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Translated by Pharmaceuticals and Medical Devices Agency



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 Istradefylline

September 7, 2021

**Therapeutic category** 

Antiparkinsonism agents

Non-proprietary name

Istradefylline

**Safety measure** Precautions should be revised in the package insert.

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Thamaceulical Alians Dureau, Mir M, daleu April 25, 1997 (Olu Instructi							
Current				Revision			
Precautions concerning Dosage and Administration				Precautions concerning Dosage and Administration			
The blood concentration of this drug may increase in the following				The blood concentration of this drug may increase in the following			
patients. The dosage	e should not exceed 20	mg once daily.		patients. The dosage should not exceed 20 mg once daily.			
· Patients with mode	rate liver disorder			· Patients with moderate liver disorder			
· Patients receiving o	drugs that strongly inhib	it <u>CYP3A4</u>		· Patients receiving o	lrugs that strongly inhib	oit <u>CYP3A</u>	
Drug Interactions				Drug Interactions			
This drug is mainly r	metabolized by CYP1A	1 <u>,</u> CYP3A4, and		This drug is mainly metabolized by CYP1A1 and CYP3A (CYP3A4			
CYP3A5. In addition	, this drug inhibits <u>CYP</u>	<u>3A4/5</u> and P-		and CYP3A5). In addition, this drug inhibits <u>CYP3A</u> and P-			
glycoprotein.				glycoprotein.			
Precautions for Co-Ad	ministration			Precautions for Co-Administration			
Dimension	Signs, Symptoms,	Mechanism and		Drugs	Signs, Symptoms,	Mechanism and	
Drugs	and Treatment	<b>Risk Factors</b>			and Treatment	Risk Factors	
Drugs that strongly	When co-	Co-administration		Drugs that strongly	When co-	Co-administration	
inhibit <u>CYP3A4</u>	administered at 40	with <u>CYP3A4</u>		inhibit <u>CYP3A</u>	administered at 40	with <u>CYP3A</u>	
(itraconazole,	mg with	inhibitors may inhibit		(itraconazole,	mg with	inhibitors may inhibit	
clarithromycin, etc.)	ketoconazole, the	metabolism and		clarithromycin, etc.)	ketoconazole, the	metabolism and	
	$AUC_{0-\infty}$ of this drug	increase the blood			AUC0- $\infty$ of this	increase the blood	
	increased 2.47 fold	concentration of this			drug increased 2.47	concentration of this	

Revision in line with the Instructions for Package Inserts of Prescription Drugs, PAB Notification No. 606 by the Director General ofPharmaceutical Affairs Bureau, MHW, dated April 25, 1997 (Old instructions):Revised language is underlined.

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	and t <sub>1/2</sub> extended	drug.		fold and t1/2	drug.
	1.87 fold. Effects of			extended 1.87 fold.	
	this drug may be			Effects of this drug	
	enhanced.			may be enhanced.	
	When co-			When co-	
	administered with			administered with	
	drugs that strongly			drugs that strongly	
	inhibit <u>CYP3A4</u> , the			inhibit CYP3A, the	
	dosage of this drug			dosage of this drug	
	should not exceed			should not exceed	
	20 mg once daily.			20 mg once daily.	
Drugs that inhibit	Effects of this drug		Drugs that inhibit	Effects of this drug	
CYP3A4	may be enhanced.		<u>CYP3A</u>	may be enhanced.	
(erythromycin,			(erythromycin,		
fluconazole, etc.)			fluconazole, etc.)		
Drugs that induce	Effects of this drug	Co-administration	Drugs that induce	Effects of this drug	Co-administration
CYP3A4	may be attenuated.	with <u>CYP3A4</u>	<u>CYP3A</u>	may be attenuated.	with CYP3A
(rifampicin,		inducers may	(rifampicin,		inducers may
carbamazepine,		promote metabolism	carbamazepine,		promote metabolism
etc.)		and decrease the	etc.)		and decrease the
Food containing St.		blood concentration	Food containing St.		blood concentration
John's Wort		of this drug.	John's Wort		of this drug.
Drugs that act as	Effects of the drugs	Co-administration	Drugs that act as	Effects of the drugs	Co-administration

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CYP3A4 substrates	listed on the left	with this drug may		CYP3A substrates	listed on the left	with this drug may
(midazolam,	may be enhanced.	inhibit metabolism		(midazolam,	may be enhanced.	inhibit metabolism
atorvastatin, etc.)		and increase the		atorvastatin <u>,</u>		and increase the
		blood concentration		lomitapide mesilate,		blood concentration
		of the drugs that act		etc.)		of the drugs that act
		as <u>CYP3A4</u>				as CYP3A
		substrates.				substrates.
			-			

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			
7. PRECAUTIONS CONCERNING DOSAGE AND	7. PRECAUTIONS CONCERNING DOSAGE AND			
ADMINISTRATION	ADMINISTRATION			
7.2 The blood concentration of this drug may increase in the following	7.2 The blood concentration of this drug may increase in the following			
patients. The dosage should not exceed 20 mg once daily.	patients. The dosage should not exceed 20 mg once daily.			
· Patients with moderate liver disorder	· Patients with moderate liver disorder			
<ul> <li>Patients receiving drugs that strongly inhibit <u>CYP3A4</u></li> </ul>	<ul> <li>Patients receiving drugs that strongly inhibit <u>CYP3A</u></li> </ul>			
10. INTERACTIONS	10. INTERACTIONS			
This drug is mainly metabolized by CYP1A1, CYP3A4, and	This drug is mainly metabolized by CYP1A1 and CYP3A (CYP3A4			
CYP3A5. In addition, this drug inhibits <u>CYP3A4/5</u> and P-	and CYP3A5). In addition, this drug inhibits CYP3A and P-			

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glycoprotein.			Τ	glycoprotein.			
10.2 Precautions for Co-Administration				10.2 Precautions for Co-Administration			
Drugo	Signs, Symptoms,	Mechanism and		Drugs	Signs, Symptoms,	Mechanism and	
Drugs	and Treatment	Risk Factors			and Treatment	Risk Factors	
Drugs that strongly	Effects of this drug	Co-administration		Drugs that strongly	Effects of this drug	Co-administration	
inhibit <u>CYP3A4</u>	may be enhanced.	with <u>CYP3A4</u>		inhibit <u>CYP3A</u>	may be enhanced.	with <u>CYP3A</u>	
(itraconazole,		inhibitors may inhibit		(itraconazole,		inhibitors may inhibit	
clarithromycin, etc.)		metabolism and		clarithromycin, etc.)		metabolism and	
		increase the blood				increase the blood	
		concentration of this				concentration of this	
		drug.				drug.	
		The $AUC_{0-\infty}$ of this				The $AUC_{0-\infty}$ of this	
		drug increased and				drug increased and	
		t <sub>1/2</sub> extended when				t <sub>1/2</sub> extended when	
		co-administered				co-administered	
		with ketoconazole.				with ketoconazole.	
Drugs that inhibit	Effects of this drug	Co-administration		Drugs that inhibit	Effects of this drug	Co-administration	
CYP3A4	may be enhanced.	with CYP3A4		<u>CYP3A</u>	may be enhanced.	with <u>CYP3A</u>	
(erythromycin,		inhibitors may inhibit		(erythromycin,		inhibitors may inhibit	
fluconazole, etc.)		metabolism and		fluconazole, etc.)		metabolism and	
		increase the blood				increase the blood	
		concentration of this				concentration of this	
		drug.				drug.	
Drugs that induce	Effects of this drug	Co-administration		Drugs that induce	Effects of this drug	Co-administration	

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CYP3A4 (rifampicin,	may be attenuated.	with <u>CYP3A4</u>	<u>CYP3A</u> (rifampicin,	may be attenuated.	with <u>CYP3A</u>
carbamazepine,		inducers may	carbamazepine,		inducers may
etc.)		promote metabolism	etc.)		promote metabolism
Food containing St.		and decrease the	Food containing St.		and decrease the
John's Wort		blood concentration	John's Wort		blood concentration
		of this drug.			of this drug.
Drugs that act as	Effects of the drugs	Co-administration	Drugs that act as	Effects of the drugs	Co-administration
CYP3A4 substrates	listed on the left	with this drug may	CYP3A substrates	listed on the left	with this drug may
(midazolam,	may be enhanced.	inhibit metabolism	(midazolam,	may be enhanced.	inhibit metabolism
atorvastatin, etc.)		and increase the	atorvastatin <u>,</u>		and increase the
		blood concentration	lomitapide mesilate,		blood concentration
		of the drugs that act	etc.)		of the drugs that act
		as <u>CYP3A4</u>			as <u>CYP3A</u>
		substrates.			substrates.

Note: Designated as a drug requiring preparation of a Drug Guide for Patients

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