Pharmaceuticals and Medical Devices Safety Information

No. 381 March 2021

Table of Contents

This *Pharmaceuticals and Medical Devices Safety Information (PMDSI)* publication is issued reflective of safety information collected by the Ministry of Health, Labour and Welfare (MHLW). It is intended to facilitate safer use of pharmaceuticals and medical devices by healthcare providers. The PMDSI is available on the Pharmaceuticals and Medical Devices Agency (PMDA) Medical Product Information web page (http://www.pmda.go.jp/english/index.html) and on the MHLW website (http://www.mhlw.go.jp/, only in Japanese).

Available information is listed here

Access to the latest safety information is available via the PMDA Medi-navi.

The PMDA Medi-navi is an e-mail mailing list service that serves to provide essential safety information released by MHLW and PMDA. Subscribing to the Medi-navi will allow you to receive this information on the day of its release.

Register here

Published by
Ministry of Health, Labour and Welfare

Pharmaceutical Safety and Environmental Health Bureau, Labour and Welfare,
Ministry of Health, Labour and Welfare
1-2-2 Kasumigaseki, Chiyoda-ku, Tokyo
100-8916 Japan

Translated by
Pharmaceuticals and Medical Devices Agency

Pharmaceuticals and Medical Devices Agency
3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo
100-0013 Japan E-mail: safety.info@pmda.go.jp

Pharmaceuticals and Medical Devices Safety Information

No. 381 March 2021

Ministry of Health, Labour and Welfare & Pharmaceutical Safety and Environmental Health Bureau, Labour and Welfare, Japan

[Outline of Information]

E: Distribution of Dear Healthcare Professional Letters of Emergency Communications, *R:* Distribution of Dear Healthcare Professional Letters of Rapid Communications, *P*: Revision of Precautions, *C*: Case Reports

Reporting of safety information such as adverse reactions to the Minister of Health, Labour and Welfare is a duty of medical and pharmaceutical providers.

If medical and pharmaceutical providers such as physicians, dentists, and pharmacists detect adverse reactions, infections associated with drugs or medical devices, or medical device adverse events, it is mandatory for such providers to report them to the Minister of Health, Labour and Welfare directly or through the marketing authorization holder. As medical and pharmaceutical providers, drugstore and pharmacy personnel are also required to report safety issues related to drugs and medical devices.

Abbreviations

ADR	Adverse drug reaction
BRAF	V-Raf murine sarcoma viral oncogene homolog B
EPPV	Early Post-marketing Phase Vigilance
FY	Fiscal Year
JFMDA	Japan Federation of Medical Devices Associations
MAH	Marketing authorization holder
MHLW	Ministry of Health, Labour and Welfare
PAH	Pulmonary arterial hypertension
PMDA	Pharmaceuticals and Medical Devices Agency
PSD	Pharmaceutical Safety Division
PSEHB	Pharmaceutical Safety and Environmental Health Bureau

1

Digitization of Package Inserts

1. Introduction

Digitization of package inserts, which was decided as a result of the revision of the Act on Securing Quality, Efficacy, and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960; hereinafter referred to as the "PMD Act") in 2019, will be implemented on August 1 of this year.

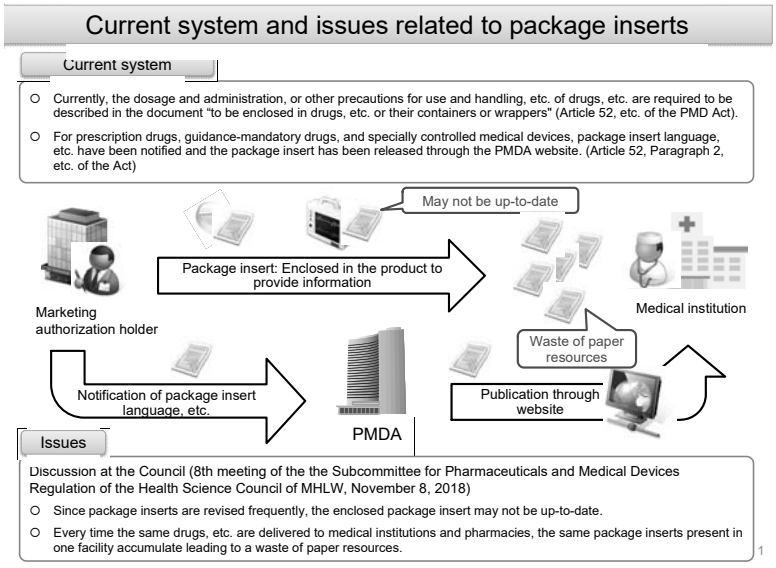
This section introduces the details of the digitization of package inserts.

2. Purpose and outline of revision

Under the current PMD Act, in order to communicate information on proper use and safety of drugs, medical devices, and cellular and tissue-based products, etc. (hereinafter referred to as "drugs, etc."), documents attached to drugs, etc. such as package inserts are used.

For provision of information on the proper use and safety of drugs, etc., it is necessary to have the latest scientific knowledge as the basis of such information. Communicating the latest information was found to be difficult, however, in the paper form because package inserts enclosed in the stock products of wholesalers and medical institutions for example are not updated regarding revisions of precautions that may be implemented.

In addition, the practice of enclosing identical package inserts in all identical products has been challenged as a waste of paper resources in consideration of identical drugs, etc. being delivered in large numbers to medical institutions.



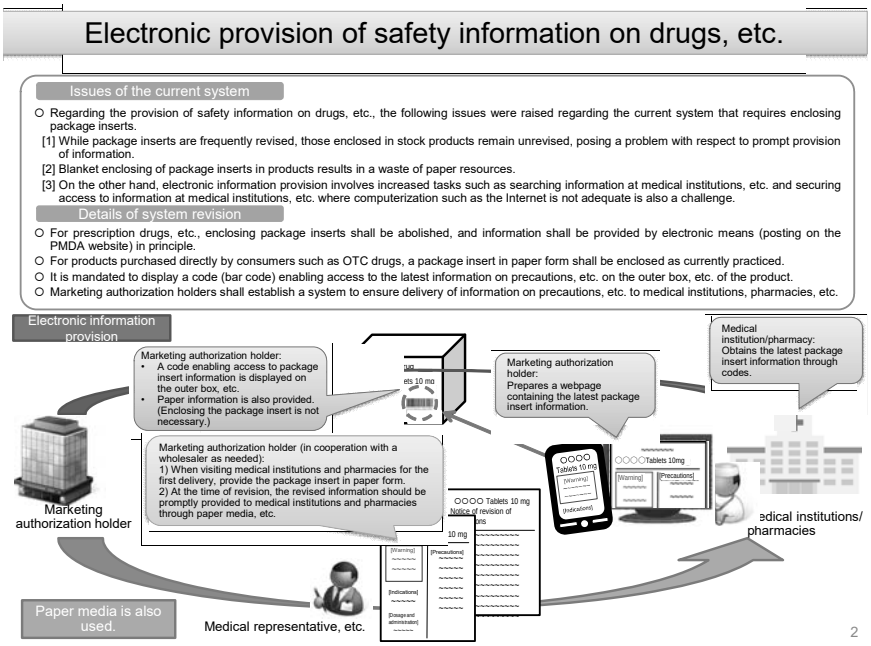
In view of these issues, provision of information on proper use and safety of drugs, etc. using paper-based media (package inserts, etc.) will be abolished as a rule.

In place of providing information in paper form, necessary precautions, etc. for use and handling of prescription drugs, medical devices (excluding medical devices intended to be provided primarily for the ordinary use of general consumers) and cellular and tissue-based products (hereinafter referred to as "information on precautions, etc." Note 1) will be basically provided through electronic means including publication on the website of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA"). In addition, by reading the code (GS1 code) displayed on the containers or wrappers of sales packaging units of drugs, etc.

(hereinafter referred to as "containers, etc.") with a smartphone, for example, the corresponding page on the PMDA website can be accessed. Note 2

Note 1) Although the content of the information itself is unaltered, the previous name of the information "package insert language, etc." was changed to "information on precautions, etc."

Note 2) A document containing information on precautions, etc. attached to drugs, etc., will be called a "package insert" as it was before the revision of the act. A "digitized package insert" is a document containing information on precautions, etc. published on the PMDA website.



For drugs, etc. directly sold, etc. to general consumers, for handy reference of the contents for each use, which is highly needed in this population, information will be provided by paper package inserts, etc. containing information on precautions, etc. as it was prior to the revision of the act.

The scope of drugs, etc. for which information will be provided by package inserts, etc. is as follows:

Scope of drugs, etc. for which information on precautions, etc. must be contained in package inserts, etc.

(1) Guidance-mandatory drugs, OTC drugs, pharmacy-compounded drugs
(2) All quasi drugs
(3) All cosmetics
(4) Medical devices provided primarily for the ordinary use of general consumers
Specifically, those designated by ministerial ordinances and announcements such as inhalers for household use, electric therapy apparatus for household use, hearing aids, and adhesive plasters.

* Cellular and tissue-based products are not supposed to be sold, etc. directly to general consumers, and therefore information will be provided by electronic means instead of in paper form for all products.

3. Browsing package inserts using electronic methods (app)

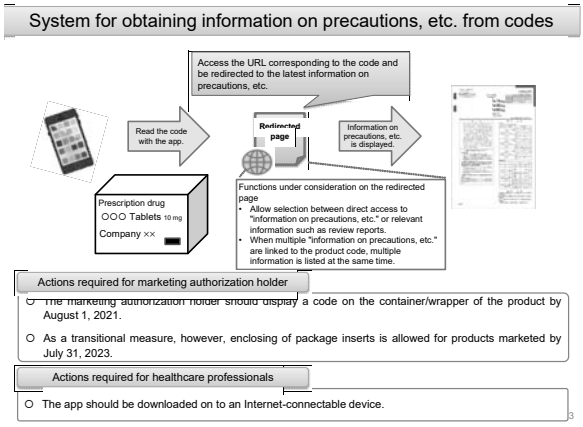
As explained in 2, information on the proper use and safety of drugs, etc. will be provided by electronic methods in principle, instead of in paper form.

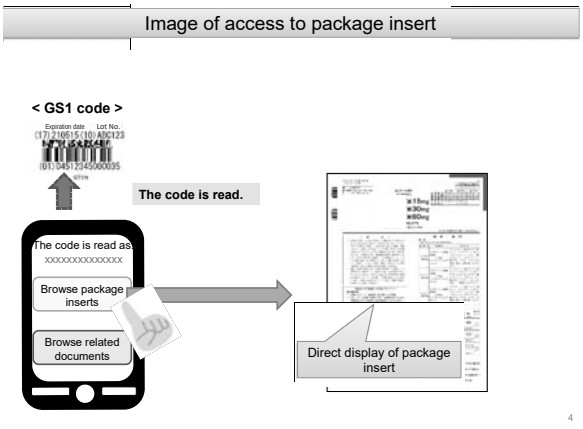
It is also possible to search on the PMDA website. As a simple method of access, applications will be available on smartphones, etc. (hereinafter referred to as "app") to read the code (GS1 code) displayed on the containers, etc. of drugs, etc. for quick access to the latest information on the PMDA website.

This app is jointly developed at present by the Distribution System Research Institute (GS1 Japan), the Federation of Pharmaceutical Manufacturers' Associations of Japan, and the Japan

Federation of Medical Devices Association. The app will be provided free of charge and its use is recommended.

Introduction of the app to medical professionals will be started in early May. In providing and disseminating the app, we will work in collaboration with industries to facilitate convenient use by medical professionals in clinical practice through posting easy-to-understand leaflets and explanatory videos on the PMDA website and other means.





4. When information by paper media, etc. is required

On August 1 of this year, provision of information on proper use and safety of drugs, etc. using paper-based media (such as package inserts) will be abolished as a rule.

However, we consider that there still are situations where paper media, etc. are necessary due to an environment inadequate for using information and communication technology for example.

To cope with such circumstances, under the new system, the marketing authorization holders of drugs, etc. will provide information to healthcare professionals who need information in paper media, etc.

Specifically:

[1] When drugs, etc. are purchased for the first time.

[2] When information on precautions, etc. for drugs, etc. has been revised.

The marketing authorization holder will provide the information in paper form to physicians, dentists, pharmacists, etc. who handle the drug, etc. in question.

In addition to the cases described in the above [1] and [2], when so requested by healthcare professionals, information will be provided appropriately in the manner desired by the recipients as their usual practice (paper media, e-mail, etc.).

5. Maintenance or disaster responses on the PMDA website

A backup site as well as a bulk downloading function of package inserts for prescription drugs have been built on the PMDA's website to maintain browsing of digitized package inserts in the event of disasters or maintenance of the website.

During maintenance of the PMDA's website, the backup site will replace it to allow browsing of digitized package inserts without disruption.

Anticipating the inability to access the Internet in the event of disasters, etc. as well, routine downloading in non-crisis times of digitized package inserts necessary for respective clinical practices will be available. Please note that the bulk downloading function for package inserts of prescription drugs will be in service from April this year and registration with My Drug List for Safety Update, an optional service of the PMDA medi-navi, is required to use the function.

6. Conclusion

Digitization of package inserts will begin on August 1 of this year. We hope that this digitization of package inserts will further promote the proper and safe use of drugs, etc. in medical

practice.

The app required to access information on precautions, etc. is currently under development. We plan to provide information on the release schedule and usage of the app in a future issue of PMDSI as well.

[References]

· Provision of Information on Precautions, etc. for Drugs, etc.
https://www.mhlw.go.jp/content/000741989.pdf (only in Japanese)
· Questions and Answers (Q&A) on Provision of Information on Precautions, etc. for Drugs, etc."
https://www.mhlw.go.jp/content/000741990.pdf (only in Japanese)
· Points for Consideration concerning Notification, etc. of Information on Precautions, etc.
https://www.mhlw.go.jp/content/000741991.pdf (only in Japanese)
·Digitization of Package Inserts page
https://www.pmda.go.jp/safety/info-services/0003.html (only in Japanese)
·My Drug List for Safety Update Service
https://www.pmda.go.jp/safety/info-services/medi-navi/0012.html (only in Japanese)
·GS1-128 Reading App Q&A Service for Medical Devices by the Japan Federation of Medical Devices Associations (JFMDA) (only in Japanese)
(intended for medical devices-related companies)
·(web delivery) Digitization of Package Inserts Briefing
Available: March 22 to July 30 2021
Go to the Seminar page on the JFMDA website
https://www.jfmda.gr.jp/course/ (only in Japanese)

2
Safety in Co-administration of Sildenafil (indicated for pulmonary arterial hypertension) and Amiodarone (oral dosage form)

1. Introduction

Sildenafil citrate (hereinafter referred to as “sildenafil”) is a drug indicated for pulmonary arterial hypertension (hereinafter referred to as “PAH”) or for “erectile dysfunction,” and amiodarone hydrochloride (oral dosage form) (hereinafter referred to as “amiodarone”) is a drug indicated for life-threatening recurrent arrhythmia such as ventricular fibrillation, only when other antiarrhythmic agents are ineffective or unfeasible. The 2 drugs (*1) were mutually specified as contraindicated for co-administration.

*1 Co-administration with amiodarone (injections) is subjected to Precautions for Co-administration.

Recently, based on the consideration at the 10th FY 2020 Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs and Food Sanitation Council (hereinafter referred to as the “Subcommittee on Drug Safety”) held on January 15, 2021, precautions of package inserts have been revised with respect to the contraindication for co-administration between sildenafil (preparations indicated for PAH) (hereinafter referred to as “sildenafil (PAH)”) and amiodarone. This section will introduce the details of the revision.

2. Background

First, the basis on which co-administration between sildenafil and amiodarone was contraindicated will be described.

Mild QT interval prolongation effects that have been observed in its clinical trial were identified in the course of the marketing authorization review of vardenafil hydrochloride hydrate (hereinafter referred to as “vardenafil”), which is a phosphodiesterase 5 inhibitor. Taking into account the fact that the 2 drugs are both class III antiarrhythmic agents that possess strong QT interval prolongation effects, co-administration of amiodarone and vardenafil was contraindicated.

Mild QT interval prolongation effects were also observed for sildenafil in the same clinical trial, and co-administration with amiodarone was similarly contraindicated for sildenafil.

*2 Sildenafil was only indicated for erectile dysfunction initially. Co-administration with amiodarone was contraindicated in the subsequent marketing authorization review for the indication of PAH.

With respect to the contraindication for co-administration of these drugs, in March 2020, the Japanese Circulation Society and the Japanese Society of Paediatric Cardiology and Cardiac Surgery submitted a request calling for revision of the contraindication for co-administration of sildenafil indicated for PAH and amiodarone. The request states, as the major reasons for request, that amiodarone is frequently selected for the treatment of tachyarrhythmia which may complicate PAH and its oral dosage form is required for the prevention of recurrent seizure after tachycardia subsides, as well as that paediatric PAH indications of sildenafil are covered by health insurance and that there is the expected necessity of co-administration of amiodarone when serious arrhythmia occurs in a PAH patient.

MHLW considered the request from these academic societies and decided to consider the safety in the co-administration of sildenafil (PAH) and amiodarone.

3. Discussion by the Subcommittee on Drug Safety

(1) Necessity of co-administration of sildenafil (PAH) and amiodarone

Related US and EU clinical practice guidelines were reviewed, and the results were as

follows:

・Related US and EU clinical practice guidelines state that in certain situations administration of amiodarone should be considered as an option for the treatment of patients who have developed PAH and arrhythmia concurrently and oral dosage form of amiodarone, in addition to injections, is required in the treatment in the acute phase and beyond.

・Sildenafil (PAH) is the only phosphodiesterase 5 inhibitor that is approved with paediatric indication distinguished from all others. Therefore, no alternative drugs are available for the treatment of PAH in paediatric patients currently.

Taking into account the results, MHLW/PMDA considers there is a medical necessity of the co-administration of sildenafil (PAH) and amiodarone (oral dosage form).

(2) Risks in co-administration of sildenafil (PAH) and amiodarone

QT interval prolongation effects of sildenafil and the safety in co-administration of sildenafil (PAH) and amiodarone were reviewed, and it was found that:

a. QT interval prolongation effects of sildenafil

・Mild QT interval prolongation was observed with sildenafil in the clinical study in healthy adult males conducted for the marketing authorization application for vardenafil mentioned above.

・The specified drug use-results survey in Japan, other Japanese and overseas cases for sildenafil (PAH) were reviewed, and none of them clearly indicated QT interval prolongation risk posed by sildenafil.

・None of the Japanese and overseas cases involving QT interval prolongation with use of sildenafil (preparations indicated for erectile dysfunction) clearly indicated QT interval prolongation risk posed by sildenafil.

b. Safety in co-administration of sildenafil (PAH) and amiodarone

・No Japanese or overseas cases have been identified reporting adverse reactions involving QT interval prolongation that can be determined to have been caused by co-administration of sildenafil and amiodarone.

・No events with co-administration of sildenafil (PAH) and amiodarone that require a renewed precaution have been reported in Japan or overseas.

・The US, EU, Australian, and Canadian package inserts do not contraindicate co-administration of sildenafil and amiodarone.

Based on these results, it was considered that no clinically apparent risks have been identified although the risk of the QT interval prolongation could not completely be ruled out.

(3) Revision of the contraindication for co-administration of sildenafil (PAH) and amiodarone

Given the above, the Subcommittee on Drug Safety considered regarding sildenafil (PAH) that the benefits of co-administration with amiodarone outweigh the risk and therefore, determined that the contraindication for co-administration of the 2 drugs may be lifted and replaced with precautions for co-administration.

4. Closing remark

Healthcare professionals are requested to understand the gist of this revision and note that co-administration of sildenafil indicated for erectile dysfunction and amiodarone (oral dosage form) is still contraindicated. Your continued efforts for the proper use of sildenafil (PAH) and amiodarone (oral dosage form) would be appreciated.

[References]

・Materials 1-1 to 1-4 of the 10th FY 2020 Subcommittee on Safety Measures of the Committee on Drug Safety in the Pharmaceutical Affairs and Food Sanitation Council (held on January 15, 2021)
https://www.mhlw.go.jp/stf/newpage_16032.html (only in Japanese)
・Revision of Precautions (PSEHB/PSD Notification No. 0126-2 dated January 26, 2021)
https://www.mhlw.go.jp/content/000726519.pdf (only in Japanese)
English translation by PMDA
https://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0008.html

3

Important Safety Information

Regarding the revision of the Precautions of package inserts of drugs in accordance with the Notification dated February 25, 2021, this section will present the details of important revisions as well as the case summaries serving as the basis for these revisions.

1 Salbutamol sulfate

Branded name (name of company)	a. Venetlin for Inhalation 0.5% (Glaxo Smith Kline K.K.) b. Venetlin Tablets 2 mg, and the others (Glaxo Smith Kline K.K., and others) c. Venetlin Syrup 0.04% (Glaxo Smith Kline K.K.) d. Sultanol Inhaler 100 μg (Glaxo Smith Kline K.K.)
Therapeutic category	Bronchodilators
Indications	a, d. Relief of symptoms associated with airflow obstruction in the following diseases: Bronchial asthma, childhood asthma, emphysema, bronchitis acute/chronic, pulmonary tuberculosis b. Relief of symptoms associated with airflow obstruction in the following diseases: Bronchial asthma, childhood asthma, emphysema, bronchitis acute/chronic, pulmonary tuberculosis, silicotuberculosis c. Relief of bronchospasm in the following diseases: Bronchial asthma, bronchitis, asthmatoid bronchitis

PRECAUTIONS (revised language is underlined)

[Under old instructions]	
Adverse Reactions Clinically Significant adverse Reactions (newly added)	**Shock, anaphylaxis:** Shock or anaphylaxis may occur. Patients should be carefully monitored and if any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be taken.
[Under new instructions]	
11. ADVERSE REACTIONS **11.1 Clinically Significant adverse Reactions (newly added)**	Shock, anaphylaxis
Reference information	Number of cases (for which a causal relationship between the drug and event was reasonably possible) reported during the previous approximately 45-month period (April 2017 to December 2020) Cases involving shock, anaphylaxis: 1 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately: a. 980 000, b. 29 000, c. 39 000, d. 210 000 Japanese market launch: a., b. September 1973, c. February 1978, d. June 1978

Case Sultanol Inhaler

Patient		Daily dose/ administration duration	Adverse reactions
Sex Age	Reason for use (complications)		Clinical course and treatment provided
Female 70s	Bronchostenosis (sepsis, aspiration pneumonia, loss of consciousness, type 2 diabetes mellitus, hypertension, and old cerebral infarction)	800 μg For 1 day	**Anaphylaxis, wheezing, erythema, rash** Date unknown: The patient was brought to hospital by ambulance after she lost consciousness in the bathtub and incurred aspiration pneumonia. Inpatient treatment was started. Sepsis was noted, and the patient was admitted to the ICU. Day 1 of administration: Administration of salbutamol sulfate 200 μg, 4 times daily was initiated. 14:55: The patient had been intubated under artificial respiratory management when wheezing was noted on auscultation of bilateral lung fields. Considering the obstructive ventilatory pattern of the ventilator, inhalation of salbutamol sulfate was applied expecting a bronchodilatory effect. Day 1 of administration 15:25: Intensified bilateral wheezing was noted 30 minutes after the inhalation and redness of face and trunk appeared, which were considered to be anaphylaxis. Rash appeared. Day 1 of administration 15:30: Adrenaline 0.3 mg was intra-muscularly injected, an anti-allergy drug and a steroid were infused, and improvement was observed in the patient's signs. Day 1 of administration 16:50: The patient recovered from all the symptoms she developed. The biphasic anaphylaxis has not recurred since with no anaphylactic sequelae.
Concomitant drugs: Sitagliptin phosphate hydrate, amlodipine besilate, aspirin, azithromycin hydrate, lansoprazole			

4
Revision of Precautions (No.321)

This section presents details of revisions to the Precautions of package inserts and brand names of drugs that have been revised in accordance with the Notifications dated February 25, 2021.

1 Antipyretics, analgesics and anti-inflammatory agents, other agents relating to blood and body fluids

Aspirin (preparations indicated for antipyresis, analgesia, anti-inflammation, prevention of thrombus/embolus formation, Kawasaki disease)

Branded name

Aspirin "Yoshida" (Yoshida Pharmaceutical Company Limited), and the others

[Under Old instructions]

Use during Pregnancy, Delivery or Lactation (newly added)

When this drug is administered to pregnant women (excluding those within 12 weeks before due date) or women who may be pregnant, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary for indications other than Kawasaki disease. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

[Under New instructions]

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS
9.5 Pregnant Women

Pregnant women (excluding those within 12 weeks before due date) or women who may be pregnant

<Common to all indications>

(1) This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

<Indications other than Kawasaki disease>

(2) If administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary.

2 Antipyretics, analgesics and anti-inflammatory agents

[1] Aspirin (preparations indicated for antipyresis, analgesia, anti-inflammation)
[2] Aspirin/dialuminate (330 mg)

Branded name

[1] Aspirin "Yoshida" (Yoshida Pharmaceutical Company Limited), and the others
[2] Bufferin Combination Tablet A330 (Lion Corporation)

[Under Old instructions]

Use during Pregnancy, Delivery or Lactation

This drug should be administered to pregnant women (excluding those within 12 weeks before due date) only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as

necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

[Under New instructions]

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.5 Pregnant Women	Pregnant women (with those within 12 weeks before due date excluded) or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

3 Antipyretics, analgesics and anti-inflammatory agents

[1] Ampiroxicam
[2] Piroxicam (oral dosage form)

Branded name	[1] Flucam Capsules 13.5 mg, 27 mg (Pfizer Japan Inc.) [2] Baxo Capsule 10, 20 (FUJIFILM Toyama Chemical Co., Ltd.), and the others

[Under Old instructions]

Use during Pregnancy, Delivery or Lactation	The safety of this drug administered during pregnancy has not been established. Pregnant women (excluding those in their term) or women who may be pregnant should be administered this drug only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

[Under New instructions]

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.5 Pregnant Women	Pregnant women (excluding those in their third trimester) or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

4 Antipyretics, analgesics and anti-inflammatory agents

Isopropylantipyrine

Branded name	Yoshipyrine (Yoshida Pharmaceutical Company Limited)

[Under Old instructions]

Use during Pregnancy, Delivery or Lactation	Teratogenic effects have been reported in animal studies. Administration of this drug is not recommended in pregnant women or women who may be pregnant. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of

cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

5 Antipyretics, analgesics and anti-inflammatory agents

[1] Isopropylantipyrine/acetaminophen/ allylisopropylacetylurea/anhydrous caffeine
[2] Ethenzamide

Branded name

[1] SG Combination Granules (Shionogi Pharma Co., Ltd.)
[2] Ethenzamide "Yoshida" (Yoshida Pharmaceutical Company Limited)

[Under Old instructions]

Use during Pregnancy, Delivery or Lactation

This drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

6 Antipyretics, analgesics and anti-inflammatory agents

[1] Ibuprofen
[2] Celecoxib
[3] Naproxen
[4] Pranoprofen (oral dosage form)
[5] Flurbiprofen axetil
[6] Loxoprofen sodium hydrate (oral dosage form)
[7] Lornoxicam

Branded name

[1] Brufen Tablets 100, 200, Brufen Granule 20% (Kaken Pharmaceutical Co., Ltd.), and the others
[2] Celecox Tablets 100 mg, 200 mg (Astellas Pharma Inc.), and the others
[3] Naixan Tablets 100 mg (Mitsubishi Tanabe Pharma Corporation)
[4] Niflan Tablets 75 mg (Mitsubishi Tanabe Pharma Corporation), and the others
[5] Ropion Intravenous 50 mg (Kaken Pharmaceutical Co., Ltd.)
[6] Loxonin Tablets 60 mg, Loxonin Fine Granules 10% (Daiichi Sankyo Co., Ltd.), and the others
[7] Lorcam tab. 2 mg, 4 mg (Taisho Pharmaceutical Co., Ltd.), and the others

[Under Old instructions]

Use during Pregnancy, Delivery or Lactation

This drug should be administered to pregnant women (excluding those in their third trimester) or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. The safety of this drug administered during pregnancy has not been established. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

[Under New instructions]

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS **9.5 Pregnant Women**	Pregnant women (excluding those in their third trimester) or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

7 Antipyretics, analgesics and anti-inflammatory agents, analgesics, anti-itchings, astrigents and anti-inflammatory agents

[1] Etodolac
[2] Nabumetone
[3] Flurbiprofen (oral dosage form)
[4] Mefenamic acid
[5] Esflurbiprofen/mentha oil

Branded name	[1] Osteluc Tablets 100, 200 (Aska Pharmaceutical. Co., Ltd.), and the others [2] Relifen Tab. 400 mg (Sanwa Kagaku Kenkyusho Co., Ltd.) [3] Froben Tablets 40, Froben Granule 8% (Kaken Pharmaceutical Co., Ltd.) [4] Pontal Capusules 250 mg, Pontal Syrup 3.25%, Pontal Powder 50%, Pontal Fine Granules 98.5% (Daiichi Sankyo Co., Ltd.), and the others [5] Loqoa tape (Taisho Pharmaceutical Co., Ltd.)
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women (excluding those in their third trimester) or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. The safety of this drug administered during pregnancy has not been established. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

8 Antipyretics, analgesics and anti-inflammatory agents

Ketoprofen (injections)

Branded name	Capisten IM 50 mg (Kissei Pharmaceutical Co., Ltd.), and the others
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women (excluding those in their third trimester) or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. The safety of this drug administered during pregnancy has not been established. Onset of oligohydramnios following administration of a ketoprofen agent(s) for epidermis in women in the second trimester of pregnancy has been reported. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have also been reported following use of cyclooxygenase inhibitors

	(oral dosage form or suppository) in pregnant women.
[Under New instructions]	
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS **9.5 Pregnant Women**	Pregnant women (excluding those in their third trimester) or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Onset of oligohydramnios following use of a ketoprofen agent(s) for epidermis in women in the second trimester of pregnancy has been reported. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have also been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women. (deleted)* *The current language “Women who are pregnant (excluding those in their second or third trimester) or women who may be pregnant: This drug should be administered only when the therapeutic benefits are considered to outweigh the risks.” should be deleted.

9 Antipyretics, analgesics and anti-inflammatory agents

Ketoprofen (suppository)

Branded name	Ketoprofen Suppositories 50 mg "JG", Ketoprofen Suppositories 75 mg "JG" (Choseido Pharmaceutical Co., Ltd.), and the others
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women (excluding those in their third trimester) or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. The safety of this drug administered during pregnancy has not been established. Onset of oligohydramnios following administration of a ketoprofen agent(s) for epidermis in women in their second trimester of pregnancy has been reported. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have also been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.
[Under New instructions]	
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS **9.5 Pregnant Women**	Pregnant women (excluding those in their third trimester) or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Onset of oligohydramnios following use of a ketoprofen agent(s) for epidermis in women in the second trimester of pregnancy has been reported. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have also been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women. (deleted)* *The current language “Second trimester of pregnancy: This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. Caution should be exercised such as limiting to the minimum effective use. Onset of oligohydramnios following use of a ketoprofen agent(s) for epidermis in women in the second trimester of pregnancy has been reported.” should be deleted.

10 Antipyretics, analgesics and anti-inflammatory agents

Zaltoprofen

Branded name	Soleton Tablets 80 (Nippon Chemiphar Co., Ltd.), and the others
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. The safety of this drug administered during pregnancy has not been established. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.
[Under New instructions]	
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS **9.5 Pregnant Women**	Pregnant women or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women. Foetal ductus arteriosus systole following administration of this drug in late pregnancy has been reported in animal studies with rats.

11 Antipyretics, analgesics and anti-inflammatory agents

[1] Dibucaine hydrochloride/sodium salicylate/calcium bromide
[2] Bucolome
[3] Flufenamate aluminum
[4] Mofezolac

Branded name	[1] Neo Vitacain Injection 2 mL, 5 mL, Neo Vitacain Injection Syringe 2 mL, 5 mL (Vitacain Pharmaceutical Co., Ltd.) [2] Paramidin Capsules 300 mg (Aska Pharmaceutical. Co., Ltd.) [3] Opyrin tab. 125 mg, 250 mg (Taisho Pharmaceutical Co., Ltd.) [4] Disopain Tablets 75 (Nipro ES Pharma co., Ltd.)
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If administration of this drug is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. The safety of this drug administered during pregnancy has not been established. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

12 Antipyretics, analgesics and anti-inflammatory agents

Sulpyrine hydrate

Branded name	Sulpyrine Injection 250 mg "NP" (Nipro Corporation), and the others
[Under Old instructions]	

Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

13 Antipyretics, analgesics and anti-inflammatory agents

Tiaprofenic acid

Branded name	Surgam Tablets 100 mg, 200 mg (Sanofi K.K.)
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	The safety of this drug administered during pregnancy has not been established. Pregnant women (excluding those in their term) or women who may be pregnant should be administered this drug only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

14 Antipyretics, analgesics and anti-inflammatory agents

Migrenin

Branded name	Migrenin "Kenei" (KENEI Pharmaceutical Co., Ltd.)
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	Administration of this drug is not recommended in pregnant women or women who may be pregnant. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

15 Agents used for common cold

[1] Salicylamide/acetaminophen/anhydrous caffeine/chlorpheniramine maleate
[2] Salicylamide/acetaminophen/anhydrous caffeine/promethazine methylenedisalicylate

Branded name	[1] Pelex combination granule (TAIHO Pharmaceutical Co., Ltd.), and the others [2] PL Combination Granules (Shionogi Pharma Co., Ltd.), and the others
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women (those within 12 weeks before due date or in their third trimester) or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. If such administration is deemed necessary, caution should be exercised such as limiting to the minimum effective use and monitoring amniotic fluid as necessary. Renal impairment and decreased urine output in foetuses as well as

accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

16 Analgesics, anti-itchings, astringents and anti-inflammatory agents

[1] Ibuprofen piconol
[2] Glycol salicylate/l-menthol
[3] Methyl salicylate/dl-camphor/capsicum extract
[4] Methyl salicylate/dl-camphor/l-menthol
[5] Methyl salicylate/glycol salicylate/l-menthol/d-camphor/diphenhydramine/benzyl nicotinate
[6] Methyl salicylate/l-menthol/dl-camphor/glycyrrhetinic acid
[7] Suprofen

Branded name

[1] Vesicum Ointment 5%, Vesicum Cream 5% (Hisamitsu Pharmaceutical Co., Inc.), and the others
[2] GS PLASTER C「YUTOKU」(Yutoku Pharmaceutical Ind. Co., Ltd.)
[3] Honesip (Sioe Pharmaceutical Co., Ltd.)
[4] MS onshippu「TAIHO」(OKAYAMA TAIHO Pharmaceutical Co., Ltd.), and the others
[5] Air-Salonpas (Hisamitsu Pharmaceutical Co., Inc.)
[6] Stickzenol A (Mikasa Seiyaku co., ltd)
[7] Sulprotin Ointment 1%, Sulprotin Cream 1% (Teva Takeda Pharma Ltd.), and the others

[Under Old instructions]

Use during Pregnancy, Delivery or Lactation (newly added)

This drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. The safety of this drug in pregnant women has not been established.
Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

17 Analgesics, anti-itchings, astringents and anti-inflammatory agents, anti-dermoinfectives, emollients

[1] Indometacin (agents for epidermis)
[2] Ketoprofen (agents for epidermis)
[3] Diclofenac sodium (agents for epidermis)
[4] Piroxicam (agents for epidermis)
[5] Felbinac
[6] Flurbiprofen (agents for epidermis)
[7] Loxoprofen sodium hydrate (agents for epidermis)
[8] Salicylic acid (dry powder, ointment, patches)

Branded name

[1] Idomethine Kowa Gel 1%, Idomethine Kowa Sol 1%, Idomethine Kowa Cream 1% (Kowa Company, Ltd.), and the others
[2] Sector Gel 3%, Sector Lotion 3%, Sector Cream 3% (Hisamitsu Pharmaceutical Co., Inc.), and the others
[3] Voltaren Gel 1%, Voltaren Lotion 1%, Voltaren Tape 15 mg, 30 mg (Dojin Iyaku-Kako Co., Ltd.), and the others
[4] Baxo Ointment 0.5% (FUJIFILM Toyama Chemical Co., Ltd.), and the others

	[5] Napageln Ointment 3%, Napageln Lotion 3%, Napageln Cream 3% (Teikoku Seiyaku Co., Ltd.), and the others [6] Yakuban tape 20 mg, 40 mg, 60 mg (TOKUHON Corporation), and the others [7] Loxonin Gel 1% (Daiichi Sankyo Co., Ltd.), Loxonin Tape 50 mg, 100 mg, Loxonin Pap 100 mg (LEAD CHEMICAL Co., Ltd.), and the others [8] 5% Salicylic Acid Ointment Toho, 10% Salicylic Acid Ointment Toho (Toho Pharmaceutical Co., Ltd.), and the others
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation (newly added)	Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

18 Analgesics, anti-itchings, astringents and anti-inflammatory agents

Methyl salicylate

Branded name	Methyl Salicylate「Toho」(Toho Pharmaceutical Co., Ltd.)
[Under Old instructions]	
(newly added)	Use during Pregnancy, Delivery or Lactation This drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. The safety of this drug in pregnant women has not been established. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

19 Analgesics, anti-itchings, astringents and anti-inflammatory agents

Heparinoid/adrenal extract/salicylic acid

Branded name	Zestak Cream (Mikasa Seiyaku co., ltd)
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women or women who may be pregnant only when the therapeutic benefits are considered to outweigh the risks. The safety of this drug in pregnant women has not been established.
(newly added)	Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

20 Other agents relating to blood and body fluids

[1] Aspirin (preparations indicated for prevention of thrombus/embolus formation, Kawasaki disease)
[2] Aspirin/dialuminate (81 mg)
[3] Aspirin/lansoprazole
[4] Clopidogrel sulfate/aspirin

Branded name	[1] Bayaspirin tablets 100 mg (Bayer Yakuhin Ltd.), and the others [2] Bassamin-A81 (Teva Takeda Pharma Ltd.), and the others [3] Takelda Combination Tablets (Teva Takeda Yakuhin Ltd.) [4] ComPlavin Combination Tablets (Sanofi K.K.), and the others
[Under Old instructions]	
Use during Pregnancy, Delivery or Lactation	This drug should be administered to pregnant women (excluding those within 12 weeks before due date) or women who may be

	pregnant only when the therapeutic benefits are considered to outweigh the risks. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.
[Under New instructions]	
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.5 Pregnant Women	Pregnant women (excluding those within 12 weeks before due date) or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

21 Other agents relating to blood and body fluids

Aspirin/vonoprazan fumarate

Branded name	Cabpirin Combination Tablets (Takeda Pharmaceutical Company Limited.)
[Under New instructions]	
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.5 Pregnant Women	Pregnant women (with those within 12 weeks before due date excluded) or women who may be pregnant This drug should be administered only when the therapeutic benefits are considered to outweigh the risks. Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

22 Bronchodilators

Salbutamol sulfate

Branded name	Venetlin for Inhalation 0.5% (GlaxoSmithKline K.K.), and the others
[Under Old instructions]	
Adverse Reactions Clinically Significant Adverse Reactions (newly added)	**Shock, anaphylaxis:** Shock or anaphylaxis may occur. Patients should be carefully monitored and if any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be taken.
[Under New instructions]	
11. ADVERSE REACTIONS 11.1 Clinically Significant Adverse Reactions (newly added)	Shock, anaphylaxis

23 Cellular and tissue-based products

Tisagenlecleucel

Branded name	Kymriah suspension for intravenous infusion (Novartis Pharma K.K.)
[Under Old instructions]	
Malfunction/Adverse Reactions Clinically Significant Adverse Reactions (newly added)	Infusion reaction, anaphylaxis Infusion reaction or anaphylaxis may occur. Patients should be carefully monitored and appropriate measures should be taken if any abnormalities are observed.

5

List of Products Subject to Early Post-marketing Phase Vigilance

Early Post-marketing Phase Vigilance (EPPV) was established in 2001. This unique system for newly-approved drug products refers to any safety assurance activities that are conducted within a period of 6 months just after marketing of a new drug. The MAH responsible for a new drug in the EPPV period is required to collect adverse drug reactions (ADRs) data from all medical institutions where the drug is used and to take safety measures as appropriate. The aim of EPPV is to promote the rational and appropriate use of drugs in medical treatments and to facilitate prompt action for the prevention of serious ADRs. EPPV is specified as a condition of product approval.

(As of 28 February 2021)

◎: Products for which EPPV was initiated after February 1, 2021

	Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
◎	Thalidomide*1 Thaled Capsules 25, 50, 100	Fujimoto Pharmaceutical Corporation	February 24, 2021
◎	Coronavirus modified uridine RNA vaccine (SARS-CoV-2) Comirnaty intramuscular injection	Pfizer Japan Inc.	February 16, 2021
◎	Semaglutide (genetical recombination) Rybelsus tablets 3 mg, 7 mg, 14 mg	Novo Nordisk Pharma Ltd.	February 5, 2021
	Rivaroxaban*2 Xarelto tablets 15 mg, 10 mg, Xarelto fine granules 15 mg, 10 mg, Xarelto OD tablets 15 mg, 10 mg	Bayer Yakuhin Ltd.	January 22, 2021
	Cetuximab sarotalocan sodium (genetical recombination) Akalux IV Infusion 250 mg	Rakuten Medical Japan K.K.	January 1, 2021
	Recombinant adsorbed quadrivalent human papillomavirus virus-like particle vaccine (yeast origin) *3 Gardasil Aqueous Suspension for Intramuscular Injection Syringes	MSD K.K.	December 25, 2020
	Baricitinib*4 Olumiant tablets 4 mg, 2 mg	Eli Lilly Japan K.K.	December 25, 2020
	Midazolam Buccolam Oromucosal Solution 2.5 mg, 5 mg, 7.5 mg, 10 mg	Takeda Pharmaceutical Company Limited.	December 10, 2020
	Enarodustat Enaroy tablets 2 mg, 4 mg	Japan Tabacco Inc.	December 8, 2020
	Incobotulinumtoxin A Xeomin 50 units for Intramuscular injection, Xeomin 100 units for Intramuscular injection, Xeomin 200 units for Intramuscular injection	Teijin Pharma Limited.	December 4, 2020
	Roxadustat*5 Evrenzo Tablets 20 mg, 50 mg, 100 mg	Astellas Pharma Inc.	November 27, 2020

Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
Dapagliflozin propylene glycolate hydrate*6 Forxiga 5 mg Tablets, Forxiga 10 mg Tablets	AstraZeneca K.K.	November 27, 2020
Cabozantinib malate*7 Cabometyx tablets 20 mg, 60 mg	Takeda Pharmaceutical Company Limited.	November 27, 2020
Binimetinib*8 Mektovi Tablets 15 mg	Ono Pharmaceutical Co., Ltd.	November 27, 2020
Encorafenib*8 Braftovi Capsules 50 mg, 75 mg	Ono Pharmaceutical Co., Ltd.	November 27, 2020
Brodalumab (genetical recombination) *9 Lumicef Subcutaneous Injection 210 mg Syringe	Kyowa Kirin Co., Ltd.	November 27, 2020
Baloxavir marboxil*10 Xofluza Tablets 20 mg, Xofluza Granules 2%	Shionogi & Co., Ltd.	November 27, 2020
Sofpironium bromide Ecclock gel 5%	Kaken Pharmaceutical Co., Ltd.	November 26, 2020
Niraparib tosilate hydrate Zejula capsules 100 mg	Takeda Pharmaceutical Company Limited.	November 20, 2020
Filgotinib maleate Jyseleca Tablets 100 mg, 200 mg	Gilead Sciences K.K.	November 18, 2020
Paliperidone palmitate*11 Xeplion TRI Aqueous Suspension for IM Injection 175 mg, 263 mg, 350 mg, 525 mg	Janssen Pharmaceutical K.K.	November 18, 2020
Oxycodone hydrochloride hydrate*12 OxyContin TR Tablets 5 mg, 10 mg, 20 mg, 40 mg	Shionogi Pharma Co., Ltd.	October 29, 2020
Glucagon Baqsimi Nasal Powder 3 mg	Eli Lilly Japan K.K.	October 2, 2020
Aripiprazole hydrate*13 Abilify prolonged release aqueous suspension for IM injection 300 mg, 400 mg, Abilify prolonged release aqueous suspension for IM injection 300 mg syringe, Abilify prolonged release aqueous suspension for IM injection 400 mg syringe	Otsuka Pharmaceutical Co., Ltd.	September 25, 2020
Trastuzumab deruxtecan (genetical recombination) *14 Enhertu For Intravenous Drip Infusion 100 mg	Daiichi Sankyo Co., Ltd.	September 25, 2020
Ravulizumab (genetical recombination) *15 Ultomiris for Intravenous Infusion 300 mg	Alexion Pharma Godo Kaisha	September 25, 2020
Tildrakizumab (genetical recombination) Ilumya Subcutaneous Injection 100 mg Syringe	Sun Pharma Japan Limited	September 23, 2020
Siponimod fumaric acid Mayzent tablets 0.25 mg, 2 mg	Novartis Pharma K.K.	September 14, 2020
Ferric carboxymaltose Ferinject solution for injection/infusion 500 mg	Zeria Pharmaceutical Co., Ltd.	September 1, 2020

*1 Crow-Fukase (POEMS) syndrome

*2 Treatment and reduction in the risk of recurrence of venous thromboembolism

*3 Prevention of the following diseases caused by infection with human Papillomavirus (HPV) Types 6, 11, 16, and 18
・Cervical cancer (squamous cell carcinoma and adenocarcinoma) and its precancerous lesions (cervical intraepithelial neoplasia (CIN) grades 1, 2 and 3 and cervical adenocarcinoma *in situ* (AIS))
・Vulval intraepithelial neoplasia (VIN) grades 1, 2 and 3 and vaginal intraepithelial neoplasia (VaIN) grades 1, 2 and 3
・Anal cancer (squamous cell carcinoma) and its precancerous lesions (anal intraepithelial neoplasia (AIN) grades 1, 2, and 3)
・Condyloma acuminatum
(Only underlined diseases in men are subject to EPPV)

*4 Atopic dermatitis with inadequate response to conventional treatments

*5 Nephrogenic anaemia

*6 Chronic heart failure (only in patients who are receiving standard of care)

*7 Unresectable hepatocellular carcinoma that has progressed after chemotherapy

*8 Unresectable advanced or recurrent BRAF-mutant colorectal cancer that has progressed after chemotherapy

*9 Ankylosing spondylitis and non-radiographic axial spondyloarthritis that respond inadequately to existing therapies

*10 Treatment and prevention of influenza virus infection types A and B

*11 Schizophrenia (only in patients who have been adequately treated with 4-week intramuscular paliperidone palmitate)

*12 Relief of moderate to severe chronic pain difficult to manage with non-opioid analgesics or other opioid analgesics

*13 Suppression of recurrence and relapse of mood episodes in bipolar I disorder

*14 HER2 positive unresectable advanced or recurrent gastric cancer that has progressed after chemotherapy

*15 Atypical haemolytic uraemic syndrome

< Errata, p.11 *2 in the English version of PMDSI No.380 >

Original	Revised
*2 Prevention of the following diseases caused by infection with human Papillomavirus (HPV) Types 6, 11, 16, and 18 ・ Cervical cancer (squamous cell carcinoma and adenocarcinoma) and its precancerous lesions (cervical intraepithelial neoplasia (CIN) grades 1, 2 and 3 and cervical adenocarcinoma *in situ* (AIS)) ・ Vulval intraepithelial neoplasia (VIN) grades 1, 2 and 3 and vaginal intraepithelial neoplasia (VaIN) grades 1, 2 and 3 ・Anal cancer (squamous cell carcinoma) and its precancerous lesions (anal intraepithelial neoplasia (AIN) grades 1, 2, and 3) ・Condyloma acuminatum	*2 Prevention of the following diseases caused by infection with human Papillomavirus (HPV) Types 6, 11, 16, and 18 ・ Cervical cancer (squamous cell carcinoma and adenocarcinoma) and its precancerous lesions (cervical intraepithelial neoplasia (CIN) grades 1, 2 and 3 and cervical adenocarcinoma *in situ* (AIS)) ・ Vulval intraepithelial neoplasia (VIN) grades 1, 2 and 3 and vaginal intraepithelial neoplasia (VaIN) grades 1, 2 and 3 ・<u>Anal cancer (squamous cell carcinoma) and its precancerous lesions (anal intraepithelial neoplasia (AIN) grades 1, 2, and 3)</u> <u>・Condyloma acuminatum</u> (Only underlined diseases in men are subject to EPPV.)