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Pharmaceuticals and Medical Devices Agency

Revision of Precautions

Ritonavir

September 13, 2022

Therapeutic category

Anti-virus agents

Non-proprietary name

Ritonavir

Safety measure

Precautions should be revised.

Pharmaceuticals and Medical Devices Agency

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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 the following drugs: Quinidine sulfate hydrate, bepridil hydrochloride hydrate, flecainide acetate, propafenone hydrochloride, amiodarone hydrochloride, pimozide, piroxicam, ampiroxicam, ergotamine tartrate/anhydrous caffeine/isopropylantipyrine, dihydroergotamine mesilate, ergometrine maleate, methylergometrine maleate, eletriptan hydrobromide, vardenafil hydrochloride hydrate, sildenafil citrate (Revatio), tadalafil (Adcirca), azelnidipine, azelnidipine/olmesartan medoxomil, rifabutin, blonanserin, rivaroxaban, lomitapide mesilate, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)], diazepam, clorazepate dipotassium, estazolam, flurazepam hydrochloride, triazolam, midazolam, lurasidone hydrochloride, <u>riociguat,</u> or voriconazole

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><u>Riociguat</u></td><td><u>It has been reported</u></td><td><u>The inhibitory activity</u></td></tr>
</table>
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	that the blood concentration of riociguat was increased and the clearance of riociguat was decreased when co-administered with ketoconazole.	of ritonavir against cytochrome P450 and transporters (P-gp, BCRP) may cause similar drug interactions.

10.2 Precautions for Co-administration

(N/A)

10.2 Precautions for Co-administration

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Riociguat	The blood concentration of riociguat may increase. When co-administration with ritonavir is necessary, patients should be monitored for their conditions and dose reduction of riociguat should be considered as necessary.	The clearance of riociguat is decreased by the inhibition of CYP1A1 and CYP3A by ritonavir.

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