# Pharmaceuticals and Medical Devices Safety Information

**July 2026**
**No. 430**

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This *Pharmaceuticals and Medical Devices Safety Information (PMDSI)* publication is issued when safety information collected by the Ministry of Health, Labour and Welfare (MHLW) is made available. 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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# Pharmaceuticals and Medical Devices Safety Information No.430

**Ministry of Health, Labour and Welfare**

## [ Outline of Information ]

| No. | Subject | Measures | Outline of Information | Page |
|---|---|---|---|---|
| 1 | **Revision of "PRECAUTIONS" for lithium carbonate** | *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 JDIIP project of the Ministry of Health, Labour and Welfare 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. This project specifies that a working group composed of experts shall be established to select a candidate drug, organize and evaluate the information accumulated to date and compile a draft revision of the package insert for the drug as a report.<br>Recently, the language concerning contraindications, etc. of lithium carbonate for pregnant women has been revised based on the deliberation of 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. | 4 |
| 2 | **Serious hepatic impairment caused by avacopan** | | Avacopan (brand name: Tavneos Capsules 10 mg) is a drug that has actions including those to improve the pathological condition of ANCA-associated vasculitis by inhibiting C5a-C5a receptor (C5aR) signaling-mediated neutrophil priming through its selective C5aR antagonistic action, thereby relieving antineutrophil cytoplasmic antibody-mediated amplification of vasculitis induced by neutrophils.<br>In Japan, this drug was approved in September 2021 for the indications of "microscopic polyangiitis" and "granulomatosis with polyangiitis." Both of these diseases are designated as intractable diseases, and this drug is designated as an orphan drug. According to the estimation by the marketing authorization holder, this drug was administered to 8,503 patients between February 2025 and January 2026. | 7 |

| | | | | |
|---|---|---|---|---|
| | | | Recently, cases of serious hepatic impairment associated with administration of this drug have been collected, and these cases include those for which a causal relationship between the drug and the event is reasonably possible. Therefore, the MHLW/PMDA issued Dear Healthcare Professional Letters of Rapid Safety Communications on May 21, 2026 to request the marketing authorization holder to promptly alert healthcare professionals etc. This section will introduce the details of this action. | |
| 3 | **Avacopan and 8 others** | *P* | Revision of Precautions (No. 370) | 10 |
| 4 | **List of Products Subject to Early Post-marketing Phase Vigilance** | | Products for which EPPV was initiated after May 31, 2026 | 15 |

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

**Reporting of safety information such as adverse reactions to the MHLW is a duty of healthcare professionals.**

When healthcare professionals including physicians, dentists, and pharmacists notice any adverse reactions, infections, or malfunctions associated with drugs, medical devices, or regenerative medical products, please report safety information to the MHLW directly or through the marketing authorization holders. Pharmacists and registered salespersons in a drugstore or pharmacy are also required to report any adverse reactions.

Please submit your report through the  Report Reception Site.

(This service is available only in Japanese.)
https://www.pmda.go.jp/safety/reports/hcp/0002.html

# 1.

# Revision of "PRECAUTIONS" for lithium carbonate

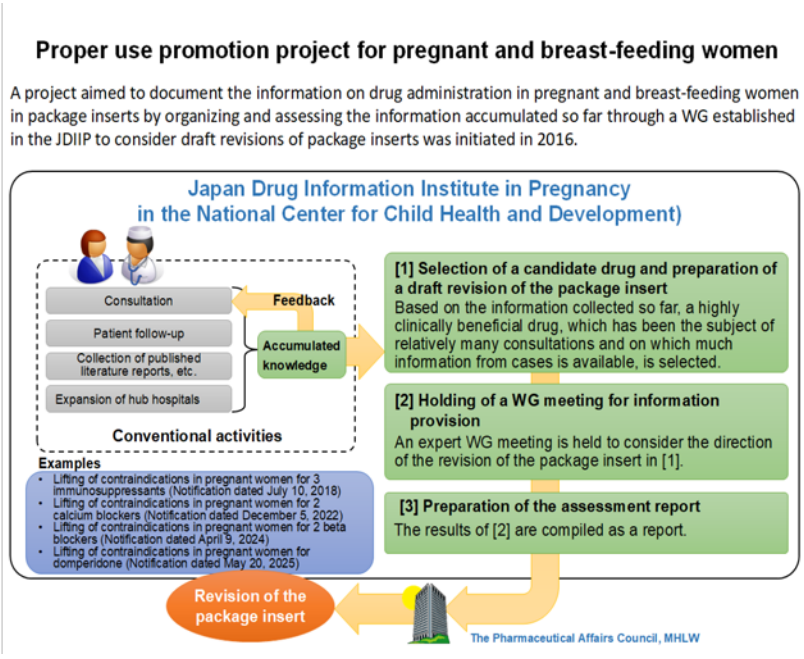
## 1. Introduction

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 in 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 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 composed of experts (hereinafter referred to as "WG") has been established to select a candidate drug, organize and evaluate the information accumulated to date and compile a draft revision of the package insert for the drug as a report (Figure 1).

(Fig.1)



Recently, the language concerning contraindications, etc. of lithium carbonate for pregnant women has been revised based on the deliberation of 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

Lithium carbonate (hereinafter referred to as "this drug") has been approved for marketing in Japan for the indications of mania and manic state of manic depressive illness. This drug is positioned as a first-choice drug for bipolar disorder. It was decided at the time of approval of the brand-name product of lithium carbonate that administration of lithium carbonate to pregnant women or women who may be pregnant is contraindicated since the teratogenicity was reported in animal experiments during the development phase and an increase in the frequency of congenital cardiovascular anomaly was reported in the epidemiological studies in humans.

On the other hand, since the most common age of onset of bipolar disorder corresponds to the age of childbearing potential, the timing of pregnancy/delivery and treatment often overlap. It is known that the risk of recurrence increases substantially after childbirth when a patient with bipolar disorder becomes pregnant. Since recurrence after childbirth may cause serious consequences such as suicide, it is considered desirable for patients with bipolar disorder to receive appropriate treatment. The Japanese Society of Psychiatry and Neurology submitted a request to the WG to lift the contraindication in pregnant women since there are a certain number of patients who do not sufficiently respond to alternative therapeutic drugs for pregnant women in manic state including valproate and antipsychotic drugs and the treatment options and opportunities to become pregnant are restricted in patients with bipolar disorder who wish to become pregnant. In response to this request, the WG investigated the appropriateness of contraindicating lithium carbonate in pregnant women/nursing mothers, etc. As a result, it was revealed that some epidemiological studies in humans suggest teratogenicity while others did not demonstrate the risk of malformation. After this result and the influences of the recurrence in mothers due to treatment discontinuation were taken into consideration, a report was compiled stating that pregnant women or women who may be pregnant may be deleted from the CONTRAINDICATIONS section in the package insert for this drug and that it is appropriate to add a precautionary statement to the effect that "lithium carbonate should not be administered to pregnant women or women who may be pregnant unless the administration is considered therapeutically essential" to the Pregnant Women section.

The WG report pointed out as follows: Since pregnancy may change blood concentrations of this drug, which may affect the therapeutic effect, and neonatal abstinence syndrome or lithium poisoning may occur in neonates born from pregnant women who received this drug, it is considered necessary to monitor patients' conditions including blood concentrations of this drug, symptoms of bipolar disorder, and course of pregnancy during pregnancy. However, the results of a survey on the implementation status of blood lithium concentration measurement conducted by the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA") using the National Database of Health Insurance Claims (NDB) suggest that periodic measurement of blood lithium concentrations has not been performed in many patients. Therefore, it is considered essential to provide administration of this drug in collaboration with a medical institution that can perform perinatal management for pregnant women, fetuses, and neonates and under the supervision of a physician who can fully manage and explain the risks of this drug, etc. when this drug is administered to patients for whom administration of this drug is considered appropriate even during pregnancy.

## 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 12th FY 2025 Subcommittee on Drug Safety held on March 25, 2026 concluded that the electronic package insert of lithium carbonate may be revised as follows, and the revision was made on June 16 in the same year:

- "Pregnant women or women who may be pregnant" should be deleted from the CONTRAINDICATIONS section in the package insert, and a precautionary statement that "lithium carbonate should not be administered to pregnant women or women who may be pregnant unless the administration is considered therapeutically essential" should be added to the Pregnant Women

section.

- Since the opportunity for women with reproductive potential to receive this drug is considered to increase, the precautionary statement that "If this drug is used in women of childbearing potential, teratogenicity of this drug should be fully explained, and the appropriateness of use of this drug should be carefully determined. However, the dose-response relationship between this drug and the risk of congenital anomaly has not been demonstrated" should be added to the "Persons with Reproductive Potential" section.
- A precautionary statement to the effect that a physician with knowledge and experience in the treatment of bipolar disorder who can fully manage and explain the risks of this drug, etc. should determine the appropriateness of administering this drug to a pregnant woman under close collaboration with psychiatrists and physicians responsible for perinatal medicine (including obstetrics and neonatal medicine) should be included in the package insert. A precautionary statement to the effect that it is necessary to collaborate with institutions that can perform appropriate perinatal management, including management of the effects of this drug on pregnant women, fetuses, and neonates (such as neonatal abstinence syndrome and changes in serum lithium concentrations) should also be added.
- A precautionary statement to the effect that serum concentrations of this drug should be measured frequently and patients should be carefully monitored should be added because changes in serum lithium concentrations due to pregnancy may affect the therapeutic effect.

## 4. In closing

This revision is not intended to proactively recommend the use of this drug in "pregnant women or women who may be pregnant". If this drug is used for inevitable reasons, the appropriateness of the use should be carefully determined after the risk of teratogenicity of this drug has been fully explained to a woman of childbearing potential, and the administration should be provided in collaboration with a medical institution that can perform perinatal management for pregnant women, fetuses, and neonates and under the supervision of a physician with knowledge and experience in the treatment of bipolar disorder who can fully manage and explain the risks of this drug, etc. Healthcare professionals are requested to understand the purpose of the revision this time and continuously cooperate in ensuring the proper use of the drug.

In the future, the Ministry of Health, Labour and Welfare will continue to collect and evaluate safety information on drugs that may be used by pregnant women/nursing mothers and take necessary actions such as revision of the package inserts through this project.

## 5. References


- Proper use promotion project for pregnant and breast-feeding women
  https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iyakuhin/ninshin_00002.html
- Materials 1-1 to 1-4 of the 12th FY 2025 Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs Council (held on March 25, 2026)
  https://www.mhlw.go.jp/stf/newpage_71874.html
- Revisions of PRECAUTIONS (PSB/PSD Notification No. 0616-1 dated June 16, 2026)
  https://www.mhlw.go.jp/content/11120000/001711417.pdf

# 2.

# Serious hepatic impairment caused by avacopan

## 1. Introduction

Avacopan (brand name: Tavneos Capsules 10 mg; hereinafter referred to as "this drug") is a drug that has actions including those to improve the pathological condition of ANCA-associated vasculitis by inhibiting C5a-C5a receptor (C5aR) signaling-mediated neutrophil priming through its selective C5aR antagonistic action, thereby relieving antineutrophil cytoplasmic antibody (hereinafter referred to as ANCA)-mediated amplification of vasculitis induced by neutrophils.

In Japan, this drug was approved in September 2021 for the indications of "microscopic polyangiitis" and "granulomatosis with polyangiitis." Both of these diseases are designated as intractable diseases, and this drug is designated as an orphan drug. According to the estimation by the marketing authorization holder, this drug was administered to 8,503 patients between February 2025 and January 2026.

Recently, cases of serious hepatic impairment associated with administration of this drug have been collected, and these cases include those for which a causal relationship between the drug and the event is reasonably possible. Therefore, the MHLW/PMDA issued Dear Healthcare Professional Letters of Rapid Safety Communications (hereinafter referred to as "Blue Letter") on May 21, 2026 to request the marketing authorization holder to promptly alert healthcare professionals, etc. This section will introduce the details of this action.

## 2. Serious hepatic impairment caused by this drug

Based on the clinical study results submitted at the time of application for approval, the precautions concerning hepatic impairment have been provided in the "Clinically Significant Adverse Reactions" section of the electronic package insert of this drug since the approval in September 2021.

Since the launch of this drug in 2022, cases of serious hepatic impairment in patients taking this drug, including 20 fatal cases, have been reported (as of the time of issuance of Blue Letter). For the cases of death, a causal relationship between the drug and the adverse reaction is evaluated every time they are reported based on the obtained information, and cases for which the causal relationship was not determined have been accumulated. However, cases of vanishing bile duct syndrome for which a causal relationship with avacopan was considered reasonably possible were identified. Therefore, the electronic package insert was revised on May 1, 2026 to add vanishing bile duct syndrome to the section of hepatic impairment in "Clinically Significant Adverse Reactions."

On May 15, 2026, the marketing authorization holder provided information to the effect that avacopan should be carefully administered with attention paid to serious hepatic impairment to medical practice settings on the basis of the accumulated reported cases.

Consideration of further safety measures resulted in a determination that it is necessary to provide precautions by not only adding a description of serious hepatic impairment to the "Warnings" section in the electronic package insert but also indicating the frequency of liver function tests according to the timing after the start of administration and the state of liver function that requires discontinuation of this drug specifically in order to detect hepatic impairment early and prevent the symptoms from progressing to a severe condition. Thus, a Blue Letter was issued to request healthcare professionals to ensure the proper use of this drug.

Based on the contents of the precautions to be provided, it was decided to request healthcare professionals in the medical practice settings to ensure proper management through monitoring of

patients by reliably performing liver function tests after the start of administration, especially in patients who newly started receiving this drug and by periodically performing liver function tests even in patients who continuously receive this drug.

## 3. Matters to be noted

Attention should be paid especially to the following points when this drug is used in order to detect hepatic impairment early and prevent the symptoms from progressing to a severe condition.

(1) **Serious hepatic impairment including vanishing bile duct syndrome** may occur, and **fatal cases have also been reported**. **Patients should be carefully monitored through periodic liver function tests** before and during the administration of this drug.
(2) Patients should be **carefully monitored** and **attention should be paid to the occurrence of subjective and objective symptoms**. **Patients should be instructed to consult a physician or pharmacist immediately** if any abnormalities are observed.
(3) **If serious hepatic impairment is observed** during administration of this drug, appropriate measures such as **discontinuing administration of this drug** should be taken.
(4) Since hepatic impairment mostly **occurs within 3 months** after the start of administration, **liver function tests should be periodically performed at least once every 2 weeks for 3 months** after the start of administration and **at least once every 4 weeks for the subsequent 3 months**.
(5) **If ALT or AST increases to more than 3 times the upper limit of the reference range during administration of this drug, administration of this drug should be interrupted, and the patient's condition should be promptly evaluated.**

Patients taking this drug should be instructed to consult a physician or pharmacist promptly if there is any change in their physical condition instead of discontinuing the administration at their own discretion and to discuss the matter thoroughly with the physician or pharmacist about appropriate treatment while undergoing liver function tests. In line with the issuance of the Blue Letter, we prepared materials to help patients and their families understand the symptoms that may occur in persons with hepatic impairment and to encourage them to immediately seek medical attention if such symptoms are observed in their daily lives. Please utilize them.

The Blue Letter lists 20 fatal cases of hepatic impairment. Of these, cases for which a causal relationship between the drug and the event is considered reasonably possible at the present moment are Case No. 10 and Case No. 18 ("a causal relationship is unknown" for the other cases). For Case No. 18, the clinical course is shown in the "Outline of vanishing bile duct syndrome 2 (fatal case)" section.

## 4. Future actions

The revision of the electronic package insert this time has been made to provide precautions concerning serious hepatic impairment. Cases of serious hepatic impairment reported so far and cases of adverse reactions to be newly reported in the future will be continuously evaluated and analyzed to take safety measures as needed. Healthcare professionals are requested to submit reports of adverse reactions, etc. 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 adverse reactions, etc. caused by administration of this drug including serious hepatic impairment are observed.

## 5. Adverse Drug Reaction Relief System

"Adverse Drug Reaction Relief System" (hereinafter referred to as "Relief System") is established for the purpose of relieving people suffering from adverse health effects such as diseases or disabilities that were caused by adverse reactions of pharmaceuticals, even if such pharmaceuticals were properly used, through prompt and simple procedures. This is a public service funded by contributions etc. made by marketing authorization holders of pharmaceuticals and biological products to fulfill their social responsibilities.

Patients who have experienced serious hepatic impairment caused by administration of this drug to date may be eligible for the Relief System. Patients who newly started this drug may also be eligible for the Relief System if any adverse health effects occur despite proper use of this drug including compliance with the precautionary points that were added to the package insert as a result of the recent revision.

Healthcare professionals are requested to cooperate in providing information on the Relief System to people suffering from adverse health effects and preparing documents necessary for making claims including medical certificates.

Please refer to the PMDA website for an overview of the Relief System, procedures for making claims for relief benefits, frequently asked questions, and the contact information.

https://www.pmda.go.jp/relief-services/adr-sufferers/0001.html

## 6. References


- Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letter): Precautions concerning serious hepatic impairment in patients treated with "Tavneos Capsules 10 mg"
  https://www.mhlw.go.jp/content/11125000/001702349.pdf

# 3.

# Revisions of PRECAUTIONS (No. 370)

This section provides details of the revisions to the PRECAUTIONS and brand names of drugs that have been revised in accordance with the Notifications dated May 21, June 5, and June 16, 2026.

---

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

## Avacopan

**Brand name (newly added)**

Tavneos Capsules 10 mg (Kissei Pharmaceutical Co., Ltd.)

**8. IMPORTANT PRECAUTIONS**

1. WARNINGS

Serious hepatic impairment including vanishing bile duct syndrome may occur, and fatal cases have also been reported. Patients should be carefully monitored through periodic liver function tests before and during the administration of this drug. If serious hepatic impairment is observed during administration of this drug, appropriate measures such as discontinuing administration of this drug should be taken.

Hepatic impairment may occur. Careful attention should be paid to the following points. Most of the events occurred within the first 3 months after the start of administration.

Patients should be carefully monitored through liver function tests, which should be performed before the start of administration of this drug, at least once every 2 weeks for 3 months after the start of administration of this drug, and at least once every 4 weeks for the subsequent 3 months, and periodically thereafter during the treatment period.

If ALT or AST increases to more than 3 times the upper limit of the reference range during administration of this drug, administration of this drug should be interrupted, and the patient's condition should be promptly evaluated. The administration of this drug should be discontinued in the following cases.

- ALT or AST exceeds the levels that are more than 8 times the upper limit of the reference range
- ALT or AST continuously exceeds the levels that are more than 5 times the upper limit of the reference range for more than 2 weeks
- Total bilirubin exceeds the levels that are more than 2 times the upper limit of the reference range
- ALP is more than 2 times the upper limit of the reference range
- Signs or symptoms of hepatic impairment such as jaundice and itching are observed.

If vanishing bile duct syndrome is suspected, administration of this drug should be discontinued immediately.

2 Other agents affecting central nervous system

## Donanemab (genetical recombination)

**Brand name** kisunla Intravenous Infusion 350 mg (Eli Lilly Japan K.K.)

**8. IMPORTANT PRECAUTIONS**

ARIA more commonly occurs within 24 weeks after the start of administration of this drug and serious ARIA more commonly occurs within 12 weeks after the start of the administration. Patients should be carefully monitored especially during these periods. Patients and their families/caregivers should be instructed to immediately seek medical attention if symptoms suggestive of ARIA (such as headache, confusion, nausea, vomiting, lightheadedness, dizziness, tremor, visual disturbance, language disorder, decline in cognitive function, alteration of consciousness, and seizures) are observed irrespective of the above periods. Clinical evaluation should be promptly performed. MRI scanning should be performed if occurrence of ARIA is suspected.
Even if a patient has no symptoms suggestive of ARIA, MRI scanning should be performed prior to the 2nd dose, the 3rd dose, the 4th dose, and the 7th dose of this drug, and periodically thereafter to check whether ARIA occurs or not.

3 Other agents affecting central nervous system

## Lecanemab (genetical recombination)

**Brand name** Leqembi for Intravenous Infusion 200 mg, 500 mg (Eisai Co., Ltd.)

**8. IMPORTANT PRECAUTIONS**

ARIA more commonly occurs within 14 weeks after the start of administration of this drug. Patients should be carefully monitored especially during this period. Patients and their families/caregivers should be instructed to immediately seek medical attention if symptoms suggestive of ARIA (such as headache, confusion, dizziness, visual disturbance, feeling queasy, gait disturbance, convulsion, language disorder, and muscular weakness) are observed irrespective of the above period. Clinical evaluation should be promptly performed. MRI scanning should be performed if occurrence of ARIA is suspected.
Even if a patient has no symptoms suggestive of ARIA, MRI scanning should be performed prior to the 5th dose (up to approximately 2 months after the treatment start), the 7th dose (up to approximately 3 months after the treatment start), and 14th dose (up to approximately 6 months after the treatment start), and periodically thereafter to check whether ARIA occurs or not. It is desirable to perform MRI also prior to the 3rd dose of this drug (up to approximately 1 month after the treatment start). MRI prior to the 3rd dose should be considered especially in patients with pretreatment cerebral microhaemorrhage, those with hypertension, and other patients who need to be carefully monitored for occurrence of ARIA.
If ARIA is detected on imaging, attention should be paid to the onset of symptoms under careful monitoring, and additional MRI scanning should be performed as necessary with reference to the table in the 7.1 section.

4 Psychotropic agents

## Lithium carbonate

| | |
|---|---|
| **Brand name** | Limas tablets 100, 200 (Taisho Pharmaceutical Co., Ltd.), Lithium Carbonate tablets 100 mg "Taisho," 200 mg "Taisho" (TOKUHON Corporation), Lithium Carbonate Tablets 100 mg "Fujinaga," 200 mg "Fujinaga" (Fujinaga pharm Co., Ltd.) |
| **2. CONTRAINDICATIONS (This drug is contraindicated to the following patients.)** | (Deleted) |
| **9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS (newly added)** | 9.4 Persons with Reproductive Potential<br>If this drug is used in women of childbearing potential, the teratogenicity of this drug should be fully explained, and the appropriateness of use of this drug should be carefully determined. The dose-response relationship between this drug and the risk of congenital anomaly has not been demonstrated. |
| **9.5 Pregnant Women** | This drug should not be administered to pregnant women or women who may be pregnant unless the administration is considered therapeutically essential. Teratogenic effects have been reported in animal studies (rats and mice), and heart malformation has been reported in humans.<br>This drug should be administered only to patients for whom treatment with this drug is considered appropriate. The administration of this drug should be provided in collaboration with a medical institution that can perform perinatal management for pregnant women, fetuses, and neonates and under the supervision of a physician with knowledge and experience in the treatment of bipolar disorder who can fully manage and explain the following risks of this drug, etc.<br>• Changes in serum lithium concentrations due to pregnancy may affect the therapeutic effect. Serum lithium concentrations should be measured frequently and attention should be paid to patients' conditions, etc. when this drug is administered to pregnant women. An abnormal elevation of serum lithium concentration immediately before delivery may occur in the last pregnancy trimester.<br>• Neonatal abstinence syndrome or lithium poisoning may occur in neonates born from pregnant women who received this drug. |

5 Mineral preparations

## Ferric carboxymaltose

| | |
|---|---|
| **Brand name** | Ferinject solution for injection/infusion 500 mg (Zeria Pharmaceutical Co., Ltd.) |
| **(newly added)** | 8. IMPORTANT PRECAUTIONS<br>Administration of this drug may cause hypophosphataemia, resulting in osteomalacia. Serum phosphorus concentration should be measured before the start of administration unless the measurement is not feasible for inevitable reasons. Serum phosphorus concentrations should be measured periodically during treatment as well, and phosphorus replacement should be considered as necessary. Patients should be instructed to consult a prescribing physician if symptoms suggestive of osteomalacia such as arthralgia and bone pain occur. |
| **11. ADVERSE REACTIONS** | Hypophosphataemia, osteomalacia |

| | |
|---|---|
| **11.1. Clinically Significant Adverse Reactions (newly added)** | Hypophosphataemia may occur and result in osteomalacia. |

6 Mineral preparations

## Saccharated ferric oxide

| | |
|---|---|
| **Brand name** | Fesin Intravenous Injection 40 mg (Nichi-Iko Pharmaceutical Co., Ltd.) |
| **8. IMPORTANT PRECAUTIONS (newly added)** | Administration of this drug may cause hypophosphataemia, resulting in osteomalacia. Serum phosphorus concentration should be measured before the start of administration unless the measurement is not feasible for inevitable reasons. Serum phosphorus concentrations should be measured periodically during treatment as well, and phosphorus replacement should be considered as necessary. Patients should be instructed to consult a prescribing physician if symptoms suggestive of osteomalacia such as arthralgia and bone pain occur. |
| **11. ADVERSE REACTIONS** | Hypophosphataemia, osteomalacia |
| **11.1 Clinically Significant Adverse Reactions (newly added)** | Hypophosphataemia may occur and result in osteomalacia. |

7 Other antitumor agents

## Valemetostat tosilate

| | |
|---|---|
| **Brand name** | Ezharmia Tablets 50 mg, 100 mg (Daiichi Sankyo Co., Ltd.) |
| **8. IMPORTANT PRECAUTIONS (newly added)** | Secondary malignant tumour including acute myeloid leukaemia and myelodysplastic syndrome may occur. Patients should be carefully monitored. |

8 Other chemotherapeutics

## Sulfamethoxazole/trimethoprim (oral dosage form)

| | |
|---|---|
| **Brand name** | Baktar Combination Tablets, Baktar mini Combination Tablets, Baktar Combination Granules (Shionogi Pharma Co., Ltd.), Bactramin Combination Tablets, Bactramin Combination Granules (TAIYO Pharma Co., Ltd.), and others |
| **11. ADVERSE REACTIONS** | Toxic epidermal necrolysis (TEN), oculomucocutaneous syndrome (Stevens-Johnson syndrome), erythema multiforme, acute generalised exanthematous pustulosis |
| **11.1 Clinically Significant Adverse Reactions** | |

9 Antiprotozoan agents

## Sulfamethoxazole/trimethoprim (injection)

| | |
|---|---|
| **Brand name** | Bactramin for Injection (TAIYO Pharma Co., Ltd.) |

| | |
|---|---|
| **11. ADVERSE REACTIONS** | Oculomucocutaneous syndrome (Stevens-Johnson syndrome), Toxic epidermal necrolysis (TEN), erythema multiforme, acute generalised exanthematous pustulosis |
| **11.1 Clinically Significant Adverse Reactions** | |

# 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 May 31, 2026)

◎: Products for which EPPV was initiated after May 1,2026

| | Nonproprietary name / Brand name | Name of the MAH | Date of EPPV initiation |
|---|---|---|---|
| ◎ | Gadoquatrane hydrate / Ambelvist iv injection 2 mL, Ambelvist iv injection syringes 5 mL, 7.5 mL, 10 mL | Bayer Yakuhin, Ltd. | May 26, 2026 |
| ◎ | Triheptanoin / Dojolvi oral liquid 100% | Ultragenyx Japan K.K. | May 21, 2026 |
| ◎ | Tirzepatide [*1] / Zepbound Subcutaneous Injection 2.5 mg Ateos, 5 mg Ateos, 7.5 mg Ateos, 10 mg Ateos, 12.5 mg Ateos, 15 mg Ateos | Eli Lilly Japan K.K. | May 18, 2026 |
| ◎ | Benralizumab (genetical recombination) [*2] / Fasenra Subcutaneous Injection 30 mg Syringe, Fasenra Subcutaneous Injection 30 mg Pen | AstraZeneca K.K. | May 18, 2026 |
| ◎ | Deucravacitinib [*3] / Sotyktu tablets 6 mg | Bristol-Myers Squibb K.K. | May 18, 2026 |
| ◎ | Oxymetazoline hydrochloride [*4] / Upneeq Mini ophthalmic solution 0.1% | Santen Pharmaceutical Co., Ltd. | May 15, 2026 |
| ◎ | Freeze-dried live attenuated measles and rubella combined vaccine / Mearubik II Subcutaneous Injection | The Research Foundation for Microbial Diseases of Osaka University | May 8, 2026 |
| | [1] [2] Human milk/calcium glycerophosphate/calcium gluconate hydrate/calcium chloride hydrate/anhydrous citric acid sodium/potassium citrate/magnesium monohydrogen phosphate/ zinc sulfate hydrate/sodium chloride/copper sulfate, [3] Human milk / [1] PreemieFort Enteral Solution 6, [2] 8, [3] PreemieFort Enteral Solution CF | Clinigen K.K. | April 28, 2026 |

| Nonproprietary name / Brand name | | Name of the MAH | Date of EPPV initiation |
|---|---|---|---|
| | Tucatinib ethanolate / Tukysa Tablets 50 mg, 150 mg | Pfizer Japan Inc. | April 21, 2026 |
| | Atogepant hydrate / Aquipta tablets 10mg, 30 mg, 60 mg | AbbVie GK | April 17, 2026 |
| | Doravirine/islatravir hydrate / Idvynso Combination Tablets | MSD K.K. | April 15, 2026 |
| | Depemokimab (genetical recombination) / Exdensur solution for s.c. injection 100 mg pen, Exdensur solution for s.c. injection 100 mg syringe | GlaxoSmithKline K.K. | April 15, 2026 |
| | Glycerol phenylbutyrate / Ravicti Oral Liquid 1.1 g/mL | OrphanPacific, Inc. | April 15, 2026 |
| | Motugivatrep / Avarept Ophthalmic Suspension 0.3% | Senju Pharmaceutical Co., Ltd. | April 6, 2026 |
| | Vorasidenib citric acid hydrate / Voranigo Tablets 10 mg, 40 mg | NIHON SERVIER CO., LTD | March 30, 2026 |
| | Luseogliflozin hydrate / Lusefi OD film 2.5 mg, Lusefi tablets 2.5 mg, 5 mg | Taisho Pharmaceutical Co., Ltd. | March 23, 2026 |
| | Linzagolix choline / Yselty Tablets 100 mg | KISSEI PHARMACEUTICAL CO., LTD. | March 19, 2026 |
| | Zuranolone / Zurzuvae Capsules 30 mg | Shionogi & Co., Ltd. | March 19, 2026 |
| | Sebetralstat / Ekterly Tablets 300 mg | KalVista Pharmaceuticals Ltd. | March 18, 2026 |
| | Tafasitamab (genetical recombination) / Minjuvi for intravenous infusion 200 mg | Incyte Biosciences Japan G.K. | March 18, 2026 |
| | Tagraxofusp (genetical recombination) / Elzonris I.V. Injection 1000 μg | Nippon Shinyaku Co., Ltd. | March 18, 2026 |
| | Retifanlimab (genetical recombination) / Zynyz for Intravenous Infusion 500 mg | Incyte Biosciences Japan G.K. | March 18, 2026 |
| | Sepiapterin / Sephience Granules 250 mg, 1000 mg | PTC Therapeutics K.K. | March 18, 2026 |
| | Amivantamab (genetical recombination)/vorhyaluronidase alfa (genetical recombination) / Rybrofaz Combination Subcutaneous Injection | Janssen Pharmaceutical K.K. | March 18, 2026 |
| | Mosunetuzumab (genetical recombination) / Lunsumio for Subcutaneous Injection 5 mg, 45 mg | CHUGAI PHARMACEUTICAL CO., LTD. | March 18, 2026 |
| | Belantamab mafodotin (genetical | | |

| Nonproprietary name<br>Brand name | | Name of the MAH | Date of EPPV initiation |
|---|---|---|---|
| | recombination)<br>Blenrep for I.V. infusion 100 mg | GlaxoSmithKline K.K. | March 18, 2026 |
| | Vonicog alfa (genetical recombination)<br>Vonvendi Intravenous 1300 | Takeda Pharmaceutical Company Limited. | February 19, 2026 |
| | Tezepelumab (genetical recombination) *5<br>Tezspire Subcutaneous Injection 210 mg Syringe, Tezspire Subcutaneous Injection 210 mg Pen | AstraZeneca K.K. | February 19, 2026 |
| | Adrenaline<br>neffy nasal spray 1 mg, 2 mg | Alfresa Pharma Corporation | February 12, 2026 |
| | Cantharidin<br>Ycanth topical solution 0.71% | TORII PHARMACEUTICAL CO., LTD. | February 9, 2026 |
| | Diazepam<br>Spydia Nasal Spray 5 mg, 7.5 mg, 10 mg | Aculys Pharma, Inc. | December 24, 2025 |
| | Finerenone *6<br>Kerendia tablets 10 mg, 20 mg | Bayer Yakuhin, Ltd. | December 22, 2025 |
| | Odevixibat hydrate<br>Bylvay Granules 200 μg, 600 μg | IPSEN Co., Ltd | December 18, 2025 |
| | Rimegepant sulfate hydrate<br>Nurtec OD Tablets 75 mg | Pfizer Japan Inc. | December 16, 2025 |

*1 Moderate or more severe obstructive sleep apnoea syndrome, for only patients with BMI of ≥ 27 kg/m$^2$

*2 Eosinophilia

*3 Psoriatic arthritis in patients who have not responded sufficiently to conventional therapies

*4 Acquired blepharoptosis

*5 Chronic rhinosinusitis with nasal polyps (for use only in patients who have not responded sufficiently to conventional treatments)

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