Pharmaceuticals and Medical Devices Safety Information

No. 420 June 2025

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) 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).

Available information is listed here

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

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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.

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No. 420 June 2025

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

[Outline of Information]

No.	Subject	Measures	Outline of Information	Page
1	**Revision of PRECAUTIONS for Domperidone**	*P*	In 2005, the Japan Drug Information Institute in Pregnancy (hereinafter referred to as “JDIIP”) was established in the National Center for Child Health and Development by the MHLW’s JDIIP project to collect and assess the latest scientific evidence regarding the effects of drugs on mothers and fetuses. Based on these data, the JDIIP has provided consultations for women who are pregnant or who wish to become pregnant. Since 2016, we have been engaged in a project to promote the documentation of information on drug use in pregnant women/nursing mothers, etc. in package inserts by organizing and assessing the information accumulated so far by the JDIIP. In this project, a working group (hereinafter referred to as “WG”) composed of experts has been established. The WG selects a candidate drug, organizes and evaluates the information accumulated so far, and compiles the draft revision of the package insert for the drug as a report. Recently, the language concerning contraindications, etc. for domperidone was revised based on the deliberation in the Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs Council. This section will introduce the details of the revision.	5
2	**Revisions of PRECAUTIONS for Iodixanol**	*P*	On May 20, 2025, the MHLW issued a notification instructing the addition of "cardiac arrest" to the 11.1 Clinically Significant Adverse Reactions section in the PRECAUTIONS of iodixanol (Visipaque 270 Injection 20 mL, 50 mL, 100 mL, Visipaque 320 Injection 50 mL, 100 mL). This section will introduce the details of the revision and other relevant information.	8
3	**Important Safety Information**	*P* *C*	Nemolizumab (genetical recombination) (and 3 others): Regarding the revision of the PRECAUTIONS of drugs in accordance with the Notification dated May 20, 2025, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.	9
4	**Revisions of PRECAUTIONS (No.360)**	*P*	[1] Acetazolamide [2] Acetazolamide sodium (and 20 others):	19
5	**List of Products Subject to Early Post-marketing Phase Vigilance**		List of products subject to Early Post-marketing Phase Vigilance as of April 30, 2025	28

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

ACD	Anterior Chamber Depth
ADR	Adverse Drug Reaction
ALS	Amyotrophic Lateral Sclerosis
BMI	Body Mass Index
BPDAI	Bullous Pemphigoid Disease Area Index
CCT	Central Corneal Thickness
CPR	Cardiopulmonary Resuscitation
CYP	Cytochrome P450
EPPV	Early Post-marketing Phase Vigilance
FA	Fluorescein Angiography
FY	Fiscal Year
IOP	Intraocular pressure
JDIIP	Japan Drug Information Institute in Pregnancy
LT	Lens Thickness
MAH	Marketing Authorization Holder
MHLW	Ministry of Health, Labour and Welfare
MRI	Magnetic Resonance Imaging
OCT	Optical Coherence Tomography
OD	Right Eye
OS	Left Eye
PMDA	Pharmaceuticals and Medical Devices Agency
PSB	Pharmaceutical Safety Bureau
PSD	Pharmaceutical Safety Division
SPH	Spherical Diopter Power
TARC	Thymus and Activation-Regulated Chemokine
UBM	Ultrasound Biomicroscopy
WG	Working Group

1

Revision of PRECAUTIONS for Domperidone

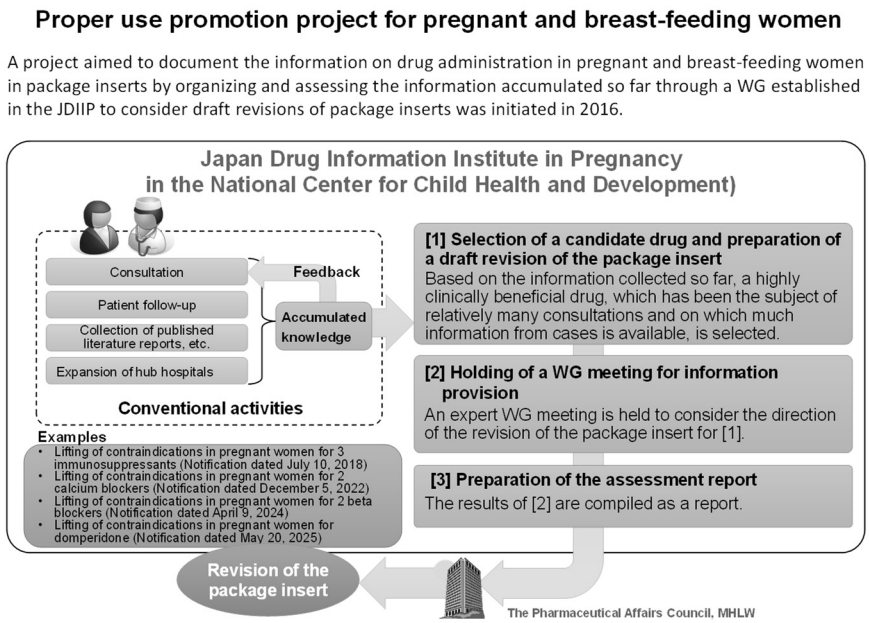
1. Introduction

When drugs are used during pregnancy, attention must be paid to the effects on the fetus as well as on the mother. On the other hand, due to difficulties with obtaining safety information on drug use during pregnancy, women who are receiving drug therapy for pre-existing diseases may choose to avoid pregnancy or to discontinue taking prescribed necessary medications. In addition, there are cases in which women who used drugs without realizing that they are pregnant become concerned about the continuation of the pregnancy.

In 2005, the Japan Drug Information Institute in Pregnancy (hereinafter referred to as “JDIIP”) was established in the National Center for Child Health and Development by the project for JDIIP to collect and assess the latest scientific evidence regarding the effects of drugs on mothers and fetuses. Based on these data, the JDIIP has provided consultations for women who are pregnant or who wish to become pregnant.

Since 2016, we have been engaged in a project to promote the documentation of information on drug use in pregnant women/nursing mothers, etc. in package inserts by organizing and assessing the information accumulated so far by the JDIIP. In this project, a working group (hereinafter referred to as “WG”) composed of experts has been established. The WG selects a candidate drug, organizes and evaluates the information accumulated so far, and compiles the draft revision of the package insert for the drug as a report (Figure 1).

(Fig.1)



Recently, the language concerning contraindications, etc. for pregnant women for domperidone has been revised based on the deliberation in the Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs Council (hereinafter referred to as "the Subcommittee on Drug Safety"). This section will introduce the details of the revision.

2. Details of the review by the WG

Domperidone (hereinafter referred to as “this drug”) was approved for marketing in Japan for the indication of diseases including chronic gastritis and gastroptosis and gastrointestinal symptoms including nausea/vomiting when receiving a drug. It was decided at the time of approval of the brand-name product of domperidone that administration of domperidone to pregnant women or women who may be pregnant is contraindicated since the teratogenicity, such as visceral/skeletal anomalies, in rat fetuses at approximately 65 times the clinical dose was reported in a study on administration during the organogenesis period of rat fetuses.

Recently, the Japan Society of Obstetrics and Gynecology and the Japanese Society of Neurology submitted a request to the working group (WG) to lift the contraindication in pregnant women. Therefore, the appropriateness of contraindicating domperidone to pregnant women/nursing mothers, etc. was investigated by the WG. As a result, taking into account the following, a report was compiled stating that pregnant women or women who may be pregnant may be deleted from 2. CONTRAINDICATIONS in the package insert for this drug and that it is appropriate to add precautions that domperidone should be administered to pregnant women or women who may be pregnant only if the potential therapeutic benefits are considered to outweigh the potential risks.

- In a study on administration during the organogenesis period of rat fetuses, teratogenicity was observed at a dose of 200 mg/day (corresponding to 65 times the maximum recommended clinical dose). While maternal toxicity and mild foetal toxicity were noted at a dose of 70 mg/kg/day (corresponding to 23 times the maximum recommended clinical dose), no teratogenic toxicity in rat fetuses was observed.
- There have been no epidemiological studies (including Japanese literature) suggesting an increase in the risk of congenital anomaly by the use of domperidone in the first trimester of pregnancy.
- In a Japanese guideline, domperidone is included in a list of drugs that are considered not to have a clinically significant impact on the fetus when it is used only in the first trimester of pregnancy. In addition, in overseas product labeling, the use of domperidone in pregnant women is not contraindicated, and it is stated that domperidone should be administered only if the potential therapeutic benefits are considered to outweigh the potential risks.

The WG report pointed out as follows: Because of the similarity between the symptoms of hyperemesis gravidarum and the gastrointestinal symptoms for which domperidone is indicated, there are a certain number of cases that result in prescribing domperidone to pregnant women who are unaware of their pregnancy. Women may become anxious about continuing their pregnancy in such cases when they notice the fact that domperidone is contraindicated for pregnant women after recognizing their pregnancy, causing them to choose to undergo an elective abortion.

3. Deliberation by the Subcommittee on Drug Safety

Based on the deliberation by the WG and the investigation results by the PMDA in response to the WG report, the 2nd FY 2025 Subcommittee on the Drug Safety held on April 25, 2025 concluded that the package insert of domperidone may be revised as follows:

- “Pregnant women or women who may be pregnant” should be deleted from 2. CONTRAINDICATIONS in the package insert, and a cautionary statement that “domperidone should be administered to pregnant women or women who may be pregnant only if the potential therapeutic benefits are considered to outweigh the potential risks.” should be added to the 9.5 Pregnant Women section.
- Regarding the description in the current 9.5 Pregnant Women section in the package insert that teratogenicity in rats has been reported, it is a result at a high dose which is approximately 65 times the clinical dose based on body surface area conversion, although the correlation between the doses and exposures in the non-clinical studies is not clear. Therefore, the ratio of the dose in the animal study to the clinical dose should be provided in the package insert as information for users to assess the risk.

4. Closing remark

The revision of the package insert this time is not intended to proactively recommend the use of this drug for the treatment of gastrointestinal symptoms in “pregnant women or women who may be pregnant” but to lift the contraindications based on the latest knowledge to avoid the following situations: Women may become anxious about continuing their pregnancy in such cases when they notice the fact that domperidone is contraindicated for pregnant women after recognizing their pregnancy, causing them to choose to undergo an unnecessary elective abortion. Careful management, including a prescription of other drugs in the same class, is considered to be necessary for those patients. Healthcare professionals are requested to understand the purpose of the revisions this time and are asked to continue their cooperation for proper use of domperidone.

5. [Reference information]

•Proper use promotion project for pregnant and breast-feeding women
https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iyakuhin/ninshin_00002.html (only in Japanese)
•Materials 2-1 and 2-2 of the 2nd FY 2025 Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs Council (held on April 25, 2025) (only in Japanese)
https://www.mhlw.go.jp/stf/newpage_57187.html (only in Japanese)
•Revisions of PRECAUTIONS (PSB/PSD Notification No. 0520-1 dated May 20, 2025)
https://www.mhlw.go.jp/content/001489567.pdf (in Japanese)
https://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0013.html (in English)

2

Revisions of PRECAUTIONS for Iodixanol

1. Introduction

On May 20, 2025, the MHLW issued a notification instructing the addition of "cardiac arrest" to the 11.1 Clinically Significant Adverse Reactions section in the PRECAUTIONS of iodixanol (Visipaque 270 Injection 20 mL, 50 mL, 100 mL, Visipaque 320 Injection 50 mL, 100 mL (hereinafter referred to as “this drug”)). This section will introduce the details of the revision and other relevant information.

2. Background

“Shock,” “anaphylaxis,” and “ventricular fibrillation” are included in the Clinically Significant Adverse Reactions section in the electronic package insert of this drug in Japan, and it can be expected that these events may lead to cardiac arrest. On the other hand, the possibility that “cardiac arrest” not associated with “shock,” “anaphylaxis,” or “ventricular fibrillation” may occur has not been warned of in the electronic package insert. Recently, a consultation was requested to the PMDA by the marketing authorization holder (MAH) of this drug regarding the revision of the package insert to include a precaution for cardiac arrest. Cases have been observed in which cardiac arrest occurred without being accompanied by apparent signs and symptoms of anaphylaxis, etc., which are already warned of in the electronic package insert. Thus, the necessity of revising the electronic package insert was discussed.

3. Detail of the review

In examining the necessity of revision, cases involving cardiac arrest were evaluated. Cases of cardiac arrest have been reported in which a causal relationship with iodixanol was considered reasonably possible, and where the cardiac arrest was not clearly associated with shock, anaphylaxis, or ventricular fibrillation, which are already warned of in the electronic package insert. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

In addition, since cardiac arrest is a serious adverse event that may lead to death, it was considered to be important to prepare emergency measures prior to administration of this drug. Therefore, it was determined that “cardiac arrest” should be added to the language in IMPORTANT PRECAUTIONS stating that emergency measures should always be prepared prior to administration of this drug.

Please also refer to 3. Important Safety Information in this article for the details of the revision and clinical courses of the cases.

4. Closing remark

Healthcare professionals are requested to pay sufficient attention to the onset of cardiac arrest after administration of this drug and to take appropriate measures such as always preparing emergency treatments prior to administration of this drug in case cardiac arrest should occur.

3

Important Safety Information

Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated May 20, 2025, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.

1 Nemolizumab (genetical recombination)

Brand name (name of company)	Mitchga Vials 30 mg, Mitchga Syringes 60 mg (Maruho Co., Ltd.)
Therapeutic category	Other antiallergic agents
Indications	<Mitchga Vials 30 mg> Treatment of the following diseases in patients who have had an inadequate response to conventional treatments: •Pruritus associated with atopic dermatitis •Prurigo nodularis <Mitchga Syringes 60 mg> Pruritus associated with atopic dermatitis (only for patients who have had an inadequate response to conventional treatments)

PRECAUTIONS (Revised language is underlined.)

11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions** **(newly added)**	Pemphigoid Blister, erosion, etc. may occur.
Reference information	Number of cases (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's database for adverse drug reactions, etc. reports Cases involving pemphigoid reported in Japan: 2 (No patient mortalities) Cases involving pemphigoid reported overseas: 2 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Mitchga Vials 30 mg: Approximately 3,700 Mitchga Syringes 60 mg: Approximately 10,000 Japanese market launch: Mitchga Vials 30 mg: June 2024 Mitchga Syringes 60 mg: August 2022

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Male 80s	Senile atopic dermatitis/atopic dermatitis (prurigo, hypertension)	60 mg 2 doses at a 4 week interval	**Bullous pemphigoid**	
				3 months before administration	No findings suggestive of bullous pemphigoid were revealed by blood tests or a skin biopsy.
				Day 1 of administration	Difluprednate ointment was topically administered to treat atopic dermatitis, but the response was inadequate. Administration of nemolizumab was initiated for the treatment of pruritus. Itching disappeared on the day of administration.
				28 days after administration	The patient received a second dose of nemolizumab (the last administration). Erythema slightly persisted on the left forearm.
				56 days after administration (day of discontinuation)	Bullous pemphigoid occurred. Multiple tense blisters were observed on the left leg and forearms, and administration of nemolizumab was discontinued. A skin biopsy was performed again. <Biopsy results> Massive eosinophilic infiltration was noted within the blisters and the subepidermal blisters. The IgG/complement component (C3) was positive in the basement membrane by the direct immunofluorescence method. An increase in anti-BP180 antibody level of up to 271 U/mL was observed in a blood test. The severity was assessed as moderate (Bullous Pemphigoid Disease Area Index: BPDAI).
				9 days after discontinuation	The patient was admitted to the hospital for the purpose of induction of oral administration of prednisolone.
				10 days after discontinuation	Oral administration of prednisolone 30 mg was initiated.
				23 days after discontinuation	No new blisters developed, and erosions steadily showed a tendency toward epithelization. The dose of oral prednisolone was reduced to 25 mg.
				25 days after discontinuation	The erosions on the legs were completely epithelized. The patient began rehabilitation.
				32 days after discontinuation	The patient was discharged from the hospital based on his favorable clinical course. Bullous pemphigoid resolved.

Laboratory test value

Test item (unit)	3 months before administration	56 days after administration	18 days after discontinuation	31 days after discontinuation	39 days after discontinuation	73 days after discontinuation
White blood cell count (/mm^3)	7600	6700	7400	18300	6300	8700
Eosinophils (%)	24.4	33	0.5	0.3	0	0.1
IgE (IU/mL)	196	2985	−	−	−	−
TARC (pg/mL)	1260	2880	−	−	−	−
Anti-BP antibody (U/mL)	<3.0	271	431	−	249	94.5

Concomitant drugs: Heparinoid, azilsartan, magnesium oxide, junchoto, alprazolam, teprenone, brotizolam, paroxetine hydrochloride hydrate, ketoprofen, pregabalin, limaprost alfadex, rupatadine fumarate, difluprednate, dimethyl isopropylazulene, diquafosol sodium, trichlormethiazide

2 Iodixanol

Brand name (name of company)	Visipaque 270 Injection 20 mL, 50 mL, 100 mL, Visipaque 320 Injection 50 mL, 100 mL (GE Healthcare Pharma Co., Ltd.)
Therapeutic category	X-ray contrast agents
Indications	<Visipaque 270 Injection> Cerebral angiography, extremities angiography, retrograde urography, endoscopic retrograde cholangiopancreatography <Visipaque 320 Injection> Extremities angiography

PRECAUTIONS (Revised language is underlined.)

8. IMPORTANT PRECAUTIONS **<Common to all indications>**	Hypersensitivity may occur regardless of dosage and dosing regimen. Serious adverse reactions such as shock <u>and cardiac arrest</u> caused by this drug is not necessarily due to iodine hypersensitivity, and no methods are currently available for predicting them. Therefore, emergency measures should be prepared prior to administration of this drug.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions** **<Common to all indications>** **(newly added)**	<u>Cardiac arrest</u>
Reference information	Number of cases (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's database for adverse drug reactions, etc. reports* Cases involving cardiac arrest reported in Japan: 0 Cases involving cardiac arrest reported overseas: 3 (1 patient mortality) *Among the cases collected in the PMDA's database for adverse drug reactions, etc. reports that resulted in cardiac arrest, the following cases were excluded: Cases which developed shock or anaphylaxis, for which a precaution had been included in the electronic package insert; cases with complications/past history, etc. that were considered to be a risk factor of cardiac arrest. Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 231,835 Japanese market launch: November 2000

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 70s	Metastases to lung Metastases to pleura CT scan (unknown)	75 mL Single dose	**Cardiac arrest associated with cor pulmonale decompensation**	
				Day 1 of administration (Day of completion)	The patient had ventilatory failure in the right lung, but she presented to the hospital on foot in a stable condition on that day. She was administered 75 mL of Iodixanol (320 mg/mL) intravenously to perform a CT scan for the metastatic diseases in the right pleura and the lung. 60 seconds after administration, cyanosis and dyspnoea were noted. Prednisolone (100 mg) was administered. Cough, cardiac arrest, and coma progressed rapidly. Resuscitation was initiated, and she was transferred to the intensive care unit. Secondary hypoxic brain damage and aspiration developed.
				3 days after administration	Mechanical ventilation was discontinued per the patient's prior wishes, and the patient died.
	Suspected concomitant drugs: None Concomitant drugs: Unknown				

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
2	Female Unknown	Intracranial aneurysm Cerebral angiogram (cerebral arterial aneurysm)	150 mL Single dose	**Brain oedema, cardiac arrest, coma, increased blood pressure, loss of consciousness, seizure**	
				Day 1 of administration (Day of completion)	The patient was administered 150 mL of Iodixanol (320 mg/mL) intravenously to perform a cerebral angiography for the cerebral arterial aneurysm. Loss of consciousness developed during the angiography, but it resolved. Seizure and cardiac arrest occurred several hours after administration. Cardiopulmonary resuscitation (CPR) was performed. CT examinations revealed brain oedema. Seizure occurred again. Increased blood pressure and brain oedema were exacerbated.
				3 days after administration	The patient became comatose.
				5 days after administration	The patient died. The cause of the death was not reported. No autopsy was performed.
	Suspected concomitant drugs: None Concomitant drugs: Unknown				

3 Indapamide

Brand name (name of company)	Natrix Tablets 1, 2 (Kyoto Pharmaceutical Industries, Ltd.)
Therapeutic category	Antihypertensives
Indications	Essential hypertension

PRECAUTIONS (Revised language is underlined.)

8. IMPORTANT PRECAUTION (newly added)	Acute myopia, angle closure glaucoma, and/or choroidal effusion may occur. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS	Acute myopia, angle closure glaucoma, choroidal effusion
11.1 Clinically Significant Adverse Reactions (newly added)	Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.
Reference information	Number of cases (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's database for adverse drug reactions, etc. reports Cases involving acute myopia, angle closure glaucoma, and/or choroidal effusion reported in Japan: 1 (No patient mortalities) Cases involving acute myopia, angle closure glaucoma, and/or choroidal effusion reported overseas: 1 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Natrix Tablets 1: Approximately 341,000 Natrix Tablets 2: Approximately 24,000 Japanese market launch: Natrix Tablets 1: February 1985 Natrix Tablets 2: December 1990

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 50s	Uncontrolled hypertension (myopia)	1 mg for 3 days	**Acute angle closure glaucoma, choroidal effusion** Past history: Hyperlipidaemia, mydriasis	
				Date unknown	The patient started to receive pravastatin sodium and amlodipine besilate.
				Day 1 of administration	Indapamide was added to treat inadequately controlled hypertension.
				Day 3 of administration (day of discontinuation)	The patient discontinued taking indapamide due to dry eyes.
				1 day after discontinuation	When the patient woke up at night, she experienced dimmed vision and eye pain. When she woke up at midnight, she had photophobia.
				3 days after discontinuation:	The patient had eye pain since the morning. She visited the department of ophthalmology at Hospital A, and she was diagnosed with angle closure glaucoma.
				4 days after discontinuation	Since the symptoms did not improve, the patient visited the department of ophthalmology at Hospital B. Intraocular pressure (IOP) values were as follows: 24 mmHg in the right eye (OD) and 25 mmHg in the left eye (OS). Since the anterior chamber depth (ACD) was shallow, Vogt-Koyanagi-Harada disease was suspected. On the same day, the patient was referred to the department of ophthalmology at Hospital C. Black spots appeared in a field of view. Her best-corrected visual acuity was 20/20 with − 9.00 D sph, − 0.75 D cyl × 20 correction in OD and 20/16 with − 8.75 D sph, − 1.25 D cyl × 150 correction in OS. The IOP was 24 mmHg and 32 mmHg in OD and OS, respectively. Pupillary reactions were normal. A slit-lamp examination revealed no inflammation in the shallow anterior chamber of either eye. A laser flare meter showed no inflammation. The central corneal thickness (CCT) and lens thickness (LT) had been slightly increased without any difference between OD and OS, compared to the prominently swollen ciliary body and choroid. An optical coherence tomography (OCT) of the anterior segment of the eye showed choroidal effusion caused by forward displacement of the lens and the edematous ciliary body, which was revealed by an ultrasound biomicroscopy. A fundus examination revealed extensive, symmetrical, bilateral choroidal effusion on the temporal side. Fluorescein angiography (FA) showed granular hyperfluorescence, tortuous vessels, vascular leakage, a nonperfusion area corresponding to the site of choroidal effusion on the temporal side, and retinal folds toward the posterior pole in both eyes. An indocyanine green angiography revealed no significant findings. The macula was intact on OCT, but the choroid was significantly thickened.

	The corner angle was 0 to 1 by Shaffer's grading, and the anterior chamber was slightly deeper in OS than in OD. A B-mode ultrasonography revealed a membranous high-intensity lesion in both eyes that emerged from the retina. It seemed that there was no continuity from the optic nerve head. A head magnetic resonance imaging (MRI) revealed no intracranial lesions, but it indicated oedema of the entire eyeball. (A T1 weighted image showed a high-signal area on the surface and in the deep layers of liquid. Fluid had accumulated symmetrically on the sclera, with a high signal on both temporal sides. The T2 weighted image showed a small amount of fluid that had accumulated in the sub-Tenon's space. A small amount of oedema was suspected around the optic nerve head.)
5 days after discontinuation:	It was considered that oedema of the ciliary body may have mainly contributed to the forward displacement of the lens. Administration of tropicamide/ phenylephrine hydrochloride ophthalmic solution and betamethasone sodium phosphate ophthalmic solution 3 times per day was initiated.
6 days after discontinuation:	The IOP decreased to 14 mmHg and 15 mmHg in OD and OS, respectively.
7 days after discontinuation:	The ACD gradually deepened to more than 2.0 mm, and the IOP normalized.
11 days after discontinuation:	Both the CCT and the LT improved. The bilateral choroidal effusion on the inferior temporal side disappeared. The eye pain resolved, as did the other optical symptoms. Myopia improved to 20/20 with − 7.50 D sph in OD and 20/20 with − 6.75 D sph, − 0.75 D cyl × 120 correction in OS, and the patient was discharged.
Approximately 2.5 months after discontinuation	FA revealed improvement in the vascular leakage and peripheral granular hyperfluorescence, and the nonperfusion area was not observed. The choroid returned to its normal thickness.

Laboratory test value

Test item (unit)		3 days after discon-tinuation	4 days after discon-tinuation	5 days after discon-tinuation	6 days after discon-tinuation	7 days after discon-tinuation	11 days after discon-tinuation	Approxi-mately 2.5 months after discon-tinuation
Best-corrected visual acuity	OD	–	20/20	–	–	–	20/20	20/16
	OS	–	20/16	–	–	–	20/20)	20/16
Spherical diopter power (SPH) (D)	OD	–	-9.00	–	–	–	-7.50	-7.50
	OS	–	-8.75	–	–	–	-6.75	-7.00
Axial length (mm)	OD	–	26.47	–	–	–	–	26.60
	OS	–	26.42	–	–	–	–	26.54
IOP (mmHg)	OD	26	24	20	14	13	18	18
	OS	29	32	27	15	16	19	18
CCT (μm)	OD	–	527	523	510	515	506	514
	OS	–	520	518	506	491	503	508
ACD (mm)	OD	–	1.340	1.549	1.953	2.195	2.649	2.559
	OS	–	1.276	1.502	2.008	2.312	2.616	2.497
LT (mm)	OD	–	4.407	4.343	4.379	4.383	4.259	4.255
	OS	–	4.427	4.453	4.436	4.435	4.287	4.296
Choroidal thickness (μm)	OD	–	342	–	–	294	189	142
	OS	–	316	–	–	221	136	136

Concomitant drugs: Pravastatin sodium, amlodipine besilate

Reference) Takahashi S, et al.: BMC Ophthalmol. 2021; 21(1): 386

4 Indapamide

Brand name (name of company)	Tenaxil Tablets 1 mg, 2 mg (Alfresa Pharma Corporation)
Therapeutic category	Antihypertensives
Indications	Essential hypertension

PRECAUTIONS (Revised language is underlined.)

8. IMPORTANT PRECAUTIONS (newly added)	Acute myopia, angle closure glaucoma, and/or choroidal effusion may occur. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS	Acute myopia, angle closure glaucoma, choroidal effusion
11.1 Clinically Significant Adverse Reactions (newly added)	Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.
Reference information	Number of cases (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's database for adverse drug reactions, etc. reports Cases involving acute myopia, angle closure glaucoma, and/or choroidal effusion reported in Japan: 1 (No patient mortalities) Cases involving acute myopia, angle closure glaucoma, and/or choroidal effusion reported overseas: 3 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 874,478 Japanese market launch: Tenaxil Tablets 1 mg: December 1990 Tenaxil Tablets 2 mg: July 1992

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Male 40s	Hypertension (none)	1 mg for 3 days	**Acute myopia, narrow anterior chamber angle**	
				Day 1 of administration	The patient was prescribed indapamide to treat hypertension by a nearby internal medicine clinic. Oral administration of indapamide at a dose of 1 mg/day was initiated in the morning. The patient noticed decreased distance visual acuity in both eyes from the evening.
				Day 2 of administration	Decreased distance visual acuity was aggravated. The patient noticed myopia.
				Day 3 of administration (day of discontinuation)	The patient consulted an ophthalmologist The anterior chamber was slightly shallow for his age and the reflection. The peripheral anterior chamber depth was classified as Van Herick grade 2, and the angle opening distance was classified as Shaffer grade 2, but the angle was open. An ultrasound biomicroscopy (UBM) was performed, which revealed supraciliochoroidal fluid collection, mild anterior rotation of the ciliary body, elevation of the iris root, and narrow anterior chamber angle. The patient was diagnosed with acute myopia and narrow anterior chamber angle, and he was instructed to discontinue oral administration of indapamide.
				3 days after discontinuation	Myopia was markedly alleviated, and uncorrected visual acuity improved. The anterior chamber depth increased. The peripheral anterior chamber depth was classified as Van Herick grade 4, and the angle opening distance was classified as Shaffer grade 3, with wide open angle. Acute myopia and narrow anterior chamber angle improved.
				2 weeks after discontinuation	A UBM examination was performed, which revealed disappearance of supraciliochoroidal fluid, leaving only a slight plateau iris shape. Thereafter, no recurrence of flat anterior chamber was noted, and intraocular inflammation and sunset glow fundus did not develop during the course.
				3 months after discontinuation	No changes in objective finding were noted.

Laboratory test value

Test item (unit)		Day 3 of administration (day of discontinuation)	3 days after discontinuation	2 weeks after discontinuation
Best-corrected visual acuity	Right eye	0.15	1.0	—
	Left eye	0.15	1.0	—
SPH (D)	Right eye	1.2 x -2.25D⌔ cyl -0.5D 80°	1.2 x -0.5D	—
	Left eye	1.2 x -2.75D⌔ cyl -0.75D 110°	1.2 x -0.5D⌔ cyl-0.5D 115°	—
Axial length (mm)	Right eye	22.86	—	—
	Left eye	22.90	—	—
IOP (mmHg)	Right eye	15	—	—
	Left eye	14	—	—

CCT (μm)	Right eye	—	—	—
	Left eye	—	—	—
ACD (mm)	Right eye	1.997	—	2.490
	Left eye	1.946	—	2.470
LT (mm)	Right eye	1.072	—	0.521
	Left eye	1.003	—	0.447
Choroidal thickness (μm)	Right eye	—	—	—
	Left eye	—	—	—
Anterior chamber volume (mm^3)	Right eye	73.014	—	109.322
	Left eye	73.963	—	108.236

Concomitant drugs: Olmesartan medoxomil/azelnidipine, eplerenone, rosuvastatin calcium

4

Revisions of PRECAUTIONS (No. 360)

This section presents details of revisions to the PRECAUTIONS and brand names of drugs that have been revised in accordance with the Notification dated May 20, 2025.

1 Diuretics

[1] Acetazolamide
[2] Acetazolamide sodium

Brand name	[1] Diamox Powder, Diamox Tablets 250 mg (Sanwa Kagaku Kenkyusho Co., Ltd.) [2] Diamox for Injection 500 mg (Sanwa Kagaku Kenkyusho Co., Ltd.)
8. IMPORTANT PRECAUTIONS (newly added)	Acute myopia, angle closure glaucoma, and/or choroidal effusion may occur. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Acute myopia, angle closure glaucoma, choroidal effusion It has been reported that reduced visual acuity, aggravation of angle closure glaucoma, and/or choroidal effusion occurred in overseas cases of patients treated with this drug for drug-induced glaucoma. Also, there have been reports that acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion occurred in overseas cases of patients administered this drug for treatments including the adjustment of intraocular pressure before and after cataract surgery. When abnormalities such as a rapid reduction in visual acuity and eye pain are observed, the possibility that they are caused by this drug should be considered. If a causal relationship to this drug is suspected, appropriate measures such as discontinuation of this drug should be taken.

2 Diuretics, antihypertensives

[1] Trichlormethiazide
[2] Benzylhydrochlorothiazide
[3] Irbesartan/trichlormethiazide

Brand name	[1] Fluitran Tablets 1 mg, 2 mg (Shionogi Pharma Co., Ltd.), and the others [2] Behyd Tablets 4 mg (Kyorin Pharmaceutical Co., Ltd.) [3] Irtra Combination Tablets LD, HD (Shionogi Pharma Co., Ltd.)
15. OTHER PRECAUTIONS **15.1 Information Based on Clinical Use (newly added)**	It has been reported that acute myopia, angle closure glaucoma, and/or choroidal effusion occurred in patients treated with other thiazide drugs.

3 Diuretics, antihypertensives

Hydrochlorothiazide

Brand name	Hydrochlorothiazide Tablets 12.5 mg “Towa,” 25 mg “Towa,” Hydrochlorothiazide OD Tablets 12.5 mg “Towa” (Towa Pharmaceutical Co., Ltd.)
8. IMPORTANT PRECAUTIONS (newly added)	Acute myopia, angle closure glaucoma, and/or choroidal effusion may occur. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Acute myopia, angle closure glaucoma, choroidal effusion Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.

4 Diuretics

Mefruside

Brand name	Baycaron Tablets 25 mg (Mitsubishi Tanabe Pharma Corporation) and the others
15. OTHER PRECAUTIONS **15.1 Information Based on Clinical Use (newly added)**	It has been reported that acute myopia, angle closure glaucoma, and/or choroidal effusion occurred in patients treated with other thiazide-like drugs.

5 Antihypertensives

Indapamide

Brand name	Natrix Tablets 1, 2 (Kyoto Pharmaceutical Industries, Ltd.)
8. IMPORTANT PRECAUTIONS (newly added)	Acute myopia, angle closure glaucoma, and/or choroidal effusion may occur. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Acute myopia, angle closure glaucoma, choroidal effusion Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.

6 Antihypertensives

Eplerenone

Brand name	Selara Tablets 25 mg, 50 mg, 100 mg (Viatris Pharmaceuticals Japan G.K.), and the others
2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.) <Common to all indications>	Patients receiving the following drugs: Itraconazole, voriconazole, posaconazole, preparations containing ritonavir, and ensitrelvir fumaric acid
10. INTERACTIONS **10.1 Contraindications for Co-administration (Do not co-administer**	

Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
Itraconazole	The plasma	The metabolism of

with the following.) **<Common to all indications>**	Voriconazole Posaconazole Preparations containing ritonavir Ensitrelvir fumaric acid	concentration of eplerenone may increase, and an increase in serum potassium levels may be induced.	eplerenone is suppressed by a strong CYP3A4-inhibitor.

7 Antihypertensives

Candesartan cilexetil/hydrochlorothiazide

Brand name	Ecard Combination Tablets LD, HD (Teva Takeda Yakuhin Ltd.), and the others
8. IMPORTANT PRECAUTIONS (newly added)	Hydrochlorothiazide may cause acute myopia, angle closure glaucoma, and/or choroidal effusion. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Acute myopia, angle closure glaucoma, choroidal effusion Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.

8 Antihypertensives

[1] Telmisartan/amlodipine besilate/hydrochlorothiazide
[2] Telmisartan/hydrochlorothiazide

Brand name	[1] Micatrio Combination Tablets (Nippon Boehringer Ingelheim Co., Ltd.) [2] Micombi Combination Tablets AP, BP (Nippon Boehringer Ingelheim Co., Ltd.), and the others
8. IMPORTANT PRECAUTIONS (newly added)	Hydrochlorothiazide, which is an ingredient of this drug, may cause acute myopia, angle closure glaucoma, and/or choroidal effusion. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Acute myopia, angle closure glaucoma, choroidal effusion Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.

9 Antihypertensives

Valsartan/hydrochlorothiazide

Brand name	Co-DIO Combination Tablets MD, EX (Novartis Pharma K.K.), and the others
8. IMPORTANT PRECAUTIONS (newly added)	Hydrochlorothiazide may cause acute myopia, angle closure glaucoma, and/or choroidal effusion. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Acute myopia, angle closure glaucoma, choroidal effusion Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.

10 Antihypertensives

Losartan potassium/hydrochlorothiazide

Brand name	Preminent Tablets LD, HD (Organon K.K.), and the others
8. IMPORTANT PRECAUTIONS (newly added)	Hydrochlorothiazide, which is an ingredient of this drug, may cause acute myopia, angle closure glaucoma, and/or choroidal effusion. Patients should be instructed to consult an ophthalmologist immediately if they experience abnormalities such as a rapid reduction in visual acuity and eye pain.
11. ADVERSE REACTIONS	Acute myopia, angle closure glaucoma, choroidal effusion
11.1 Clinically Significant Adverse Reactions	Acute myopia (including blurred vision and reduced visual acuity), angle closure glaucoma, and/or choroidal effusion may occur.

11 Other cardiovascular agents

Riociguat

Brand name	Adempas tablets 0.5 mg, 1.0 mg, 2.5 mg (Bayer Yakuhin Ltd.)
2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)	(deleted)
10. NTERACTIONS	(deleted)
10.1 Contraindications for Co-administration (Do not co-administer with the following.)	
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
Itraconazole Voriconazole	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 a day 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 CYP1A1 and/or CYP3A by these drugs.

12 Other agents affecting digestive organs

Domperidone

Brand name	Nauzelin Tablets 5, 10 Nauzelin OD tablets 5, 10 (Kyowa Kirin Co., Ltd.), Domperidone Tablets 5 mg “Kyorin,” 10 mg “Kyorin” (KYORIN Rimedio Co., Ltd.), Domperidone Tablets 5 mg “Sawai,” 10 mg “Sawai” (Sawai Pharmaceutical Co., Ltd.), Domperidone Tablets 5 mg “Tsuruhara,” 10 mg “Tsuruhara” (Tsuruhara Pharmaceutical Co., Ltd.), Domperidone Tablets 5 mg “Towa,” 10 mg “Towa” (Towa Pharmaceutical Co., Ltd.), Domperidone Tablets 5 mg “Nichi-iko,” 10 mg “Nichi-iko” (Nichi-Iko Pharmaceutical Co., Ltd.), Domperidone

	Tablets 5 mg “Nissin,” 10 mg “Nissin” (Nissin Pharmaceutical Co., Ltd.), Domperidone Tablets 5 mg “JG,” 10 mg “JG” (Choseido Pharmaceutical Co., Ltd.), Domperidone Tablets 5 mg “NIG,” 10 mg “NIG” (Nichi-Iko Gifu Plant Co., Ltd.), Domperidone Tablets 5 mg “YD,” 10 mg “YD” (Yoshindo Inc.), Domperidone tab. 5 mg “EMEC,” 10 mg “EMEC” (Alfresa Pharma Corporation), Nauzelin Dry Syrup 1% (Kyowa Kirin Co., Ltd.), Domperidone DS for Pediatric 1% “Sawai” (Sawai Pharmaceutical Co., Ltd.), Nauzelin Suppository 10, 30, 60 (Kyowa Kirin Co., Ltd.), Domperidone Suppositories 10 mg “Takata,” 30 mg “Takata” (TAKATA Pharmaceutical Co., Ltd.), Domperidone Suppositories 10 mg “JG,” 30 mg “JG” (Choseido Pharmaceutical Co., Ltd.), Domperidone Suppositories 10 mg “Nissin,” 30 mg “Nissin” (Nissin Pharmaceutical Co., Ltd.)
2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)	(deleted)
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.5 Pregnant Women	Pregnant women or women who may be pregnant should be administered this drug only if the potential therapeutic benefits are considered to outweigh the potential risks. Teratogenic effects such as skeletal and visceral anomalies have been reported at approximately 65 times the clinical dose (body surface area conversion) in animal studies (rats).

13 Other antitumor agents

Ceritinib

Brand name	Zykadia tablets 150 mg (Novartis Pharma K.K.)
2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.) (newly added)	Patients receiving the following drug: Venetoclax (relapsed or refractory chronic lymphocytic leukaemia (including small lymphocytic lymphoma) and relapsed or refractory mantle cell lymphoma during the dose escalation phase)
10. INTERACTIONS 10.1 Contraindications for Co-administration (Do not co-administer with the following.) (newly added)	

Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
Venetoclax (relapsed or refractory chronic lymphocytic leukaemia (including small lymphocytic lymphoma) and relapsed or refractory mantle cell lymphoma during the dose escalation phase)	The occurrence of tumour lysis syndrome may increase.	Strong CYP3A inhibition by ceritinib may suppress the metabolism of venetoclax, leading to an increase in the blood concentration of venetoclax.

14 Other antitumor agents

Venetoclax

Brand name	Venclexta Tablets 10 mg, 50 mg, 100 mg (AbbVie GK)
2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)	<Relapsed or refractory chronic lymphocytic leukaemia (including small lymphocytic lymphoma), relapsed or refractory mantle cell lymphoma> Patients receiving a strong CYP3A inhibitor (ritonavir, clarithromycin, itraconazole, voriconazole, posaconazole, preparations containing cobicistat, ensitrelvir, lonafarnib, or ceritinib) during the dose escalation

phase of this drug

10. INTERACTIONS **10.1 Contraindications for Co-administration (Do not co-administer with the following.)**	Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
	<Relapsed or refractory chronic lymphocytic leukaemia (including small lymphocytic lymphoma) and relapsed or refractory mantle cell lymphoma during the dose escalation phase of this drug> Strong CYP3A inhibitor Ritonavir Clarithromycin Itraconazole Voriconazole Posaconazole Preparations containing cobicistat Ensitrelvir Lonafarnib Ceritinib	The occurrence of tumour lysis syndrome may increase.	These drugs inhibit CYP3A, and therefore the blood concentration of venetoclax may increase.

15 Other antitumor agents

Borofalan (^{10}B)

Brand name	Steboronine 9000 mg/300 mL for infusion (STELLA PHARMA CORPORATION)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Necrosis, mucosal ulceration, perforation, fistula Mucosal ulceration, perforation, or fistula may occur in association with necrosis at the irradiation site.

16 Other antiallergic agents

Nemolizumab (genetical recombination)

Brand name	Mitchga Vials 30 mg, Mitchga Syringes 60 mg (Maruho Co., Ltd.)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Pemphigoid Blister, erosion, etc. may occur.

17 Antibiotic preparations acting mainly on mold

Posaconazole

Brand name	Noxafil Tablets 100 mg, Noxafil for Intravenous Infusion 300 mg (MSD K.K.)
2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)	Patients receiving the following drugs: Ergotamine tartrate/anhydrous caffeine/isopropylantipyrine, dihydroergotamine, methylergometrine, ergometrine, simvastatin, atorvastatin, pimozide, quinidine, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)],

suvorexant, finerenone, eplerenone, azelnidipine, olmesartan medoxomil/azelnidipine, lurasidone hydrochloride, blonanserin, triazolam, rivaroxaban

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

Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
Finerenone Eplerenone	The effect of these drugs may be enhanced.	The plasma concentration of these drugs is expected to increase due to inhibition of CYP3A4 by co-administration with posaconazole.

18 Antibiotic preparations acting mainly on mold
Voriconazole

Brand name

Vfend Tablets 50 mg, 200 mg, Vfend for Intravenous Use 200 mg, Vfend Dry Syrup 2800 mg (Pfizer Japan Inc.), and the others

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

Patients receiving the following drugs: Rifampicin, rifabutin, efavirenz, ritonavir, lopinavir/ritonavir, nirmatrelvir/ritonavir, carbamazepine, barbital, phenobarbital, pimozide, quinidine, ivabradine, ergot alkaloids (ergotamine/anhydrous caffeine/isopropylantipyrine, dihydroergotamine, ergometrine, methylergometrine), triazolam, ticagrelor, asunaprevir, lomitapide, blonanserin, suvorexant, rivaroxaban, azelnidipine, olmesartan medoxomil/azelnidipine, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)], anamorelin, lurasidone, isavuconazonium, finerenone, eplerenone

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

(deleted)

Drugs	Signs, symptoms, and treatment	Mechanism/risk factors
Eplerenone	The blood concentration of eplerenone may be increased by co-administration with voriconazole, and the effect may be enhanced.	Voriconazole inhibits the metabolizing enzyme of eplerenone (CYP3A4).

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	The blood concentration of riociguat may be increased by co-administration with voriconazole. When co-administration with voriconazole is necessary, patients should be monitored for their condition and dose reduction of riociguat should be considered as necessary.	Voriconazole inhibits the metabolizing enzyme of riociguat (CYP3A).

19 Other chemotherapeutics

Itraconazole

Brand name

Itrizole Capsules 50, Itrizole Oral Solution 1% (Janssen Pharmaceutical K.K.), and the others

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

Patients receiving the following drugs: Pimozide, quinidine, bepridil, triazolam, simvastatin, azelnidipine, azelnidipine/olmesartan medoxomil, nisoldipine, ergotamine/caffeine/isopropylantipyrine, dihydroergotamine, ergometrine, methylergometrine, vardenafil, eplerenone, blonanserin, sildenafil (Revatio), tadalafil (Adcirca), suvorexant, ibrutinib, ticagrelor, lomitapide, ivabradine, venetoclax [during its dose escalation phase for relapsed or refractory chronic lymphocytic leukemia (including small lymphocytic lymphoma)], lurasidone hydrochloride, anamorelin hydrochloride, finerenone, isavuconazonium sulfate, aliskiren, dabigatran, rivaroxaban

10. INTERACTIONS

(deleted)

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

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	Itraconazole may increase the blood concentration of riociguat. (It has been reported as follows: When co-administered with ketoconazole, the AUC and C_{max} of riociguat were increased by 150% and 46%, respectively. In addition, the elimination half-life was prolonged.) When co-administration with itraconazole is necessary, patients should be monitored for their condition and dose reduction of riociguat should be considered as necessary.	It is considered that the clearance of riociguat is decreased by the inhibitory activity of itraconazole against CYP1A1 and CYP3A4.

20 X-ray contrast agents

Iodixanol

Brand name

Visipaque 270 Injection 20 mL, 50 mL, 100 mL, Visipaque 320 Injection 50 mL, 100 mL (GE Healthcare Pharma Co., Ltd.)

8. IMPORTANT PRECAUTIONS <Common to all indications>

Hypersensitivity may occur regardless of dosage and dosing regimen. Serious adverse reactions such as shock and cardiac arrest caused by this drug is not necessarily due to iodine hypersensitivity, and no methods are currently available for predicting them. Therefore, emergency measures should be prepared prior to administration of this drug.

11. ADVERSE REACTIONS

11.1 Clinically Significant Adverse Reactions

Cardiac arrest

<Common to all indications>
(newly added)

21 Onasemnogene abeparvovec

Brand name	Zolgensma Intravenous Infusion (Novartis Pharma K.K.)
Important Precautions (newly added)	An infusion reaction may occur. Administration of this product should be initiated after arrangements for proper responses to an emergency are ensured in preparation for an infusion reaction.
Defects/Adverse Reactions Clinically significant adverse reactions (newly added)	Infusion reaction: An infusion reaction (rash, urticaria, flushing, vomiting, tachycardia, pyrexia, etc.) including hypersensitivity and anaphylaxis may occur. If an infusion reaction occurs, appropriate measures should be taken.

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 April 30, 2025)
◎: Products for which EPPV was initiated after April 1, 2025

	Nonproprietary name Brand name	Name of the MAH	Date of EPPV initiation
◎	Atropine sulfate hydrate[*1] Ryjusea Mini ophthalmic solution 0.025%	Santen Pharmaceutical Co., Ltd.	April 21, 2025
◎	Garadacimab (genetical recombination) Andembry S.C. Injection 200 mg Pens	CSL Behring K.K.	April 18, 2025
◎	Brivaracetam Briviact for I.V. injection 25 mg	UCB Japan Co. Ltd.	April 17, 2025
◎	Tarlatamab (genetical recombination) Imdelltra For I.V. Infusion 1 mg, 10 mg	Amgen K.K.	April 16, 2025
◎	Tirzepatide[*2] Zepbound Subcutaneous Injection Ateos 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg	Eli Lilly Japan K.K.	April 11,2025
◎	Benralizumab (genetical recombination)[*3] Fasenra Subcutaneous Injection 30 mg Pen	AstraZeneca K.K.	April 1, 2025
	Letermovir[*4] Prevymis Tablets 240 mg, Prevymis Intravenous Infusion 240 mg	MSD K.K.	March 27, 2025
	Marstacimab (genetical recombination) Hympavzi S.C. Injection 150 mg Pen	Pfizer Japan Inc.	March 24, 2025
	Teclistamab (genetical recombination) Tecvayli Subcutaneous Injection 153 mg, 30 mg	Janssen Pharmaceutical K.K.	March 19, 2025
	Mosunetuzumab (genetical recombination) Lunsumio for Intravenous Infusion 1 mg, 30 mg	Chugai Pharmaceutical Co., Ltd.	March19, 2025
	Datopotamab deruxtecan (genetical recombination) Datroway for Intravenous Drip Infusion 100 mg	Daiichi Sankyo Co., Ltd.	March 19, 2025
	Selexipag		

Nonproprietary name Brand name	Name of the MAH	Date of EPPV initiation
Uptravi Tablets for Pediatric 0.05 mg	Nippon Shinyaku Co., Ltd.	March 19, 2025
Ozanimod hydrochloride Zeposia capsules 0.92 mg, Zeposia capsules starter pack	Bristol-Myers Squibb K.K.	March 19, 2025
Tofersen Qalsody Intrathecal injection 100 mg	Biogen Japan Ltd	March 19, 2025
Zanubrutinib Brukinsa capsules 80 mg	BeiGene Japan GK	March 19, 2025
Patiromer sorbitex calcium Veltassa 8.4 g powder for suspension (single-dose package)	Zeria Pharmaceutical Co., Ltd.	March 17, 2025
Flortaucipir (^{18}F) Tauvid Injection	PDRadiopharma Inc.	March 3, 2025
Insulin Icodec (genetical recombination) Awiqli injection FlexTouch 300 units, 700 units	Novo Nordisk Pharma Ltd.	January 30, 2025
Articaine hydrochloride/adrenaline bitartrate Septocaine Combination Injection Cartridge	GC SHOWAYAKUHIN CORPORATION	January 21, 2025
Amifampridine phosphate Firdapse Tablets 10 mg	DyDo Pharma, Inc.	January 15, 2025
Benralizumab (genetical recombination)*5 Fasenra Subcutaneous Injection 30 mg Syringe	AstraZeneca K.K.	December 27, 2024
Efgartigimod alfa (genetical recombination)/vorhyaluronidase alfa (genetical recombination)*6 Vyvdura Combination Subcutaneous Injection	argenx Japan K.K.	December 27, 2024
Daridorexant hydrochloride Quviviq Tablets 25 mg, 50 mg	Nxera Pharma Japan Co., Ltd.	December 19, 2024
Aceneuramic acid Acenobel Extended Release Tablets 500 mg	Nobelpharma Co., Ltd.	December 19, 2024
Estetrol hydrate/drospirenone alyssa combination tablets	Fuji Pharma Co., Ltd.	December 3, 2024
Donanemab (genetical recombination) kisunla Intravenous Infusion 350 mg	Eli Lilly Japan K.K.	November 26, 2024
Fruquintinib Fruzaqla capsules 1 mg, 5 mg	Takeda Pharmaceutical Company Limited	November 22, 2024
Sacituzumab govitecan (genetical recombination) Trodelvy for Injection 200 mg	Gilead Sciences K.K.	November 20, 2024
Amivantamab (genetical recombination) Rybrevant Intravenous Infusion 350 mg	Janssen Pharmaceutical K.K.	November 20, 2024
Repotrectinib Augtyro capsules 40 mg	Bristol-Myers Squibb K.K.	November 20, 2024

	Nonproprietary name Brand name	Name of the MAH	Date of EPPV initiation
	Mecobalamin[*7] Rozebalamin for Injection 25 mg	Eisai Co., Ltd.	November 20, 2024
	Teprotumumab (genetical recombination) Tepezza for Intravenous Infusion 500 mg	Amgen K.K.	November 20, 2024
	Voclosporin Lupkynis Capsules 7.9 mg	Otsuka Pharmaceutical Co., Ltd.	November 20, 2024
	Tasurgratinib succinate Tasfygo Tablets 35 mg	Eisai Co., Ltd.	November 20, 2024
	Avibactam sodium/ceftazidime hydrate Zavicefta Combination for Intravenous Infusion	Pfizer Japan Inc.	November 12, 2024

*1 Slowing the progression of myopia

*2 Treatment of obesity
The use is limited to patients with either hypertension, dyslipidaemia, or type 2 diabetes mellitus who have not sufficiently responded to treatment with dietary and exercise therapy and who fall under the following conditions:
* BMI of 27 kg/m^2 or greater in the presence of at least two obesity-related comorbidities
* BMI of 35 kg/m^2 or greater

*3 Eosinophilic granulomatosis with polyangiitis in patients who have not sufficiently responded to conventional treatments

*4 Addition of a pediatric dosage for the indication below:
Prophylaxis of cytomegalovirus disease for the following:
* Allogeneic haematopoietic stem cell transplantation
* Organ transplantation

*5 Eosinophilic granulomatosis with polyangiitis in patients who have not sufficiently responded to conventional treatments

*6 Chronic inflammatory demyelinating polyradiculoneuritis

*7 Slowing the progression of functional impairment in amyotrophic lateral sclerosis (ALS)