Pharmaceuticals and Medical Devices Safety Information

No. 427 March 2026

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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) web page (https://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0002.html) and on the MHLW website (https://www.mhlw.go.jp/, only in Japanese).

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This English version of PMDSI 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.

Pharmaceuticals and Medical Devices Safety Information

No. 427 March **2026**

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

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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 healthcare professionals.

If healthcare professionals such as physicians, dentists, and pharmacists detect adverse reactions, infections, or malfunctions associated with drugs, medical devices, or regenerative medical products, please report them to the Minister of Health, Labour and Welfare directly or through the marketing authorization holder. As healthcare professionals, drugstore and pharmacy personnel are also required to report adverse reactions, etc.

Please utilize the Report Reception Site for reporting.
(This service is available only in Japanese.)

https://www.pmda.go.jp/safety/reports/hcp/0002.html

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Abbreviations

CYP	Cytochrome P
MAH	Marketing Authorization Holder

1

Revision of "PRECAUTIONS" for sulfite-containing prescription drugs, medical devices, and regenerative medicine products

1. Introduction

In drugs containing sulfites, lysine sulfite is used as an active ingredient, or sodium sulfite, sodium bisulfite, dried sodium sulfite, potassium pyrosulfite, and sodium pyrosulfite are used as an additive for the purpose of antioxidation and stabilization, etc.

On February 10, 2026, the Ministry of Health, Labour and Welfare instructed a revision of PRECAUTIONS in the digitized package inserts (hereinafter referred to as "electronic package inserts") for prescription drugs containing sulfites as an active ingredient or additive to provide thorough precautions regarding the risk of sulfite hypersensitivity. This action is also applicable to medical devices and regenerative medicine products containing sulfites. This document introduces the contents of the revision.

2. Background

In Japan, the electronic package inserts of prescription drugs containing sulfites as an active ingredient or additive have listed an alert for patients with a history of hypersensitivity to their ingredients; however, the descriptions differed among products.

The U.S. FDA called attention to the risk of hypersensitivity to prescription drugs containing sulfites for healthcare professionals in June 2024. In addition, the FDA required package inserts of prescription drugs to list precautions about it.

"Sulfites, etc." are also used as an additive for the purpose of antioxidation, preservation, and bleaching in foods in Japan. The Food Safety Commission of Japan announced the assessment of the effect of sulfites, etc. in foods on health in August 2025, listing the following 2 points as the findings of hypersensitivity in humans.

- The possibility of inducing allergy-like reactions by sulfites, etc. and ammonium hydrogen sulfite in patients with allergic diseases, etc. cannot be ruled out, but it is difficult to discuss dosages including the minimum induction dose.
- There are several reports that a few to 10% of patients with bronchial asthma are hypersensitive to sulfites, and accumulation of new findings on the mechanism of onset of hypersensitivity reactions to sulfur dioxide and sulfites should be carefully monitored.

3. Details of the actions

Based on the above trend, MHLW examined the necessity of actions for the risk of hypersensitivity to sulfites in Japan. MHLW also obtained the opinions of the Japanese Society of Allergology. As a result, MHLW decided to uniformly call attention to the risk of hypersensitivity associated with prescription drugs containing sulfites and revise the PRECAUTIONS to include the risk for patients with asthma. The following are the results of the examination.

- In published literature, case reports of adverse reactions to drugs, etc., as well as the results of assessments by the Food Safety Commission of Japan, have reported cases of hypersensitivity (asthma, respiratory failure, urticaria, etc.) due to exposure to sulfites. In particular, there are several reports suggesting that hypersensitivity to sulfites is more common in asthma patients than in non-asthma patients.
- The package inserts of prescription drugs in foreign countries (such as the US, Europe, and

Australia) state that hypersensitivity to sulfites is more common in asthma patients than in non-asthma patients.

<Reference> Examples of PRECAUTIONS for prescription drugs (when containing sulfites as an active ingredient or additive)
9.1 Patients with Complication or History of Diseases, etc.
Patients with a history of hypersensitivity to any of the ingredients of this drug
15.1 Information Based on Clinical Use
This drug contains sulfites as an active ingredient (as an additive when containing an additive agent). Sulfite hypersensitivity has been reported to be more common in asthma patients than in non-asthma patients.

4. Provision of information from healthcare professionals

Patients may not be fully aware of sulfite hypersensitivity. In addition, although the electronic package inserts state that the drug being taken contains sulfites as an active ingredient/additive, they are intended for healthcare professionals. Therefore, it is expected to be difficult for patients to avoid using products that may cause hypersensitivity by themselves. In this revision of PRECAUTIONS, MHLW considered it important to uniformly call attention to prescription drugs, etc. containing sulfites and provide healthcare professionals with information on the occurrence of hypersensitivity due to sulfites. Therefore, healthcare professionals are requested to provide explanations to patients as needed.

5. Closing remark

This revision requires actions for prescription drugs, medical devices, and regenerative medicine products, but active ingredients and additives contained in behind-the-counter drugs and over-the-counter drugs are listed in the package insert, outer box, etc. If you receive any consultation on hypersensitivity, etc. for sulfite-containing drugs from patients, healthcare professionals should take appropriate actions.

Healthcare professionals are requested to continuously cooperate to ensure the proper use of drugs by, for example, reporting safety information on drugs and medical devices in accordance with Article 68-10, Paragraph 2 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145, 1960) when they obtain information about health hazards (adverse reactions, infections, and malfunctions).

6. References

○ Food Safety Commission of Japan. Food Additive Assessment Report on Sulfites, etc. and Ammonium Hydrogen Sulfite Water. August 2025.

○ FDA alerts health care professionals, compounders and patients of potential safety risks associated with sulfite-containing compounded drugs
https://www.fda.gov/drugs/human-drug-compounding/fda-alerts-health-care-professionals-compounders-and-patients-potential-safety-risks-associated

2

Important Safety Information

Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated February 10 ,2026, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.

1 Cytarabine

Brand name (name of company)	Cylocide Injection 20 mg, 40 mg, 60 mg, 100 mg, 200 mg, Cylocide N Injection 400 mg, 1 g (Nippon Shinyaku Co., Ltd.), and the others
Therapeutic category	Antimetabolic agents, antitumor antibiotics and preparations
Indications	< Cylocide Injection 20 mg, 40 mg, 60 mg, 100 mg, 200 mg > · Acute leukaemia (including erythroleukaemia and cases of chronic myeloid leukaemia transformation) · Gastrointestinal carcinoma (gastric cancer, pancreatic carcinoma, hepatic cancer, colon cancer, and the others), lung cancer, breast cancer, female genital cancer (uterine cancer, and the others), and the others, only when co-administered with other antitumor agents (fluorouracil, mitomycin C, cyclophosphamide hydrate, methotrexate, vincristine (fluorouracil, mitomycin C, cyclophosphamide hydrate, methotrexate, vincristine sulfate, vinblastine sulfate, and the others). · Bladder tumour < Cylocide N Injection 400 mg, 1 g > · High-dose cytarabine therapy The following therapies for acute leukaemia (acute myeloid leukaemia, acute lymphocytic leukaemia) - Remission induction therapy for relapsed or refractory cases (salvage therapy) - Consolidation therapy Relapsed or refractory malignant lymphoma Only when co-administered with other antitumor agents for acute lymphocytic leukaemia and malignant lymphoma · Pretreatment for tumour-specific T-cell infusion therapy

PRECAUTIONS (Revised language is underlined.)

8. IMPORTANT PRECAUTIONS (newly added)	<u>Tumour lysis syndrome may occur. Patients should be carefully monitored by checking serum electrolyte levels, renal function, etc.</u>

11. ADVERSE REACTIONS (newly added)

Tumour lysis syndrome
If any abnormalities are observed, administration of this drug should be discontinued, appropriate measures (e.g., administration of physiological saline solution and/or hyperuricaemia therapeutic agents, and dialysis) should be taken, and patients should be carefully monitored until recovery from such symptoms.

Reference information

Number of cases* (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's safety database

Cases* involving Tumour lysis syndrome reported in Japan:4
(No patient mortalities)

* Among the cases collected in the PMDA's safety database for drugs, those for which blood test results for 2 or more of the following items (uric acid, potassium, phosphorus, and calcium) were documented in the case report forms were retrieved .

Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 14,248
Japanese market launch:
①Cylocide Injection 20 mg: April 1971
②Cylocide Injection 40 mg, 60 mg: November 1971
③Cylocide Injection 100 mg, 200 mg: October 1987
④Cylocide N Injection 400 mg: April 2000
⑤Cylocide N Injection 1 g: April 2010

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 70s	Acute myelomonocytic leukaemia (pneumonia)	140 mg for 2 days ↓ Discontinuation ↓ 140 mg unknown	**Tumour lysis syndrome** Past history: Cerebral infarction, diabetes mellitus	
				Day 1 of administration	The patient was referred and admitted to the hospital from a local hospital due to increased white blood cells. Intravenous drip infusion of cytarabine (70 mg twice) and daunorubicin hydrochloride (50 mg once) was initiated. Fluid loading, allopurinol (100 mg twice), and sodium bicarbonate (20 mL twice) were administered for prophylaxis of tumour lysis syndrome. Administration of cefepime dihydrochloride hydrate (2 g twice) was initiated for pneumonia.
				Day 2 of administration (day of discontinuation)	The patient was found unconscious in the bathroom. Since sinus bradycardia was observed, she was considered to have hyperkalaemia and secondary sick sinus syndrome associated with tumour lysis syndrome. Administration

	of cytarabine and daunorubicin hydrochloride was immediately discontinued, and she underwent haemodialysis. After haemodialysis, her potassium level promptly improved.
1 day after discontinuation (Day 1 of readministration)	Administration of cytarabine and daunorubicin hydrochloride was restarted. No adverse reaction occurred thereafter.
Day 75 of readministration	Complete remission was observed.
Day 191 of readministration	The patient was discharged from the hospital.
Date unknown	The patient died of recurrence.

Laboratory test value

Test item (unit)	Day 1 of administration	Day 2 of administration	1 day after discontinuation	Day 7 of readministration
WBC (/μL)	64,000	50,400	39,900	800
K (mEq/L)	4.5	6.7	3.9	3.2
P (mg/dL)	-	6.5	-	1.0
Uric acid (mg/dL)	2.6	4.9	2.6	0.5

Suspected concomitant drugs: Daunorubicin hydrochloride
Concomitant drugs: Allopurinol, sodium bicarbonate, cefepime dihydrochloride hydrate

2 Ibrutinib

Brand name (name of company)	Imbruvica Capsules 140 mg (Janssen Pharmaceutical K.K.)
Therapeutic category	Other antitumor agents
Indications	· Chronic lymphocytic leukemia (including small lymphocytic lymphoma) · Primary macroglobulinemia and lymphoplasmacytic lymphoma · Mantle cell lymphoma · Chronic graft-versus-host disease after hematopoietic stem cell transplant (for patients who have an inadequate response to steroids)

PRECAUTIONS (Revised language is underlined.)

8. IMPORTANT PRECAUTIONS (newly added)	Uveitis may occur. Whether ocular abnormalities occur should be examined periodically. In addition, patients should be instructed to immediately seek medical attention if any ocular abnormalities are observed.
11. ADVERSE REACTIONS (newly added)	Uveitis

Reference information

Number of cases* (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's safety database

No cases have been reported in Japan to date.
No patient mortalities have been reported in Japan to date.

*Among the cases collected in the PMDA's safety database for drugs, cases involving uveitis of grade 3 or higher by Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 for which information on test values of visual acuity and number of anterior chamber cells is included in the case report forms were retrieved.

Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 2,327
Japanese market launch:
Imbruvica Capsules 140 mg : May 2016

Case summary

<table>
<tr><th rowspan="2">No.</th><th colspan="2">Patient</th><th rowspan="2">Daily dose/
Administration duration</th><th colspan="2">Adverse reaction</th></tr>
<tr><th>Sex/
age</th><th>Reason for use
(complication)</th><th colspan="2">Clinical course and treatment</th></tr>
<tr><td rowspan="5">1</td><td rowspan="5">Male
50s</td><td rowspan="5">Chronic lymphocytic leukaemia
(ulcerative colitis)</td><td rowspan="5">420 mg
unknown
↓
Discontinuation
↓
140 mg
unknown
↓
420 mg
unknown
↓
Discontinuation</td><td colspan="2">Non-granulomatous anterior uveitis of the right eye</td></tr>
<tr><td>Day 1 of administration</td><td>Administration of ibrutinib at 420 mg was initiated for chronic lymphocytic leukaemia.</td></tr>
<tr><td>15 months after administration (day of discontinuation)</td><td>The patient visited the hospital with chief complaints of right eye pain, hyperaemia, photophobia, and filmy vision that were secondary to severe anterior uveitis of the right eye. Administration of ibrutinib was discontinued 5 days later. There were no clinical findings of active ulcerative colitis.
(Upon presentation)
Right eye: Fine keratic precipitates, posterior synechiae of the iris, anterior chamber cells (4+)
Left eye: No inflammatory findings
Best-corrected visual acuity: Right 6/6, left 6/9
The symptoms improved within 2 weeks after the initiation of tapering of steroid eye drops.
(Final)
Best-corrected visual acuity: Right 6/7.5, left 6/6</td></tr>
<tr><td>5 weeks after discontinuation (Day 1 of readministration)</td><td>Anterior uveitis resolved. Administration of ibrutinib was resumed at 140 mg, and the dose was gradually increased to 420 mg.</td></tr>
<tr><td>1 month after readministration (day of discontinuation of readministration)</td><td>Administration of ibrutinib was discontinued due to relapse of anterior uveitis. Anterior uveitis resolved with tapering of steroid eye drops. Timolol was used for secondary increase in intraocular pressure. As the condition of chronic lymphocytic leukaemia remained unchanged and inactive, administration of ibrutinib was not restarted.</td></tr>
<tr><td colspan="6">Concomitant drugs: None</td></tr>
</table>

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
2	Male 60s	Lymphoma (none)	480 mg unknown ↓ Discontinuation ↓ 240 mg unknown ↓ Discontinuation	**Panuveitis of both eyes with optic disc swelling**	
				Day 1 of administration	Administration of ibrutinib at 480 mg was initiated for second-line treatment of lymphoplasmacytic lymphoma (off-label use).
				8 months after administration	The patient visited the hospital with chief complaints of photophobia and filmy vision due to panuveitis of both eyes. Four weeks later, optic disc swelling of both eyes developed. Infectious and non-infectious causes of panuveitis were ruled out by screening tests. (Upon presentation) Right eye: 180-degree posterior synechiae of the iris, anterior chamber cells (2+) and flare (1+), cystoid macular oedema Left eye: 360-degree posterior synechiae of the iris, anterior chamber cells (2+) and flare (1+), left vitreous opacities (0.5+), cystoid macular oedema Central macular thickness: Right 369 μm, left 356 μm Best-corrected visual acuity: Right 6/9, left 6/9
				9 months after administration (day of discontinuation)	Panuveitis improved with a steroid and a mydriatic. Administration of ibrutinib was discontinued 1 month after the onset of panuveitis. (Final) Central macular thickness: Right 342 μm, left 323 μm Best-corrected visual acuity: Right 6/9, left 6/9
				1 month after discontinuation (Day 1 of readministration)	As symptoms of lymphoma recurred, ibrutinib was restarted at 240 mg.
				3 months after readministration (day of discontinuation of readministration)	The steroid was restarted for recurrence of acute panuveitis of both eyes and cystoid macular oedema. Ibrutinib was switched to acalabrutinib.
	Concomitant drugs: None				

3

Revisions of PRECAUTIONS (No. 367)

This section presents details of revisions to the PRECAUTIONS and brand names of drugs that have been revised in accordance with the Notifications dated February 10, 2026.

1 Antimetabolic agents, antitumor antibiotics and preparations

[1] Cytarabine
[2] Daunorubicin hydrochloride

Brand name	[1] Cylocide Injection 20 mg, 40 mg, 60 mg, 100 mg, 200 mg, Cylocide N Injection 400 mg, 1 g (Nippon Shinyaku Co., Ltd.), and the others [2] DAUNOMYCIN FOR INJECTION 20 mg (Meiji Seika Pharma Co., Ltd.)
8. IMPORTANT PRECAUTIONS (newly added)	Tumour lysis syndrome may occur. Patients should be carefully monitored by checking serum electrolyte levels, renal function, etc.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Tumour lysis syndrome If any abnormalities are observed, administration of this drug should be discontinued, appropriate measures (e.g., administration of physiological saline solution and/or hyperuricaemia therapeutic agents, and dialysis) should be taken, and patients should be carefully monitored until recovery from such symptoms.

2 Other antitumor agents

Axitinib

Brand name	Inlyta Tablets 1 mg, 5 mg (Pfizer Japan Inc.)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Acute pancreatitis If symptoms such as abdominal pain or pancreatic enzyme increased are observed, appropriate measures including discontinuation of treatment with this drug should be taken.

3 Other antitumor agents

Ibrutinib

Brand name	Imbruvica Capsules 140 mg (Janssen Pharmaceutical K.K.)
8. IMPORTANT PRECAUTIONS (newly added)	Uveitis may occur. Whether ocular abnormalities occur should be examined periodically. In addition, patients should be instructed to immediately seek medical attention if any ocular abnormalities are observed.
11. ADVERSE REACTIONS	Uveitis

11.1 Clinically Significant Adverse Reactions (newly added)	

4 Other antitumor agents

Fruquintinib

Brand name	Fruzaqla capsules 1 mg, 5 mg (Takeda Pharmaceutical Company Limited)
8. IMPORTANT PRECAUTIONS	Nephrotic syndrome and proteinuria may occur. Urine protein should be monitored periodically before the start of and during administration of this drug.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Nephrotic syndrome

5 Anti-virus agents

[1] Aciclovir (oral dosage form and injection)
[2] Valaciclovir hydrochloride

Brand name	[1] Zovirax Granules 40%, Zovirax Tablets 200, 400, Zovirax for I.V. infusion 250 (GlaxoSmithKline K.K.), and the others [2] Valtrex Granules 50%, Valtrex Tablets 500 (GlaxoSmithKline K.K.), and the others
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Toxic epidermal necrolysis (TEN), oculomucocutaneous syndrome (Stevens-Johnson syndrome), acute generalised exanthematous pustulosis

6 Other cardiovascular agents

Riociguat

Brand name

Adempas Tablets 0.5 mg, 1.0 mg, 2.5 mg (Bayer Yakuhin Ltd.)

10. INTERACTIONS
10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.)
(newly added)

Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
Ensitrelvir fumaric acid Lonafarnib	The blood concentration of riociguat may increase. If administration of riociguat is started in patients being treated with these drugs, starting at a dose of 0.5 mg 3 times daily should also be considered. If administration of these drugs is started while receiving riociguat, dose reduction of riociguat should be considered.	The clearance of riociguat is decreased by the inhibition of CYP3A by these drugs.

7 Agents affecting metabolism, n.e.c. (not elsewhere classified)

Lonafarnib

Brand name

Zokinvy Capsules 50 mg, 75 mg (AnGes, Inc.)

2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)

Patients receiving the following drugs: Quinidine sulfate hydrate, bepridil hydrochloride hydrate, ticagrelor, eplerenone, ergotamine tartrate/anhydrous caffeine/isopropylantipyrine, methylergometrine maleate, triazolam, anamorelin hydrochloride, ivabradine hydrochloride, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small cell lymphocytic lymphoma)], ibrutinib, blonanserin, lurasidone hydrochloride, azelnidipine containing preparations, suvorexant, tadalafil (Adcirca), vardenafil hydrochloride hydrate, lomitapide mesilate, rifabutin, finerenone, rivaroxaban, apalutamide, carbamazepine, midazolam, atorvastatin calcium hydrate containing preparations, simvastatin

10. INTERACTIONS
10.1 Contraindications for Co-administration (Do not co-administer with the following.)

(Deleted)

10. INTERACTIONS
10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.)
(newly added)

Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
Riociguat	Lonafarnib may increase the blood concentration of riociguat. When co-administration with lonafarnib is necessary, patients should be monitored for their condition and dose reduction of riociguat should be considered as necessary.	The metabolism of riociguat is suppressed by the inhibitory activity of lonafarnib against CYP3A.

8 Anti-virus agents

Ensitrelvir fumaric acid

Brand name
Xocova Tablets 125 mg (Shionogi & Co., Ltd.)

2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)
Patients receiving the following drugs: Pimozide, quinidine sulfate hydrate, bepridil hydrochloride hydrate, ticagrelor, eplerenone, ergotamine tartrate/anhydrous caffeine/isopropylantipyrine, ergometrine maleate, methylergometrine maleate, dihydroergotamine mesilate, simvastatin, triazolam, anamorelin hydrochloride, ivabradine hydrochloride, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)], ibrutinib, blonanserin, lurasidone hydrochloride, azelnidipine, azelnidipine/olmesartan medoxomil, suvorexant, daridorexant hydrochloride, vornorexant hydrate, tadalafil (Adcirca), macitentan/tadalafil, vardenafil hydrochloride hydrate, lomitapide mesilate, rifabutin, finerenone, voclosporin, lonafarnib, mavacamten, rivaroxaban, apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, fosphenytoin sodium hydrate, rifampicin, or food containing St. John's Wort

10. INTERACTIONS
10.1 Contraindications for Co-administration (Do not co-administer with the following.)
(Deleted)

10. INTERACTIONS
10.2 Precautions for Co-administration (This drug should be administered with caution when co-administered with the following.)
(newly added)

Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
Riociguat	Ensitrelvir fumaric acid may increase the blood concentration of riociguat. When co-administration with ensitrelvir fumaric acid is necessary, patients should be monitored for their conditions and dose reduction of riociguat should be considered as necessary.	The metabolism of riociguat is suppressed by the inhibitory activity of ensitrelvir fumaric acid against CYP3A.

4

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 January 31, 2026)

Nonproprietary name / Brand name		Name of the MAH	Date of EPPV initiation
	Diazepam Spydia Nasal Spray 5 mg, 7.5 mg, 10 mg	Aculys Pharma, Inc.	December 24, 2025
	Finerenone*1 Kerendia tablets 10 mg, 20 mg	Bayer Yakuhin, Ltd.	December 22, 2025
	Odevixibat hydrate Bylvay Granules 200 μg, 600 μg	IPSEN Co., Ltd	December 18, 2025
	Rimegepant sulfate hydrate Nurtec OD Tablets 75 mg	Pfizer Japan Inc.	December 16, 2025
	Midazolam Dormicum syrup 2 mg/mL	Maruishi Pharmaceutical Co., Ltd.	November 27, 2025
	Avacincaptad pegol sodium Izervay for intravitreal injection 20 mg/mL	Astellas Pharma Inc.	November 27, 2025
	Vornorexant hydrate Vorzzz tablets 2.5 mg, 5 mg, 10 mg	Taisho Pharmaceutical Co., Ltd.	November 27, 2025
	Chenodeoxycholic Acid*2 Fujichenon granular tablets 125	Fujimoto Pharmaceutical Corporation	November 21, 2025
	Bempedoic Acid Nexletol tablets 180 mg	Otsuka Pharmaceutical Co., Ltd.	November 21, 2025
	Repotrectinib*3 Augtyro capsules 40 mg, 160 mg	Bristol-Myers Squibb K.K.	November 20, 2025
	Inebilizumab (genetical recombination)*4 Uplizna for intravenous infusion 100 mg	Tanabe Pharma Corporation	November 20, 2025
	Gallium (^{68}Ga) gozetotide Locametz kit	Novartis Pharma K.K.	November 12, 2025
	Lutetium (177Lu) vipivotide tetraxetan Pluvicto injection	Novartis Pharma K.K.	November 12, 2025
	Taletrectinib adipate		November 12,

	Nonproprietary name Brand name	Name of the MAH	Date of EPPV initiation
	Ibtrozi capsules 200 mg	Nippon Kayaku Co., Ltd.	2025
	Zongertinib Hernexeos tablets 60 mg	Nippon Boehringer Ingelheim Co., Ltd.	November 12 2025
	Nusinersen Sodium Spinraza intrathecal injection 28 mg, 50 mg	Biogen Japan Ltd.	November 12, 2025
	Selumetinib sulfate Koselugo granules 5 mg, 7.5 mg	Alexion Pharma Godo Kaisha	November 12, 2025
	Nipocalimab (genetical recombination) Imaavy intravenous infusion 1200 mg	Janssen Pharmaceutical K.K.	November 12, 2025
	Palopegteriparatide Yorvipath subcutaneous injection 168 μg pen, 294 μg pen, 420 μg pen	Teijin Pharma Limited	November 6, 2025
	Gallium (^{68}Ga) chloride GalliaPharm ^{68}Ge/^{68}Ga generator	Eckert & Ziegler Radiopharma GmbH (Oversee products designated MAH) Novartis Pharma K.K.	November 5, 2025
	Remimazolam besilate[*5] Anerem 20 mg for I.V. injection	Mundipharma K.K.	November 4, 2025
	Pneumococcal 21-valent Conjugate Vaccine (joint component of nontoxic diphtheria toxin derivatives) Capvaxive for intramuscular injection syringes	MSD K.K.	October 29, 2025
	Sepetaprost Setaneo ophthalmic solution 0.002%	Santen Pharmaceutical Co., Ltd.	October 23, 2025
	Coronavirus (SARS-CoV-2) RNA Vaccine DAICHIRONA INTRAMUSCULAR INJECTION	Daiichi Sankyo Co., Ltd.	September 19, 2025
	Etrasimod L-Arginine Velsipity Tablets 2 mg	Pfizer Japan Inc.	September 12, 2025
	Miglustat[*6] Opfolda Capsules 65 mg	Amicus Therapeutics, Inc.	August 27, 2025
	Cipaglucosidase alfa (genetical recombination) Pombiliti for I.V. Infusion 105 mg	Amicus Therapeutics, Inc.	August 27, 2025
	Recombinant adsorbed 9-valent human papillomavirus virus-like particle vaccine (yeast origin)[*7] Silgard 9 Aqueous Suspension for Intramuscular Injection Syringes	MSD K.K.	August 25, 2025
	Selumetinib Sulfate Koselugo Capsules 10 mg, 25 mg	Alexion Pharma Godo Kaisha	August 25, 2025

	Nonproprietary name Brand name	Name of the MAH	Date of EPPV initiation
	Avatrombopag Maleate[*8] Doptelet tablets 20 mg	Swedish Orphan Biovitrum Japan Co., Ltd.	August 25, 2025
	Belzutifan Welireg Tablets 40 mg	MSD K.K.	August 18, 2025
	Sotatercept (genetical recombination) Airwin for Subcutaneous Injection 45 mg, 60 mg	MSD K.K.	August 18, 2025
	Talquetamab (genetical recombination) Talvey Subcutaneous Injection 3 mg, 40 mg	Janssen Pharmaceutical K.K.	August 14, 2025

*1 Chronic cardiac failure, only limited to patients receiving standard treatment for chronic heart failure

*2 Cerebrotendinous xanthomatosis

*3 NTRK fusion gene-positive advanced or recurrent solid tumor

*4 Suppression of relapse in IgG4-related diseases

*5 Sedation during gastrointestinal endoscopy

*6 Combination therapy with cipaglucosidase alfa (genetical recombination) for late onset pompe's disease

*7 Prevention of the following diseases caused by infection with human papillomavirus types 6, 11, 16, 18, 31, 33, 45, 52, and 58
• Anal cancer (squamous cell carcinoma) and its precursor lesions (anal intraepithelial neoplasia (AIN) grades 1, 2, and 3)

*8 Persistent and chronic immune thrombocytopenia