></tr><tr><td><u>Itraconazole</u> <u>Voriconazole</u></td><td><u>The blood concentration of riociguat may increase. If administration of riociguat is started in patients being</u></td><td><u>The clearance of riociguat is decreased by the inhibition of</u></td></tr></table>	Drugs	Signs, symptoms, and treatment	Mechanism/risk factors	<u>Itraconazole</u> <u>Voriconazole</u>	<u>The blood concentration of riociguat may increase. If administration of riociguat is started in patients being</u>	<u>The clearance of riociguat is decreased by the inhibition of</u>
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		<p><u>treated with these drugs, starting at a dose of 0.5 mg 3 times a day should also be considered.</u></p> <p><u>If administration of these drugs is started while receiving riociguat, dose reduction of riociguat should be considered.</u></p>	<p><u>CYP1A1 and/or CYP3A by these drugs.</u></p>
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