

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

Macitentan/tadalafil

March 17, 2026

Therapeutic category

Other cardiovascular agents

Non-proprietary name

Macitentan/tadalafil

Safety measure

PRECAUTIONS should be revised.

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Revised language is underlined.

| Current | | | Revision | | |
|---|---|---|---|---|---|
| <p>2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)</p> <p>Patients receiving a strong CYP3A4 inhibitor (itraconazole, preparations containing ritonavir, atazanavir, preparations containing darunavir, clarithromycin, preparations containing cobicistat, ensitrelvir)</p> | | | <p>2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)</p> <p>Patients receiving a strong CYP3A4 inhibitor (itraconazole, preparations containing ritonavir, atazanavir, preparations containing darunavir, clarithromycin, preparations containing cobicistat, ensitrelvir, <u>ceritinib</u>)</p> | | |
| <p>10. INTERACTIONS</p> <p>10.1 Contraindications for Co-administration (Do not co-administer with the following.)</p> | | | <p>10. INTERACTIONS</p> <p>10.1 Contraindications for Co-administration (Do not co-administer with the following.)</p> | | |
| Drugs | Signs, symptoms, and treatment | Mechanism/risk factors | Drugs | Signs, symptoms, and treatment | Mechanism/risk factors |
| <p>Strong CYP3A4 inhibitors</p> <p>Itraconazole</p> <p>Preparations containing ritonavir</p> <p>Atazanavir</p> <p>Preparations containing darunavir</p> <p>Clarithromycin</p> <p>Preparations containing cobicistat</p> <p>Ensitrelvir</p> | <p>The blood concentrations of macitentan and tadalafil may increase, which may make adverse reactions to this drug more likely to occur.</p> | <p>Strong CYP3A4 inhibition increases exposure to macitentan and tadalafil.</p> | <p>Strong CYP3A4 inhibitors</p> <p>Itraconazole</p> <p>Preparations containing ritonavir</p> <p>Atazanavir</p> <p>Preparations containing darunavir</p> <p>Clarithromycin</p> <p>Preparations containing cobicistat</p> <p>Ensitrelvir</p> <p><u>Ceritinib</u></p> | <p>The blood concentrations of macitentan and tadalafil may increase, which may make adverse reactions to this drug more likely to occur.</p> | <p>Strong CYP3A4 inhibition increases exposure to macitentan and tadalafil.</p> |