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Pharmaceuticals and Medical Devices Agency

Revision of PRECAUTIONS

Tramadol hydrochloride/acetaminophen

October 12, 2023

Therapeutic category

Antipyretics, analgesics and anti-inflammatory agents

Non-proprietary name

Tramadol hydrochloride/acetaminophen

Safety measure

PRECAUTIONS should be revised.

Pharmaceuticals and Medical Devices Agency

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

Current	Revision
Contraindications (This drug is contraindicated to the following patients.) Patients with peptic ulcer [Symptoms may be exacerbated.] Patients with serious blood abnormalities [Serious outcomes may occur.] Patients with serious renal disorder [Serious outcomes may occur.] Patients with serious cardiac function failure [The balance of the cardiovascular system may be compromised, and cardiac failure may be aggravated.] Patients with aspirin asthma (induction of asthmatic attack due to nonsteroidal preparation) [It is considered that the inhibitory activity of prostaglandin synthesis is involved in the onset of aspirin asthma.] Precautions for Dosage and Administration (N/A)	Contraindications (This drug is contraindicated to the following patients.) (deleted) (deleted) (deleted) (deleted) Patients with aspirin asthma (induction of asthmatic attack due to nonsteroidal anti-inflammatory drug) who have pain after tooth extraction [It is considered that the inhibitory activity of prostaglandin synthesis is involved in the onset of aspirin asthma.] Precautions for Dosage and Administration When this drug is administered to patients with aspirin asthma or a history of the disease who have chronic pain, the dose should be

	one tablet per dose.
Careful Administration (Careful administration of this drug is required in the following patients.) Patients with liver or renal disorder or a history of those diseases [Liver function or renal function may worsen. Also, the drug concentration in blood may remain high and the effect and adverse reactions may be enhanced.]	Careful Administration (Careful administration of this drug is required in the following patients.) Patients with liver disorder or a history of the disease [Liver function may worsen. Also, the drug concentration in blood may remain high and the effect and adverse reactions may be enhanced.] Patients with renal disorder or a history of the disease [Dose reduction and prolongation of dosing intervals should be considered. Symptoms may be exacerbated or recurrence may be promoted. Also, the drug concentration in blood may remain high and the effect and adverse reactions may be enhanced.]
Patients with a history of peptic ulcer [Recurrence of peptic ulcer may be promoted.]	Patients with peptic ulcer or a history of the disease [Symptoms may be exacerbated or recurrence may be promoted.]
Patients with blood abnormalities or a history of the disease [Blood disorder may occur.]	Patients with blood abnormalities or a history of the disease [Symptoms may be exacerbated or recurrence may be promoted.]
Patients with abnormal cardiac function [Symptoms may be exacerbated.]	Patients with abnormal cardiac function [Symptoms may be exacerbated or cardiac failure may be aggravated.]
(N/A)	Patients with aspirin asthma (induction of asthmatic attack due to

	nonsteroidal anti-inflammatory drug) or a history of the disease who have chronic pain [Adjusting the dose using not this drug but single active ingredient preparations containing acetaminophen should be considered. The maximum dose of acetaminophen for patients with aspirin asthma or a history of the disease should be 300 mg or less per dose. However, this drug contains 325 mg of acetaminophen per tablet. It is considered that the inhibitory activity of prostaglandin synthesis is involved in the onset of aspirin asthma, and the symptoms may be exacerbated or recurrence may be promoted.]

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

Revision in line with the Instructions for Electronic Package Inserts of Prescription Drugs, PSEHB Notification No. 0611-1 by the Director-General of Pharmaceutical Safety and Environmental Health Bureau, MHLW, dated June 11, 2021 (New instructions):

Revised language is underlined.

Current	Revision
2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.) Patients with peptic ulcer [Symptoms may be exacerbated.] Patients with serious blood abnormalities [Serious outcomes may occur.]	2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.) <Common to all indications> (deleted) (deleted)

Patients with serious renal disorder [Serious outcomes may occur.]	(deleted)
Patients with serious cardiac function failure [The balance of the cardiovascular system may be compromised, and cardiac failure may be aggravated.]	(deleted)
Patients with aspirin asthma (induction of asthmatic attack due to nonsteroidal preparation) or a history of the disease [It is considered that the inhibitory activity of prostaglandin synthesis is involved in the onset of aspirin asthma.]	<Pain after tooth extraction> Patients with aspirin asthma (induction of asthmatic attack due to nonsteroidal anti-inflammatory drug) or a history of the disease [It is considered that the inhibitory activity of prostaglandin synthesis is involved in the onset of aspirin asthma.]
7. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION <Non-cancerous chronic pain> (N/A)	7. PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION <Non-cancerous chronic pain> When this drug is administered to the patients with aspirin asthma or a history of the disease, the dose should be one tablet per dose.
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.1 Patients with Complication or History of Diseases, etc.	9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.1 Patients with Complication or History of Diseases, etc. <Common to all indications>
Patients with a history of peptic ulcer Recurrence of peptic ulcer may be promoted.	Patients with peptic ulcer or a history of the disease Symptoms may be exacerbated or recurrence may be promoted.

Patients with blood abnormalities or a history of the disease (excluding those with serious blood abnormalities) Blood disorder may occur.	Patients with blood abnormalities or a history of the disease Symptoms may be exacerbated or recurrence may be promoted.
Patients with abnormal cardiac function (excluding those with serious cardiac function failure) Symptoms may be exacerbated.	Patients with abnormal cardiac function Symptoms may be exacerbated or cardiac failure may be aggravated.
(N/A)	<Non-cancerous chronic pain> Patients with aspirin asthma (induction of asthmatic attack due to nonsteroidal anti-inflammatory drug) or a history of the disease Adjusting the dose using not this drug but single active ingredient preparations containing acetaminophen should be considered. The maximum dose of acetaminophen for patients with aspirin asthma or a history of the disease should be 300 mg or less per dose. However, this drug contains 325 mg of acetaminophen per tablet. It is considered that the inhibitory activity of prostaglandin synthesis is involved in the onset of aspirin asthma, and the symptoms may be exacerbated or recurrence may be promoted.
9.2 Patients with renal impairment Patients with serious renal disorder This drug should not be administered. Serious outcomes may occur.	9.2 Patients with renal impairment (deleted)

Patients with renal disorder or a history of the disease (excluding those with serious renal disorder) Renal function may worsen. Also, the drug concentration in blood may remain high and the effect and adverse reactions may be enhanced.	Patients with renal disorder or a history of the disease Dose reduction and prolongation of dosing intervals should be considered. Symptoms may be exacerbated or recurrence may be promoted. Also, the drug concentration in blood may remain high and the effect and adverse reactions may be enhanced.

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

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