

# Pharmaceuticals and Medical Devices Safety Information

No. 426 February 2026

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This *Pharmaceuticals and Medical Devices Safety Information (PMDSI)* publication is issued reflective of safety information collected by the Ministry of Health, Labour and Welfare (MHLW). It is intended to facilitate safer use of pharmaceuticals and medical devices by healthcare providers. The PMDSI is available on the Pharmaceuticals and Medical Devices Agency (PMDA) web page (<https://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0002.html>) and on the MHLW website (<https://www.mhlw.go.jp/>, only in Japanese).

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# Pharmaceuticals and Medical Devices Safety Information

No. 426 February 2026

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

## [ Outline of Information ]

No.	Subject	Measures	Outline of Information	Page
1	Revision of "PRECAUTIONS" in the package insert of ELEVIDYS for Intravenous Infusion	P	A regenerative medical product "ELEVIDYS for Intravenous Infusion" was approved for the indication of Duchenne muscular dystrophy in Japan. The package insert was revised because of two fatal cases of acute hepatic failure reported overseas. The Subcommittee on Medical Device and Regenerative Medical Product Safety Committee on Drug Safety Pharmaceutical Affairs Council was held to discuss the cooperative framework of the related academic societies in revising the related materials and taking safety measures against hepatic impairment, in order to further ensure the safety measures against hepatic impairment that led to the revision of the package insert. This article introduces a series of safety measures to be taken when using ELEVIDYS.	4
2	Important Safety Information	P C	<ul style="list-style-type: none"> <li>• Burosumab (genetical recombination):</li> <li>• Imeglimin hydrochloride</li> </ul> Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated January 13 ,2026, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.	6
3	Revisions of PRECAUTIONS (No. 366)	P	[1] Aspirin (and 4 others) ,and 7 others	12
4	List of Products Subject to Early Post-marketing Phase Vigilance		List of products subject to Early Post-marketing Phase Vigilance as of December 31, 2025	15

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

MAH	Marketing Authorization Holder
NTRK	Neurotrophic tropomyosin receptor kinase
OTC	Over The Counter
PSB/PSD	Pharmaceutical Safety Bureau /Pharmaceutical Safety Division
PTH	Parathyroid hormone

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# Revision of "PRECAUTIONS" in the package insert of ELEVIDYS for Intravenous Infusion

## 1. Introduction

"Delandistrogene moxeparvovec" (ELEVIDYS for Intravenous Infusion; hereinafter referred to as "ELEVIDYS") is a regenerative medical product for gene therapy developed using a non-replicating recombinant adeno-associated virus vector expressing the microdystrophin protein. The product was approved with conditions and a time limit in Japan on May 13, 2025 for the indication of Duchenne muscular dystrophy (DMD) in patients who are anti-AAVrh74 antibody-negative, ambulatory, and aged 3 to under 8.

In June 2025, the marketing authorization holder reported a fatal case of acute hepatic failure in a non-ambulatory DMD patient overseas, which is outside the indication criteria in Japan. Hepatic impairment has been regarded as an adverse reaction requiring attention since the time of approval, and a warning had been included in the package insert. The package insert was revised on August 28, 2025 to include additional descriptions of specific liver function tests to be performed and measures to be taken at the onset of hepatic impairment because the case reported in June was the second case of fatal acute hepatic failure reported overseas.

To ensure the implementation of safety measures against hepatic impairment, revisions of the proper use guide for healthcare professionals, the information materials for patients and families, and the guidelines for proper use developed by the Japanese Society of Child Neurology used in clinical settings (hereinafter referred to as "the related materials") were also needed in line with the package insert revision to provide more specific safety information. Although the guidelines for proper use already recommend that medical institutions using ELEVIDYS establish a system that enables coordination with other clinical departments/institutions in case adverse reactions occur, more thorough safety measures need to be ensured. To address the situation, the Subcommittee on Medical Device and Regenerative Medical Product Safety Committee on Drug Safety Pharmaceutical Affairs Council (hereinafter referred to as the "Subcommittee") was held on November 27, 2025 to discuss the safety measures.

This article introduces a series of safety measures to be taken when using ELEVIDYS described above.

## 2. The revised contents of the package insert

Hepatic impairment associated with the administration of ELEVIDYS is known to be caused by an immune reaction to adeno-associated virus vector. Serious hepatic impairment has been reported in the clinical study of ELEVIDYS and in the overseas post-marketing surveillance. Therefore, hepatic impairment has been listed as a warning in the section of Clinically Significant Adverse Reactions of the package insert, and the information on the administration of corticosteroids to reduce hepatic impairment and liver function monitoring has been provided since the time of approval of ELEVIDYS.

The causal relationship with ELEVIDYS could not be ruled out based on the evaluation of the two overseas cases of acute hepatic failure with fatal outcomes. Although non-ambulatory DMD patients are not included in the indication criteria in Japan, the Ministry of Health, Labour and Welfare (MHLW) determined appropriate to revise the section of PRECAUTIONS to specify acute hepatic failure as a clinically significant adverse reaction. In addition, recommendations to perform liver function tests and imaging procedures for acute hepatic failure and take appropriate measures, such as postponing treatment when abnormalities are detected were added.

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Although infection was also considered a potential cause of death in the fatal case of acute liver failure known at the time of the approval review for ELEVIDYS, an autopsy had not yet been performed. Therefore, the MHLW determined appropriate to revise to include precautions for infection in the package insert and provide any new post-marketing information in a timely manner to the medical institutions. Based on the evaluation of the additional new information on the autopsy findings for the case, the MHLW determined appropriate to add a warning against the risk of infection associated with corticosteroids used in combination with ELEVIDYS.

### 3. Discussion at the Subcommittee

The Subcommittee invited experts from the Japanese Society of Child Neurology and the Japan Society of Hepatology as witnesses and discussed the revision of the related materials based on the package insert revision described above and the cooperative framework of related academic societies in taking safety measures against hepatic impairment.

The revision of the related materials concerning the implementation of liver function tests before administration of ELEVIDYS, decision on whether to administer ELEVIDYS, and a cooperative framework to address hepatic impairment occurring after administration of ELEVIDYS was discussed and approved. Regarding the cooperative framework of the related academic societies in taking safety measures, the issuance of a notification to request cooperation from the related academic societies in ensuring safety was approved.

Based on the outcomes of the Subcommittee meeting, the notifications were issued to the related academic societies on December 17, 2025 to ensure thorough safety measures against hepatic impairment. The Japanese Society of Child Neurology was requested to require medical institutions using ELEVIDYS in accordance with the guidelines for proper use to implement appropriate safety measures and establish an appropriate environment for the use of ELEVIDYS upon certification and ensure that the knowledge of and experience in the use of ELEVIDYS are shared among the certified medical institutions and appropriate cooperating institutions capable of responding to serious adverse reactions, such as hepatic impairment are secured. The Japan Society of Hepatology was requested to cooperate in responding to the occurrence of hepatic impairment.

With these measures, medical institutions using ELEVIDYS will be able to use a multilayered cooperative framework, including cooperating institutions with hepatologists capable of treating children, an expert panel consisting of pediatric neurologists, hepatologists, and hepatology surgeons, and cooperation of the Japan Society of Hepatology, in the event of hepatic impairment.

### 4. Conclusion

The necessity of ELEVIDYS is high, especially in terms of public health because it is the only gene therapy product for Duchenne muscular dystrophy approved in Japan. On the other hand, extreme caution is needed when responding to hepatic impairment. For example, a cooperative framework of relevant medical institutions should be ensured in advance, and hepatic impairment should be treated promptly and appropriately. Healthcare professionals at the medical institutions using ELEVIDYS are requested to cooperate in the proper use of ELEVIDYS based on the understanding of the purpose of the package insert revision and the related safety measures.

#### [References]

- FY2025 First Meeting of the Subcommittee on Medical Device and Regenerative Medical Product Safety Committee on Drug Safety Pharmaceutical Affairs Council (held on November 27, 2025)  
[https://www.mhlw.go.jp/stf/newpage\\_66307.html](https://www.mhlw.go.jp/stf/newpage_66307.html) (only in Japanese)
- Revision of "PRECAUTIONS" (PSB/PSD Notification No. 0828-1 dated August 28, 2025)  
<https://www.mhlw.go.jp/content/11125000/001526070.pdf> (only in Japanese)

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## Important Safety Information

Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated January 13, 2026, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.

### 1 Burosumab (genetical recombination)

<b>Brand name (name of company)</b>	①Crysvita Subcutaneous Injection 10 mg, 20 mg, 30 mg, ②Crysvita Subcutaneous Injection Syringe 10 mg, 20 mg, 30 mg (Kyowa Kirin Co., Ltd.)
<b>Therapeutic category</b>	Agents affecting metabolism, n.e.c. (not elsewhere classified)
<b>Indications</b>	FGF23-related hypophosphatemic rickets/osteomalacia

#### PRECAUTIONS (Revised language is underlined.)

#### 8. IMPORTANT PRECAUTIONS (newly added)

Increase in serum calcium or PTH may occur in patients treated with this drug. Serum calcium and PTH levels should be measured prior to and periodically during treatment with this drug.

#### 9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC

Patients with hypercalcaemia or those with risk factors for hypercalcaemia (hyperparathyroidism, immobilisation, dehydration, hypervitaminosis D, renal impairment, etc.)

#### BACKGROUNDS

#### 9.1 Patients with Complications or History of Diseases, etc.

Patients with moderate to severe hypercalcaemia prior to starting treatment with this drug should not receive this drug until hypercalcaemia is adequately treated. Hypercalcaemia may develop or worsen. In particular, severe hypercalcaemia after administration of this drug has been reported in patients with tertiary hyperparathyroidism.

#### 11. ADVERSE REACTIONS (newly added)

#### 11.1 Clinically Significant Adverse Reactions Hypercalcaemia

Attention should be paid to the onset of clinical symptoms considered to be due to hypercalcaemia (irritation, malaise, inappetence, constipation, etc.). When moderate to severe hypercalcaemia is detected, treatment with this drug should be discontinued until hypercalcaemia is adequately treated.

#### Reference information

Among cases collected in the PMDA's safety database for drugs, cases which correspond to MedDRA PT "Hypercalcaemia" and "Blood calcium increased" were retrieved:

Cases (for which a causal relationship between the drug and the event is reasonably possible) involving Hypercalcaemia reported in Japan: 2 (No patient mortalities)

Number of patients using the drug as estimated by the MAH during the previous 1-year period:①approximately 679②before launch(as of

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October 2025 )

Japanese market launch:

①Crysvita Subcutaneous Injection: December 2019

②Crysvita Subcutaneous Injection Syringe: November 2025

### Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction		
	Sex/ age	Reason for use (complication)		Clinical course and treatment		
1	Female 50s	X-linked hypophosphataemia (tertiary hyperparathyroidism, hypercalcaemia, hyperlipidaemia, hypertension, chronic kidney disease, hyperuricaemia)	30 mg once every 4 weeks (13 doses, with variation in dosing intervals) ↓ Discontinuation	<b>Worsening of tertiary hyperparathyroidism Worsening of hypercalcaemia</b>		
				Day 1 of administration	Administration of burosumab (genetical recombination) was initiated. Worsening of tertiary hyperparathyroidism developed.	
				87 days after administration	Worsening of hypercalcaemia developed.	
				286 days after administration (day of discontinuation)	Administration of burosumab (genetical recombination) was discontinued due to worsening of tertiary hyperparathyroidism and worsening of hypercalcaemia.	
				2 months after discontinuation	Administration of evocalcet 1 mg/day was initiated for worsening of tertiary hyperparathyroidism (continued until 7 months after discontinuation).	
				Date unknown	The patient underwent parathyroidectomy.	
				67 days after discontinuation	Worsening of hypercalcaemia was resolving.	
				214 days after discontinuation	Worsening of tertiary hyperparathyroidism was resolving.	
<b>Laboratory test value</b>						
	Test item (unit)	Day 1 of administration	87 days after administration	171 days after administration	255 days after administration	67 days after discontinuation
	Serum calcium (mg/dL)	10.2	11.7	11.2	11.3	10.0
	iPTH (pg/mL)	205.9	251.2	243.0	248.6	239.2
Concomitant drugs: Atorvastatin calcium hydrate, nifedipine, probenecid						

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No.	Patient		Daily dose/ Administration duration	Adverse reaction				
	Sex/ age	Reason for use (complication)		Clinical course and treatment				
2	Female 50s	Hereditary hypophosphataemic rickets (chronic kidney disease, nephrocalcinosis, tertiary hyperparathyroidism, hyperuricaemia, hypertension)	70 mg (once every 4 weeks) ↓ Discontinuation ↓ 20 mg (once every 4 weeks) ↓ Discontinuation	<b>Hypercalcaemia</b>				
				Day 1 of administration	Administration of burosumab (genetical recombination) 70 mg every 4 weeks was initiated (discontinued after 1 dose).			
				2 days after administration	Vomiting, inappetence, and weakness were observed.			
				6 days after administration	Hypercalcaemia (15.2 mg/dL) was observed, and the patient was admitted to hospital.			
				7 days after administration	After admission, zoledronic acid hydrate was administered. Elcatonin and fluid were administered for 3 days.			
				9 days after administration	Administration of evocalcet 2 mg was initiated for hypercalcaemia. The dose was gradually increased to 12 mg over 3 months.			
				13 days after administration	The patient was discharged from the hospital.			
				70 days after administration (Day 1 of readministration)	Burosumab (genetical recombination) was administered at a reduced dose of 20 mg every 4 weeks.			
				77 days after administration	Hypercalcaemia (11.5 mg/dL) was confirmed again.			
				98 days after administration (day of discontinuation of readministration)	Readministration was discontinued.			
				42 days after discontinuation	Calcium normalized with dose escalation of evocalcet.			
				148 days after discontinuation	Parathyroidectomy was performed, and administration of evocalcet was discontinued after the surgery.			
				173 days after discontinuation and thereafter	Hypocalcaemia developed postoperatively, but it was corrected with oral administration of calcium and vitamin D preparations. Thereafter, calcium was well controlled with a vitamin D preparation alone.			
				*The number of days after administration refers to the 70-mg dose.				
<b>Laboratory test value</b>								
Test item (unit)	Day 1 of administra- tion	6 days after administra- tion	56 days after administra- tion	70 days after administra- tion (Day 1 of readministr a- -tion)	77 days after administra- tion	84 days after administra- tion	98 days after administra- tion (day of discontinua tion of readministr a- -tion)	42 days after discontinua- -tion
Serum calcium (mg/dL)	11.6	15.2	10.2	9.8	11.5	11.0	11.2	8.5
iPTH (pg/mL)	536	671	441	492	-	586	454	705
Concomitant drugs: Allopurinol, azilsartan, amlodipine besilate, telmisartan								

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## 2 Imeglimin hydrochloride

<b>Brand name (name of company)</b>	Twymeeg Tablets 500 mg (Sumitomo Pharma Co., Ltd.)
<b>Therapeutic category</b>	Antidiabetic agents
<b>Indications</b>	Type 2 diabetes mellitus

### PRECAUTIONS (Revised language is underlined.)

<b>11. ADVERSE REACTIONS (newly added)</b>	<u>Severe decreased appetite, vomiting</u> <u>Cases with decreased appetite and vomiting, leading to dehydration have been reported.</u>
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**Reference information** Among cases collected in the PMDA's safety database for drugs, cases which correspond to MedDRA PT "Decreased appetite" and "Vomiting," cases assessed as CTCAE (ver. 5.0) Grade 3 or higher:

Cases (for which a causal relationship between the drug and the event is reasonably possible) involving severe decreased appetite, vomiting reported in Japan: 7 (No patient mortalities)

Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 320,454  
Japanese market launch:  
Twymeeg Tablets 500 mg: September 2021

### Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 80s	Diabetes mellitus (hypertension, dyslipidaemia, dementia, right knee osteoarthritis, lumbar spinal stenosis, insomnia)	2,000 mg for 12 days	<b>Inappetence, vomiting, dehydration, constipation</b> The patient had been taking linagliptin for diabetes mellitus for 8 years.	
				Day 1 of administration	Administration of imeglimin hydrochloride was initiated. After initiation of oral administration, appetite decreased.
				Day 9 of administration	The patient had no bowel movement for 6 days, and constipation developed.
				Day 10 of administration	Inappetence and vomiting developed, and fluid intake was difficult.

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Day 12 of administration (day of discontinuation)	Administration of imeglimin hydrochloride was discontinued. Administration of linagliptin was continued.
2 days after discontinuation	The patient visited the hospital due to persisting inappetence. Decreased kidney function and hyperkalaemia due to dehydration were observed. Fluid intake was possible. An abdominal X-ray showed constipation and gas retention in the large intestine. She received fluid replacement and metoclopramide hydrochloride 10 mg by intravenous injection and sennoside 24 mg before bedtime.
4 days after discontinuation	Vomiting and constipation improved, but decreased food intake persisted. Mosapride citrate 15 mg was administered.
8 days after discontinuation	The patient was admitted to hospital due to difficulty continuing to live in a facility. She became able to eat all staple foods, and fluid replacement was no longer required. Abdominal CT showed no abnormality. Renal function and dehydration improved.
11 days after discontinuation	The patient was discharged from the hospital.

#### Laboratory test value

Test item (unit)	Day 1 of administration	2 days after discontinuation	8 days after discontinuation	52 days after discontinuation
Creatinine (mg/dL)	0.77	1.01	0.91	0.67
BUN (mg/dL)	13.7	27.3	12.3	7.6
K (mmol/L)	3.3	5	3.8	3.3
Uric acid (mg/dL)	-	8.4	-	4
eGFR (ml/min)	52.79	39.23	43.97	61.47
Fasting blood sugar (mg/dL)	281	124	142	209
HbA1c (% NGSP)	8.3	-	-	7.1

Concomitant drugs: Amlodipine besilate, linagliptin, donepezil hydrochloride, suvorexant, valsartan, memantine hydrochloride, Yokukansan, simvastatin

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No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
2	Male 90s	Type 2 diabetes mellitus (renal impairment [excluding diabetic nephropathy], dyslipidaemia, chronic cardiac failure, atrial fibrillation, prostatic hyperplasia)	1,000 mg for 13 days	<b>Vomiting, dehydration</b>	
				Insulin glargine and teneligliptin hydrobromide hydrate were used for diabetes mellitus.	
				Day 1 of administration	Administration of imeglimin hydrochloride was initiated. The amount of food intake gradually decreased.
				Day 13 of administration (day of discontinuation)	The patient was admitted to hospital due to vomiting and dehydration (serum creatinine 2.18 mg/dL). Administration of imeglimin hydrochloride was discontinued. Metoclopramide hydrochloride 10 mg and lactated Ringer's solution (1,000) were administered. Queasy disappeared after the treatment.
				1 day after discontinuation	The patient resumed eating.
				5 days after discontinuation	Renal function/dehydration was resolving (serum creatinine 0.96 mg/dL), and fluid replacement was terminated.
<b>Laboratory test value</b>					
Test item (unit)		Day 1 of administration	Day 13 of administration	5 days after discontinuation	
Serum creatinine (mg/dL)		1.14	2.18	0.96	
BUN (mg/dL)		30.4	36.3	-	
Concomitant drugs: Insulin glargine (genetical recombination), teneligliptin hydrobromide hydrate, dutasteride, silodosin, azosemide, spironolactone, diltiazem hydrochloride, clopidogrel sulfate, pitavastatin calcium, isosorbide dinitrate					

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## Revisions of PRECAUTIONS (No. 366)

This section presents details of revisions to the PRECAUTIONS and brand names of drugs that have been revised in accordance with the Notifications dated January 13, 2026.

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

**[1] Aspirin**

**[2] Aspirin/dialuminate**

**[3] Aspirin/vonoprazan fumarate**

**[4] Aspirin/lansoprazole**

**[5] Clopidogrel sulfate/aspirin**

**Brand name** [1] Bayaspirin tablets 100 mg, and the others (Bayer Yakuhin, Ltd., and the others)  
[2] Bufferin Combination Tablets A81, and the others (Lion Corporation, and the others)  
[3] Cabpirin Combination Tablets (Takeda Pharmaceutical Company Limited)  
[4] Takelda Combination Tablets (T's Pharma Co., Ltd.)  
[5] ComPlavin Combination Tablets, and the others (Sanofi K.K., and the others)

### 11. ADVERSE REACTIONS

**11.1 Clinically Significant Adverse Reactions (newly added)**

Acute coronary syndrome accompanying allergic reaction

**2** Antidiabetic agents

**Imeglimin hydrochloride**

**Brand name** Twymeeg Tablets 500 mg (Sumitomo Pharma Co., Ltd.)

### 11. ADVERSE REACTIONS

**11.1 Clinically Significant Adverse Reactions (newly added)**

Severe decreased appetite, vomiting

Cases with decreased appetite and vomiting, leading to dehydration have been reported.

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

**Burosumab (genetical recombination)**

**Brand name** Crysvita Subcutaneous Injection 10 mg, 20 mg, 30 mg, Crysvita Subcutaneous Injection Syringe 10 mg, 20 mg, 30 mg (Kyowa Kirin)

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**8. IMPORTANT PRECAUTIONS (newly added)**

**9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS**

**9.1 Patients with Complications or History of Diseases, etc.**

**11. ADVERSE REACTIONS (newly added)**

Co., Ltd.)

Increase in serum calcium or PTH may occur in patients treated with this drug. Serum calcium and PTH levels should be measured prior to and periodically during treatment with this drug.

Patients with hypercalcaemia or those with risk factors for hypercalcaemia (hyperparathyroidism, immobilisation, dehydration, hypervitaminosis D, renal impairment, etc.)

Patients with moderate to severe hypercalcaemia prior to starting treatment with this drug should not receive this drug until hypercalcaemia is adequately treated. Hypercalcaemia may develop or worsen. In particular, severe hypercalcaemia after administration of this drug has been reported in patients with tertiary hyperparathyroidism.

**11.1 Clinically Significant Adverse Reactions**

**Hypercalcaemia**

Attention should be paid to the onset of clinical symptoms considered to be due to hypercalcaemia (irritation, malaise, inappetence, constipation, etc.). When moderate to severe hypercalcaemia is detected, treatment with this drug should be discontinued until hypercalcaemia is adequately treated.

**4 Cold medicines, antipyretics and analgesics**

**[1] Antipyretics and analgesics (OTC drug)**

**[2] Preparations containing aspirin aluminum (OTC drug)**

**Brand name**

[1]-1 Bufferin A (Lion Corporation), and the other OTC drugs  
[1]-2 New Asunamin Z (SATO YAKUHIN KOGYO Co.,Ltd.), and the other OTC drugs

**Consultation (newly added)**

[2] -

If the following symptoms are observed after taking this drug, they may be adverse reactions. In such cases, the use of this drug should be immediately discontinued, and a physician, pharmacist, or registered salesclerk should be consulted, presenting them with this document.

The following serious symptoms may occur rarely. In such cases, medical attention should be sought immediately.

Name of symptom	Symptoms
<u>Acute coronary syndrome</u> <u>accompanying allergic reaction</u>	<u>Symptoms such as tight chest pain, difficulty breathing, feeling of tight chest pressure, jaw pain, pain in the left arm, chilliness, lightheadedness, sweaty, pyrexia, decrease in consciousness, swelling around the lips, itching, urticaria, rash, throat itching, and palpitations may occur.</u>

**5 Idecabtagene vicleucel**

**Brand name**

Abecma for intravenous infusion (Bristol-Myers Squibb K.K.)

**11. ADVERSE REACTIONS**

Infection

**11.1 Clinically**

**Significant Adverse Reactions**

Severe infections caused by bacteria, fungi, and viruses, etc. (sepsis, pneumonia, etc.) may occur. Fatal cases have been reported. In addition, febrile neutropenia may occur. If any abnormalities are observed, appropriate measures such as administration of antibiotics

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should be taken. In addition, progressive multifocal leukoencephalopathy (PML) has been reported. If neurological symptoms occur, appropriate tests for the differentiation (cerebrospinal fluid tests and imaging diagnostics with MRI, etc.) should be performed.

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## **6 Ciltacabtagene autoleucel**

**Brand name** Carvykti Suspension for Intravenous Infusion (Janssen Pharmaceutical K.K.)

**11. ADVERSE REACTIONS** Infection

**11.1 Clinically Significant Adverse Reactions** Severe infections caused by bacteria, fungi, or viruses, etc. (sepsis, pneumonia, etc.) may occur. Fatal cases have been reported. In addition, febrile neutropenia may occur. If any abnormalities are observed, appropriate measures such as administration of antibiotics should be taken. In addition, progressive multifocal leukoencephalopathy (PML) has been reported. If neurological symptoms occur, appropriate tests for the differentiation (cerebrospinal fluid tests and imaging diagnostics with MRI, etc.) should be performed.

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## **7 Tisagenlecleucel**

**Brand name** Kymriah for i.v. infusion (Novartis Pharma K.K.)

**11. ADVERSE REACTIONS** Infection

**11.1 Clinically Significant Adverse Reactions** Severe infections caused by bacteria, fungi, or viruses, etc. (sepsis, pneumonia, etc.) may occur. Fatal cases have been reported. In addition, febrile neutropenia may occur. If any abnormalities are observed, appropriate measures such as administration of antibiotics should be taken. In addition, progressive multifocal leukoencephalopathy (PML) has been reported. If neurological symptoms occur, appropriate tests for the differentiation (cerebrospinal fluid tests and imaging diagnostics with MRI, etc.) should be performed.

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## **8 Ciltacabtagene autoleucel**

**Brand name** Carvykti Suspension for Intravenous Infusion (Janssen Pharmaceutical K.K.)

**11. ADVERSE REACTIONS** Enterocolitis

**11.1 Clinically Significant Adverse Reactions (newly added)** Enterocolitis considered to be due to an immune reaction may occur. Some cases may result in intestinal perforation. Patients should be carefully monitored. If any abnormalities such as severe or prolonged diarrhoea are observed, appropriate measures should be taken.

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## 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 December 31, 2025)

⊙: Products for which EPPV was initiated after December 1, 2025

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

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

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Nonproprietary name		Name of the MAH	Date of EPPV initiation
Brand name			
	Avatrombopag Maleate* <sup>8</sup> Doptelet tablets 20 mg	Swedish Orphan Biovitrum Japan Co., Ltd.	August 25, 2025
	Belzutifan Welireg Tablets 40 mg	MSD K.K.	August 18, 2025
	Sotatercept (genetical recombination) Airwin for Subcutaneous Injection 45 mg, 60 mg	MSD K.K.	August 18, 2025
	Talquetamab (genetical recombination) Talvey Subcutaneous Injection 3 mg, 40 mg	Janssen Pharmaceutical K.K.	August 14, 2025
	Erdafitinib Balversa Tablets 3 mg, 4 mg, 5 mg	Janssen Pharmaceutical K.K.	July 16, 2025
	Tislelizumab (genetical recombination) Tevimbra I.V. Infusion 100 mg	BeOne Medicines Japan	July 1, 2025

- \*1 Chronic cardiac failure, only limited to patients receiving standard treatment for chronic heart failure
- \*2 Cerebrotendinous xanthomatosis
- \*3 NTRK fusion gene-positive advanced or recurrent solid tumor
- \*4 Suppression of relapse in IgG4-related diseases
- \*5 Sedation during gastrointestinal endoscopy
- \*6 Combination therapy with cipaglucosidase alfa (genetical recombination) for late onset pompe's disease
- \*7 Prevention of the following diseases caused by infection with human papillomavirus types 6, 11, 16, 18, 31, 33, 45, 52, and 58
  - Anal cancer (squamous cell carcinoma) and its precursor lesions (anal intraepithelial neoplasia (AIN) grades 1, 2, and 3)
- \*8 Persistent and chronic immune thrombocytopenia

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