

Summary of Investigation Results

Preparations containing acetaminophen (oral dosage form, suppositories, injections) (prescription drug)

January 17, 2023

Non-proprietary name

See attachment.

Brand name (marketing authorization holder)

See attachment.

Japanese market launch

See attachment.

Indications

See attachment.

Summary of revisions

“Drug-induced hypersensitivity syndrome” should be added to the Clinically Significant Adverse Reactions section.

Investigation results and background of the revision

Cases involving drug-induced hypersensitivity syndrome reported in Japan were evaluated. Cases for which a causal relationship between preparations containing acetaminophen and drug-induced hypersensitivity syndrome was reasonably possible have been reported in Japan. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of Precautions, MHLW/PMDA concluded that revision of Precautions was necessary.

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Reference: Number of cases* and patient mortalities involving drug-induced hypersensitivity syndrome reported in Japan

a.-c.

A total of 44 cases have been reported to date (including 6 cases for which a causal relationship between the drug and event was reasonably possible).

A total of 3 patient mortalities have been reported to date. (A causal relationship between the drug and deaths subsequent to the event could not be established for any of these cases.)

e.

A total of 3 cases have been reported to date. (A causal relationship between the drug and event could not be established for any of these cases.)

No patient mortalities have been reported to date.

i.

1 case has been reported to date. (A causal relationship between the drug and event could not be established for this case.)

No patient mortalities have been reported to date.

d., f.-h., j.

No cases have been reported to date.

*Cases collected in the PMDA's database for adverse drug reactions, etc. reports

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the "Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency" (PMDA Administrative Rule No. 20-8, dated December 25, 2008).

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.

Attachment

No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	Indications
a.	Acetaminophen (oral dosage form)	Calonal powder, Calonal tablets 200, 300, 500, Calonal Fine Gran. 20%, 50%, Calonal Syrup 2%, and the others	AYUMI Pharmaceutical Corporation, and the others	Powder: May 2010 Tablets 200: July 1996 Tablets 300: July 2003 Tablets 500: February 2015 Fine Gran. 20%: July 1984 Fine Gran. 50%: July 2003 Syrup: June 2000	<Powder, tablets, granules> ·Analgesia for the following diseases and symptoms: Headache, ear pain, symptomatic neuralgia, lumbago, myalgia, bruising pain, sprain pain, painful menses, postpartum pain, pain due to cancer, toothache, pain after dental treatment, osteoarthritis ·Antipyresis and analgesia for the following diseases: Acute upper respiratory inflammation (including acute upper respiratory inflammation associated with acute bronchitis) ·Antipyresis and analgesia in the field of pediatrics <syrup>

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No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	Indications
					Antipyresis and analgesia in the field of pediatrics
b.	Acetaminophen (suppositories)	(1) Alpiny Suppositories 50, 100, 200, and the others (2) Anhiba pediatric suppository 50 mg, 100 mg, 200 mg, and the others (3) Calonal Supp. 50 for Pediatric, Calonal Supp. 100, 200, 400, and the others	(1) Hisamitsu Pharmaceutical Co., Inc., and the others (2) Mylan EPD G.K., and the others (3) AYUMI Pharmaceutical Corporation, and the others	(1) 50 mg: July 1984 (1) 100 mg: February 1980 (1) 200 mg: July 1984 (2) 50 mg: July 1994 (2) 100 mg: February 1980 (2) 200 mg: September 1981 (3) 50 mg: January 2010 (3) 100 mg, 200 mg: October 1987 (3) 400 mg: July 2015	Antipyresis and analgesia in the field of pediatrics
c.	Acetaminophen (injections)	acelio Bag for Intravenous Injection 1000 mg	Terumo Corporation	February 2017	Pain and pyrexia when administration of oral preparations and suppositories is difficult
d.	Pyrazolone-based	SG Combination	Shionogi Pharma Co.,	July 2003	Antipyresis for common cold, ear pain, sore throat,

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	antipyretics, analgesics and anti-inflammatory combination drug (4)	Granules	Ltd.		painful menses, headache, toothache, symptomatic neuralgia, traumatic pain
e.	Tramadol hydrochloride/acetaminophen	Tramcet Combination Tablets, and the others	Janssen Pharmaceutical K.K., and the others	July 2011	Analgesia for the following diseases that cannot be managed by treatment with non-opioid analgesics: ·Non-cancerous chronic pain ·Pain after tooth extraction
f.	Diprophylline/dihydrocodeine phosphate/dl-methylephedrine hydrochloride/diphenhydramine salicylate/acetaminophen/	Coughcode-N Combination Tablets	Mylan EPD G.K.	August 2002	Antitussive, pain relief, and antipyresis in common cold syndrome Antitussive in bronchitis

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No.	Non-proprietary name	Brand name	Marketing authorization holder	Japanese market launch	Indications
	bromovalerylurea				
g.	Non-pyrine common cold medicine (2)	Pelex combination granule	TAIHO Pharmaceutical Co., Ltd.	September 1967	Improvement and alleviation in the following symptoms accompanying common cold or upper respiratory inflammation: Nasal discharge, nasal congestion, pharyngeal/laryngeal pain, cough, sputum, headache, arthralgia, myalgia, pyrexia
h.	Non-pyrine common cold medicine (3)	Pediatric Pelex combination granule	TAIHO Pharmaceutical Co., Ltd.	August 1972	Improvement and alleviation in the following symptoms accompanying common cold or upper respiratory inflammation: Nasal discharge, nasal congestion, pharyngeal/laryngeal pain, cough, sputum, headache, arthralgia, myalgia, pyrexia
i.	Non-pyrine common cold medicine (4)	PL Combination Granules, and the others	Shionogi Pharma Co., Ltd., and the others	February 1962	Improvement and alleviation in the following symptoms accompanying common cold or upper respiratory inflammation:

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					Nasal discharge, nasal congestion, pharyngeal/laryngeal pain, headache, arthralgia, myalgia, pyrexia
j.	Non-pyrine common cold medicine (5)	PL Combination Granules for Infants	Shionogi Pharma Co., Ltd.	April 1962	Improvement and alleviation in the following symptoms accompanying common cold or upper respiratory inflammation: Nasal discharge, nasal congestion, pharyngeal/laryngeal pain, headache, arthralgia, myalgia, pyrexia