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*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

## Lopinavir/ritonavir

September 13, 2022

### **Therapeutic category**

Anti-virus agents

### **Non-proprietary name**

Lopinavir/ritonavir

### **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](mailto: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.

Current			Revision		
<p>2. CONTRAINDICATIONS</p> <p>Patients receiving the following drugs: Pimozide, ergotamine tartrate/anhydrous caffeine/isopropylantipyrine, dihydroergotamine mesilate, ergometrine maleate, methylergometrine maleate, midazolam, triazolam, lurasidone hydrochloride, vardenafil hydrochloride hydrate, sildenafil citrate (Revatio), tadalafil (Adcirca), blonanserin, azelnidipine, azelnidipine/olmesartan medoxomil, rivaroxaban, lomitapide mesilate, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)], <u>riociguat</u>, voriconazole, or grazoprevir hydrate</p>			<p>2. CONTRAINDICATIONS</p> <p>Patients receiving the following drugs: Pimozide, ergotamine tartrate/anhydrous caffeine/isopropylantipyrine, dihydroergotamine mesilate, ergometrine maleate, methylergometrine maleate, midazolam, triazolam, lurasidone hydrochloride, vardenafil hydrochloride hydrate, sildenafil citrate (Revatio), tadalafil (Adcirca), blonanserin, azelnidipine, azelnidipine/olmesartan medoxomil, rivaroxaban, lomitapide mesilate, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)], voriconazole, or grazoprevir hydrate</p>		
<p>10. INTERACTIONS</p> <p>10.1 Contraindications for Co-administration</p>			<p>10. INTERACTIONS</p> <p>10.1 Contraindications for Co-administration</p>		
Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors	(deleted)		
<u>Riociguat</u>	<u>It has been reported that the blood concentration of riociguat was increased and the clearance of</u>	<u>The inhibitory activity of lopinavir/ritonavir against cytochrome P450 and that of ritonavir against</u>			

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	<u>riociguat was decreased when co-administered with ketoconazole.</u>	<u>transporters (P-gp, BCRP) may cause similar drug interactions.</u>							
<p>10.2 Precautions for Co-administration (N/A)</p>			<p>10.2 Precautions for Co-administration</p> <table border="1"> <thead> <tr> <th data-bbox="1131 443 1391 539">Drugs</th> <th data-bbox="1391 443 1697 539">Signs, Symptoms, and Treatment</th> <th data-bbox="1697 443 2000 539">Mechanism and Risk Factors</th> </tr> </thead> <tbody> <tr> <td data-bbox="1131 539 1391 1118"><u>Riociguat</u></td> <td data-bbox="1391 539 1697 1118"><u>The blood concentration of riociguat may increase. When co-administration with lopinavir/ritonavir is necessary, patients should be monitored for their conditions and dose reduction of riociguat should be considered as necessary.</u></td> <td data-bbox="1697 539 2000 1118"><u>The clearance of riociguat is decreased by the inhibition of CYP1A1 and CYP3A by lopinavir/ritonavir.</u></td> </tr> </tbody> </table>	Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors	<u>Riociguat</u>	<u>The blood concentration of riociguat may increase. When co-administration with lopinavir/ritonavir is necessary, patients should be monitored for their conditions and dose reduction of riociguat should be considered as necessary.</u>	<u>The clearance of riociguat is decreased by the inhibition of CYP1A1 and CYP3A by lopinavir/ritonavir.</u>
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N/A: Not Applicable. No corresponding language is included in the current Precautions.

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