

Pharmaceuticals and Medical Devices Safety Information

August 2026
No. 431

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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).

Available information is listed

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Pharmaceuticals and Medical Devices

Safety Information No.431

Ministry of Health, Labour and Welfare

[Outline of Information]

No.	Subject	Measures	Outline of Information	Page
1	Safety measures for use of colchicine in relief of gout attacks	<i>P</i>	Colchicine (hereinafter referred to as "this drug") was launched in November 1964 and has been currently used for the indications of relief and prophylaxis of gout attacks and familial Mediterranean fever. Recently, multiple cases of toxic symptoms that were caused by administration of this drug at high doses exceeding 1.5 mg per day and resulted in death have been reported in Japan. Based on the accumulation of these cases, revision of the PRECAUTIONS in the package insert, which was electronized on February 24, 2026, was instructed to provide precautions. Furthermore, to ensure the safety measures for this drug even more, partial changes in the approved items in "DOSAGE AND ADMINISTRATION" for "Relief of gout attacks" were approved on June 2, 2026. This document introduces a series of safety measures taken for this drug.	4
2	Proper use of continuous glucose monitoring system		A continuous glucose monitoring system (CGM) is a medical device that can continuously measure glucose levels in the interstitial fluid to enable an understanding of variations in blood glucose levels and has a significant advantage over self-monitoring of blood glucose (SMBG) in daily blood glucose control. On the other hand, CGM measurements may deviate from blood glucose levels in principle, and therefore providing treatment such as insulin administration based on CGM measurements alone is not recommended. In order to use CGM safely and appropriately, it is essential that companies, academic societies, and the government cooperate to promote understanding of users and ensure proper use. This document introduces information on the proper use of CGM.	6
3	Doxorubicin hydrochloride, and 5 others	<i>P</i> <i>C</i>	Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated July 14, 2026, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.	9
4	Cefcapene pivoxil hydrochloride hydrate (for pediatric use), and 20 others	<i>P</i>	Revisions of PRECAUTIONS (No. 371)	20
5	List of Products Subject to Early Post-marketing Phase Vigilance		List of products subject to Early Post-marketing Phase Vigilance as of June 30, 2026	27

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

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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>



1.

Safety measures for use of colchicine in relief of gout attacks

1. Introduction

Colchicine (hereinafter referred to as "this drug") was launched in November 1964 and has been currently used for the indications of relief and prophylaxis of gout attacks and familial Mediterranean fever.

Recently, multiple cases of toxic symptoms that were caused by administration of this drug at high doses exceeding 1.5 mg per day and resulted in death have been reported in Japan. Based on the accumulation of these cases, revision of the PRECAUTIONS in the package insert, which was electronized on February 24, 2026 (hereinafter referred to as electronic package insert), was instructed to provide precautions. Furthermore, to ensure the safety measures for this drug even more, partial changes in the approved items in "DOSAGE AND ADMINISTRATION" for "Relief of gout attacks" were approved on June 2, 2026.

This document introduces a series of safety measures taken for this drug.

2. Background of changes in DOSAGE AND ADMINISTRATION

The dosage and administration of this drug for "relief of gout attacks" had been specified as follows so far: "Usual adult dosage is 3 to 4 mg of colchicine orally administered per day in 6 to 8 divided doses. The dose may be adjusted according to the patient's age and symptoms as appropriate". However, since risks of acute toxic symptom, etc. resulting from administration of this drug at high doses have been known, a statement as below was added to the "PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION" section in June 2010 to provide precautions.

- The frequency of occurrence of gastrointestinal disorders, such as diarrhoea increases as the dose increases. It is desirable to limit the daily dose to 1.8 mg.

In recent years, however, toxic symptoms that were caused by this drug (gastrointestinal disorder, blood disorder, renal disorder, liver disorders, etc.) and resulted in death have been reported in patients who received this drug at high doses exceeding 1.5 mg per day, although these doses were within the range of the approved dosage and administration. In most patients in the fatal cases for which the dose was identified, higher doses than 1.5 mg per day were administered. Based on the above information, the Ministry of Health, Labour and Welfare instructed revision of PRECAUTIONS ("WARNINGS," "PRECAUTIONS CONCERNING DOSAGE AND ADMINISTRATION," "IMPORTANT PRECAUTIONS," and "Clinically Significant Adverse Reactions") on February 24, 2026. As a result, statements to the effect that cases of toxic symptoms that led to death have been reported in patients who received this drug at high doses and that high-dose administration of this drug should be avoided except when it is inevitable were added to provide precautions. In this revision, a dose exceeding 1.5 mg, which is an acceptable dosage based on the specification of this drug (0.5 mg tablet), was specified as a high dose.

In addition to these safety measures, the marketing authorization holder requested a change in the dosage and administration in association with this revision of the electronic package insert. Therefore, the appropriateness of the dosage and administration was also examined, and evidence on the efficacy and safety was evaluated.

As a result of evaluation of evidence on the efficacy and safety of this drug, it was found that in an overseas clinical study (AGREE Study), while the incidence of gastrointestinal disorder was higher in the high-dose group than in the low-dose group, there was no major difference in the efficacy between the two groups. As another finding, it was found that the Japanese guideline (Guideline for the management of hyperuricemia and gout, 3rd Edition [Supplement Version in 2022]) has provided a recommendation in terms of administration of this drug as follows: This drug should be administered at 1.0 mg (0.5 mg tablet × 2) as the initial dose, followed by the addition of 0.5 mg 1 hour later, and at a low dose of 1 to 2 tablets per day thereafter.

Based on the above findings, the current dose setting assuming a high-dose administration has been reviewed, and from the viewpoint of ensuring the safety assurance even more, the dosage and administration of this drug concerning "relief of gout attacks" was changed as follows (partial change was approved on June 2, 2026).

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< DOSAGE AND ADMINISTRATION >

The usual adult dosage is 0.5 to 1.0 mg of colchicine orally administered once or twice daily. However, the total daily dose should not exceed 1.5 mg.

3. In closing

Although precautions regarding risks associated with high-dose administration of this drug have been continuously provided, cases of death in patients who received this drug at high doses exceeding 1.5 mg per day have been reported. Accordingly, a series of safety measures were taken in order to draw more attention to the relevant risks.

When using this drug, follow the dosage and administration described in the package insert to avoid use of doses exceeding the approved dose. The administration should be provided with care to elderly patients, patients with renal or hepatic impairment, and patients receiving concomitant drugs that inhibit CYP3A4 or P-glycoprotein because toxic symptoms may occur in these patients even at non-high doses. Healthcare professionals are encouraged to understand the purpose of this series of safety measures, carefully check the electronic package insert, make a careful judgment by referring to the latest guidelines in Japan, and continue to cooperate for proper use of drugs.

< Reference >

- Points to consider for the use of colchicine (PSB/MDED Notification No. 0602-1 and PSB/PSD Notification No. 0602-1, dated June 2, 2026)
- Revisions of PRECAUTIONS (PSB/PSD Notification No. 0224-1 dated February 24, 2026)
- Guideline for the management of hyperuricemia and gout, 3rd Edition (Supplement Version in 2022)

2.

Proper use of continuous glucose monitoring system

1. Introduction

A continuous glucose monitoring system is a system to continuously measure blood or tissue glucose levels. It is a medical device usually composed of an electrochemical sensor to be inserted subcutaneously and a portable receiver, which receives an electrical signal derived from sensor electrodes, converts it to a glucose level, and stores and displays the level. While self-monitoring of blood glucose (hereinafter referred to as "SMBG"), the most common blood glucose measurement method, is designed to have patients measure their own blood glucose level by using a simple blood glucose meter after collecting blood by pricking their fingertips by themselves, a glucose monitoring system measures the glucose level in interstitial fluid using a sensor attached to the upper arm or abdomen. Currently, a device that can continuously measure glucose level is mainly used. This type of device has been called continuous glucose monitoring (CGM), which allows patients to check the fluctuation pattern of glucose levels to use it for routine management of diabetes mellitus. Six types of CGM are now available in Japan (Table 1).

Since the glucose level displayed in CGM is a level estimated from the glucose level in the subcutaneous tissue fluid, a deviation from the actual blood glucose level may occur. Therefore, CGM is not intended to be used as a sole basis for treatment such as insulin administration. In recent years, a CGM integrated with an insulin pump has been released. This device automatically adjusts the dose of insulin based on the glucose level obtained from CGM. However, its use is premised on concomitant use of SMBG in a certain situation, and it is essential for healthcare professionals, patients, and their families to fully understand the characteristics of CGM to appropriately manage diabetes mellitus using CGM. This document summarizes the information on proper use of CGM for further understanding.

Table 1 CGM currently available in Japan (as of March 31, 2026)

Brand name	Name of the (designated) MAH	Approval Number
Dexcom G7 CGM System	DexCom Japan G.K.	30500BZI00035000
Dexcom G6 CGM System	Cobridge Co.,Ltd.	30200BZI00004000
FreeStyle Libre 2	Abbott Japan LLC	30300BZX00119000
FreeStyle Libre Pro	Abbott Japan LLC	22800BZX00227000
FreeStyle Libre	Abbott Japan LLC	22800BZX00212000
Medtronic Guardian Connect	Medtronic Japan Co., Ltd.	22900BZX00321000

*In addition to the above products, FreeStyle Libre 3 (Abbott Japan LLC. Approval number: 30600BZX00002000) and Simpler glucose sensor system (Medtronic Japan Co., Ltd. Approval number: 30700BZX00168000) have obtained marketing approval.

2. Precautionary statement concerning the measurement errors in the package insert

With respect to the concordance rate between glucose levels measured by CGM and plasma glucose levels, the following data were obtained from the comparison with plasma glucose levels obtained using YSI analyzer based on the clinical results of currently approved CGMs: The mean absolute relative difference was 9.2% and mean concordance rate within 20% error margin * was 81% to 94%, indicating that approximately 10% to 20% error can occur. Furthermore, it is known that the deviation is likely to occur particularly when the variation in blood glucose levels is large. For this reason, the following precautionary statements are included in the package inserts, although the description is slightly different depending on the characteristics of the product, and measuring glucose levels using SMBG in addition to CGM is requested during the treatment.

- [Purpose of use or effects]: The measurement results obtained by CGM should be used in combination with results

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obtained from a self-blood glucose meter as appropriate for self-management of diabetes mellitus within the scope agreed with a physician in advance.

- [WARNINGS] and [PRECAUTIONS]: If there is any discrepancy between the measurement results and the symptoms or if a patient is taking a drug that may affect glucose levels, the treatment should be based on the results of self-monitoring of blood glucose levels.

*Rate of measurements with error margin within $\pm 20\%$ of the reference levels. For Dexcom G7, the error margin was within $\pm 20\%$ for YSI glucose levels of 100 mg/dL or higher and within ± 20 mg/dL for YSI glucose levels of less than 100 mg/dL. For Medtronic Guardian Connect, the error margin was within $\pm 20\%$ for YSI glucose levels of 80 mg/dL or higher and within ± 20 mg/dL for YSI glucose levels of less than 80 mg/dL.

3. Concept of malfunctions, etc. reports related to measurement errors

As a tool for evaluating the accuracy of blood glucose measuring devices, an indicator called an error grid has been used. It is a chart which plots the measurements obtained by a device and reference values to show the level of clinical risks posed by the deviations between these values. The representative error grid is the consensus error grid proposed by Parkes in 2000. The error grid is used for certification standards for SMBG and regulatory application and evaluation of blood glucose measuring devices by the FDA. However, this tool is basically designed to be used for SMBG, and it has been suggested that the design does not fully reflect the recent trends in the dissemination of CGM and the latest information on treatments for diabetes mellitus. In Japan, when a discrepancy between the values measured by CGM and SMBG occurs, it may be subject to reporting of malfunctions, etc. based on Article 68-10 of the Pharmaceutical and Medical Device Act, but the degree of errors subject to the reporting has currently been examined individually by marketing authorization holders according to the performance or functions of the product. Whether or not the error grid can be applied as a criterion for determining clinically significant error is still under consideration, and further adjustment is needed in the future.

4. Academic guidelines

When CGM was first approved in Japan, the Japan Diabetes Society and the government discussed how to ensure the proper use of this product, and the guideline for the proper use was released by the relevant society. This guideline also states that CGM is a device that can be used for self-management of diabetes mellitus, but attention should be paid to the risk associated with adjustment of insulin dose only based on CGM measurements and that CGM produces a measurement error of 10% to 20% from blood glucose level on average. Furthermore, with respect to use of this product, the guideline points out that it is important for patients to fully understand the characteristics of CGM and method of using it and circumstances that require confirmation of blood glucose levels with SMBG and for the healthcare professionals to perform medical care in a medical team to interpret data obtained from CGM and make clinical judgments and give instructions appropriately.

5. In closing

CGM may cause a deviation from blood glucose levels in principle and requires a certain caution in interpretation of the measurements; however, it is useful for grasping daily variation in blood glucose and has been introduced in Japan with great expectations from relevant academic societies and patient groups. CGM is a device used by patients at home. Patients need to wear and adjust the sensor and receiver by themselves. In addition, CGM has such a characteristic that it requires concomitant use of SMBG appropriately in management of blood glucose levels as mentioned above, and therefore it is important for patients to use this product with a full understanding of the characteristics of this product and method of using it while asking physicians for advice. To promote the proper use, it is essential for the marketing authorization holders, relevant academic societies, and the government to work on patient education and appropriate clinical judgements in collaboration. The relevant parties are encouraged to provide continued cooperation. Healthcare professionals are encouraged to provide cooperation by reporting malfunctions or adverse health effects related to CGM including deviation between CGM and SMBG to the regulatory authority through the PMDA's website for receiving the reports as well as the marketing authorization holders when these events were identified. The obtained information will be used for various safety measures as important basic information for surveys and investigations including revision of PRECAUTIONS.

6. References

- Package insert, literature, URL of academic society guideline, etc.
 - Medical device package insert information search system (PMDA website)
<https://www.pmda.go.jp/PmdaSearch/kikiSearch/>
 - Draft certification standards for glucose measuring devices for self-testing. Formulation of certification standards for specially controlled medical devices (PMDA website)
<https://www.pmda.go.jp/files/000229679.pdf>

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- Guidelines for Proper Use of Continuous Glucose Monitoring Devices (website of the Japan Diabetes Society)
https://www.jds.or.jp/modules/important/index.php?content_id=111
- Website for receiving adverse reactions/malfunctions, etc. reports reported from healthcare professionals to PMDA (PMDA website)
<https://www.pmda.go.jp/safety/reports/hcp/0002.html>

3.

Important Safety Information

Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated July 14, 2026, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.

1 Doxorubicin hydrochloride

Brand name (name of company)	Doxil Injection 20 mg (Baxter Japan K.K.)
Therapeutic category	Antitumor antibiotics and preparations
Indications	○ Ovarian cancer which has progressed after cancer chemotherapy ○ AIDS-related Kaposi's sarcoma

PRECAUTIONS (A revised description is underlined.)

8. IMPORTANT PRECAUTIONS (newly added)

Renal-limited thrombotic microangiopathy may occur. Patients should be carefully monitored through such methods as periodic blood tests, renal function tests, and urine tests.

11. ADVERSE REACTIONS

Renal-limited thrombotic microangiopathy

11.1 Clinically Significant Adverse Reactions (newly added)

Reference information

Number of cases (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's safety database
Cases involving renal-limited thrombotic microangiopathy reported in Japan:
1 patient (No patient mortalities)
Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 13,000
Japanese market launch: Doxil Injection 20 mg: February 2007

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 70s	Serous cystadenocarcinoma ovary/recurrent cancer/ovarian adenocarcinoma (Serous cystadenocarcinoma ovary, ovarian serous cystadenoma)	Unknown for 5 years ↓ Discontinuation	Renal-limited thrombotic microangiopathy	
				7 years before administration	Multiple tumors were observed in the right lung, liver, and right pelvis. Adenocarcinoma was diagnosed based on liver biopsy results. Bilateral salpingo-oophorectomy was performed, and a definitive diagnosis of serous adenocarcinoma (stage IV) was made. After surgery, combination therapy with paclitaxel and carboplatin was performed (every 3 weeks for 6 cycles). Thereafter, right lower lung lobectomy, partial hepatectomy, and combination therapy with paclitaxel and carboplatin (once weekly for 6 cycles) were performed. However, recurrence occurred twice in the abdominal cavity, which needed surgical resection.
				Day 1 of administration	As drug-induced erythema developed, the treatment was switched from chemotherapy to treatment with doxorubicin hydrochloride, and induction therapy was performed for 6 cycles.
				5 months after administration	Maintenance therapy was started.
				5 years after administration	Hypertension (approximately 150/80 mmHg) and urine protein/creatinine ratio (treatment discontinuation) of 0.8 g/gCr were noted. Proteinuria did not improve even with administration

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				of olmesartan; therefore, doxorubicin hydrochloride was suspected to be one of the causes of proteinuria, and treatment with doxorubicin hydrochloride was discontinued (a total of 36 cycles of treatment with doxorubicin hydrochloride were provided in 5 years. Cumulative dose was 1,447 mg/m ²). Proteinuria persisted, and renal function further deteriorated, and improvement in oedema of both the lower limbs was also not obtained. Therefore, the patient was admitted to the hospital. Mild pitting oedema was noted in both the lower limbs, but no obvious skin lesion was observed. The patient did not meet the diagnostic criteria for nephrotic syndrome. Schizocytes were not detected in a peripheral blood smear sample.
			1 year after discontinuation	Mild interstitial fibrosis and tubular atrophy were identified based on kidney biopsy, but the lesions were mainly located in the glomeruli. One of the glomeruli presented with global sclerosis, and the others lobular thickening of glomerular capillary tuft, mild mesangial expansion, and segmental mesangiolysis. Electron microscopy revealed marked mesangiolysis, and therefore glomerular thrombotic microangiopathy (TMA) with mesangiolysis was diagnosed. Based on comprehensive evaluation, pegylated liposomal doxorubicin (PLD)-induced renal-limited thrombotic microangiopathy was diagnosed.
			1 and a half years after discontinuation	Treatment for hypertension was switched from olmesartan to sacubitril valsartan. Blood pressure had decreased from 146/68 mmHg to 132/52 mmHg. No recurrence of ovarian cancer was observed, and slowing progression of kidney function decreased was also observed. However, proteinuria persisted.

Laboratory test value		
Test item (unit)	5 years after administration	1 year after discontinuation
Urine specific gravity	-	1.013
Urine protein	-	(2 +)
Urinary occult blood	-	(-)
Red blood cell count in urine	-	1-4/HPF
White blood cell count in urine	-	< 1/HPF
Urine protein/creatinine ratio (g/g)	0.8	1.9
Urine protein (g/day)	-	1.3
Beta-N-acetyl-D-glucosaminidase (IU/g)	-	19.2
Beta-2 microglobulin in urine (μg/g)	-	6.864
Total protein (g/day)	-	7.7
Blood albumin (g/dL)	-	3.9
Aspartate aminotransferase (IU/L)	-	28
Alanine aminotransferase (IU/L)	-	18
Lactate dehydrogenase (IU/L)	-	245
Urea nitrogen (mg/dL)	-	26.4
Creatinine (mg/dL)	0.59	1.19

Concomitant drugs: None

2 Insulin aspart (genetical recombination)

Brand name (name of company)	Fiasp Injection 100 U/mL (Novo Nordisk Pharma Ltd.)
Therapeutic category	Other hormone preparations
Indications	Diabetes mellitus in cases where insulin therapy is indicated

PRECAUTIONS (A revised description is underlined.)

8. IMPORTANT PRECAUTIONS (newly added)

Gelling of this drug may occur when exposed to high temperatures exceeding 37 degrees C. Use of a portable insulin pump at high temperature may cause gelling of insulin to cause occlusion in the insulin pump, which may prevent the pump from appropriately delivering this drug and consequently serious hyperglycaemia.

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diabetic ketoacidosis, etc. may occur. Patients should be instructed as follows:

- Avoid use of a portable insulin pump in an environment of high temperature exceeding 37 degrees C.
- Check the inside of the insulin pump, and if there is any change in the appearance of the injection solution, do not use it.

Reference information

Japanese market launch: Fiasp Injection 100 units/mL: February 2020

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 60s	Type 1 diabetes mellitus (none)	Basal 0.5 U/hr for 11 days ↓ Discontinuation	Diabetic ketoacidosis Height: Unknown, Weight: Unknown History of adverse reactions: Yes Alcohol drinking, smoking, allergy: Yes Engaged in activities in an environment of high temperature	
				Day 1 of administration	Insulin treatment was switched from insulin glulisine (genetical recombination) to insulin aspart (genetical recombination) to improve blood glucose control. The treatment was started using a portable insulin pump.
				Day 7 of administration	Malaise developed.
				Day 9 of administration	Vomiting occurred.
				Day 10 of administration	The patient contacted the manufacturer because the insulin pump was not in good condition.
				Day 11 of administration (day of discontinuation)	The patient visited the emergency department with vomiting, inability to move, and hyperglycaemia that started several days ago. The patient received a diagnosis of diabetic ketoacidosis and started receiving treatment in an ICU. Insulin aspart (genetical recombination) was immediately discontinued.
				2 days after completion	The symptoms were improving, allowing the patient to be transferred to the general ward.
				Laboratory test value	
				Test item (unit)	Day 11 of administration (day of discontinuation)
				HbA1c (%)	9.4
				GLU (mg/dL)	784
				K (mEq/L)	5.6
				Na (mEq/L)	129
				pH	7.245
				pCO ₂ (mmHg)	27.8
				pO ₂ (mmHg)	56.6
				cHCl ⁻ (mmol/L)	12
				cCl ⁻ (mmol/L)	93
				β-HB (μmol/L)	9757
				Concomitant drugs: Pitavastatin calcium hydrate, thiamazole	

3 Atezolizumab (genetical recombination)

Brand name (name of company)	Tecentriq for Intravenous Infusion 840 mg, 1200 mg (Chugai Pharmaceutical Co., Ltd.)
Therapeutic category	Other antitumor agents
Indications	< Common to drug products > ○ Unresectable advanced or recurrent non-small cell lung cancer ○ Postoperative adjuvant treatment for PD-L1 positive non-small cell lung cancer ○ Extensive-stage small-cell lung cancer ○ Unresectable alveolar soft part sarcoma ○ Relapsed or refractory extranodal NK/T-cell lymphoma, nasal type < Tecentriq for Intravenous Infusion 1200 mg > ○ Unresectable hepatocellular carcinoma ○ Unresectable thymic carcinoma < Tecentriq for Intravenous Infusion 840 mg > ○ PD-L1 positive, hormone receptor (HR)-negative, and human epidermal growth factor receptor 2 (HER2)-negative inoperable or recurrent breast cancer

PRECAUTIONS (A revised description is underlined.)

11. ADVERSE REACTIONS

11.1 Clinically Significant Adverse Reactions (newly added)

Reference information

Vasculitis

Large vessel vasculitis, medium vessel vasculitis, and small vessel vasculitis [including antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, IgA vasculitis, and cutaneous vasculitis] may occur.

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

Cases involving vasculitis reported in Japan:

6 patients (No patient mortalities)

Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 18,920

Japanese market launch: Tecentriq for Intravenous Infusion 840 mg: November 2019
Tecentriq for Intravenous Infusion 1200 mg: April, 2018

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Male 60s	Right lower lobe lung adenocarcinoma (hypertension, dyslipidaemia)	1200 mg/ per dose for 1 day ↓ Discontinuation	Leukocytoclastic vasculitis [PS at the start of administration of atezolizumab (genetical recombination)] 0 [Presence of primary lesion] Yes: Right lower lobe [Metastases] Liver, bone (site: Th7, left femur) [Prior medications] Osimertinib mesylate [History of radiotherapy] Yes (dose: 30 Gy, site: Bone)	
				Day 1 of administration (day of discontinuation)	ABCP therapy was started as the second-line treatment (administration of atezolizumab [genetical recombination], bevacizumab [genetical recombination], carboplatin, and paclitaxel was started).
				2 days after discontinuation	Administration of celecoxib and lansoprazole was started.
				3 days after discontinuation	Skin eruption was observed in the lower leg, and leukocytoclastic vasculitis (Grade 3 at worst) developed. Treatment: Prednisolone
				4 days after discontinuation	Skin eruption extended, which was determined to be a significant finding.
				7 days after discontinuation	Pyrexia developed.
				10 days after discontinuation	Although celecoxib and lansoprazole were discontinued, skin eruption and pyrexia did not improve. Skin biopsy was performed.

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			17 days after discontinuation	Skin biopsy revealed leukocytoclastic vasculitis, and other conditions including infection were ruled out. Vasculitis was thus diagnosed. Administration of prednisolone 60 mg/day (1 mg/kg/day) was started.			
			37 days after discontinuation	The dose of prednisolone was reduced every 2 weeks. Hepatic enzyme increased was noted. Hepatitis developed (Grade 4 at worst).			
			45 days after discontinuation	AST and ALT worsened. It was considered that irAE hepatitis was manifested by dose reduction of prednisolone to 40 mg. The condition became stable after initiation of mycophenolate mofetil.			
			112 days after discontinuation	Leukocytoclastic vasculitis and hepatitis were resolving. The dose of prednisolone was reduced on an outpatient basis.			
			Date unknown	The treatment was shifted to best supportive care (BSC).			
Laboratory test value							
Test item (unit)		1 day before administration	3 days after discontinuation	15 days after discontinuation	30 days after discontinuation	37 days after discontinuation	45 days after discontinuation
AST (GOT) (IU)		19	24	98	27	32	239
ALT (GPT) (IU)		8	13	68	80	45	705
Al-P (IU)		131	131	139	375	-	275
CK (CPK) (IU)		179	142	1191	21	-	16
IgA		-	-	-	178	-	-
IgG		-	-	-	715	-	-
IgM		-	-	-	22	-	-
LDH (IU)		178	165	442	180	-	-
CRP (mg/dL)		1.01	1.15	8.92	1.36	-	1.38
γ-GTP (IU)		19	21	41	302	-	165
Haemoglobin (g/dL)		12.1	12.6	11.0	11.7	-	12.0
Platelets (10 ⁴ /μL)		28.7	23.0	30.5	56.1	-	25.1
Red blood cells (10 ⁴ /mm ³)		383	393	361	369	-	386
White blood cells (cells/mm ³)		6020	7500	7880	10130	-	10800
Concomitant drugs: Bevacizumab (genetical recombination), carboplatin, paclitaxel, precipitated calcium carbonate/cholecalciferol/magnesium carbonate, amlodipine besilate, fenofibrate, azilsartan, celecoxib, lansoprazole							

4 Guselkumab (genetical recombination)

Brand name (name of company)	Tremfya Subcutaneous Injection 100 mg syringe, 200 mg syringe, Tremfya Subcutaneous Injection 200 mg pen, Tremfya Intravenous Infusion 200 mg (Janssen Pharmaceutical K.K.)
Therapeutic category	Agents affecting metabolism, n.e.c. (not elsewhere classified)
Indications	< Tremfya Subcutaneous Injection 100 mg syringe > ○ Following diseases in patients who have not responded sufficiently to conventional therapies: Plaque psoriasis, psoriatic arthritis, pustular psoriasis, erythrodermic psoriasis, and palmoplantar pustulosis ○ Remission induction therapy and maintenance therapy for moderate to severe ulcerative colitis (for use only in patients who have not sufficiently responded to conventional treatments) ○ Moderate to severe active Crohn's disease (for use only in patients who have not sufficiently responded to conventional treatments) < Tremfya Subcutaneous Injection 200 mg syringe, Tremfya Subcutaneous Injection 200 mg pen > ○ Remission induction therapy and maintenance therapy for moderate to severe ulcerative colitis (for use only in patients who have not sufficiently responded to conventional treatments) ○ Moderate to severe active Crohn's disease (for use only in patients who have not sufficiently responded to conventional treatments) < Tremfya Intravenous Infusion 200 mg > ○ Remission induction therapy for moderate to severe ulcerative colitis (for use only in patients who have not sufficiently responded to conventional treatments)

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	○ Moderate to severe active Crohn's disease (for use only in patients who have not sufficiently responded to conventional treatments)
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PRECAUTIONS (A revised description is underlined.)

8. IMPORTANT PRECAUTIONS (newly added)

Hepatic impairment including autoimmune hepatitis may occur. Patients should be carefully monitored for their condition through such methods as periodic liver function tests.

11. ADVERSE REACTIONS

Hepatic impairment

11.1 Clinically Significant Adverse Reactions (newly added)

Hepatic impairment including autoimmune hepatitis 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 safety database
Cases involving hepatic impairment reported in Japan:
3 patients (No patient mortalities)
Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 3,832
Japanese market launch: Tremfya Subcutaneous Injection 100 mg syringe: May 2018
Tremfya Subcutaneous Injection 200 mg syringe, Tremfya Subcutaneous Injection 200 mg pen, Tremfya Intravenous Infusion 200 mg: May, 2025

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 10s	Plaque psoriasis (Atopic dermatitis)	100 mg at the initial dose, at Week 4, and every 8 weeks thereafter for 2 cycles ↓ Discontinuation	Liver disorder The patient had severe nail psoriasis.	
				Day 1 of administration Day 147 after administration (day of discontinuation)	Administration of guselkumab (genetical recombination) was started. Liver disorder developed. ALP 2071 IU/L AST 50 IU/L ALT 59 IU/L Administration of guselkumab (genetical recombination) was discontinued after the fourth dose of guselkumab (genetical recombination) on the same day.
				Day 69 after discontinuation	Liver disorder had resolved. No treatment was provided for liver disorder.
				Laboratory test value	

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5 Nivolumab (genetical recombination)

Brand name (name of company)	Opdivo I.V. Infusion 20 mg, 100 mg, 120 mg, 240 mg (Ono Pharmaceutical Co., Ltd.)
Therapeutic category	Other antitumor agents
Indications	○ Malignant melanoma ○ Unresectable advanced or recurrent non-small cell lung cancer ○ Preoperative adjuvant treatment for non-small-cell lung cancer ○ Unresectable or metastatic renal cell carcinoma ○ Relapsed or refractory classical Hodgkin lymphoma ○ Recurrent or metastatic head and neck cancer ○ Unresectable advanced or recurrent gastric cancer ○ Unresectable advanced or recurrent malignant pleural mesothelioma ○ Malignant mesothelioma (excluding malignant pleural mesothelioma) ○ Unresectable advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer ○ Unresectable advanced or recurrent esophageal cancer ○ Postoperative adjuvant therapy for esophageal cancer ○ Carcinoma of unknown primary ○ Postoperative adjuvant therapy for urothelial carcinoma ○ Unresectable urothelial carcinoma ○ Unresectable advanced or recurrent epithelial skin malignancies ○ Unresectable hepatocellular carcinoma

PRECAUTIONS (A revised description is underlined.)

11. ADVERSE REACTIONS

Vasculitis

11.1 Clinically Significant Adverse Reactions (newly added)

Large vessel vasculitis, medium vessel vasculitis, and small vessel vasculitis [including antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, IgA vasculitis, and cutaneous vasculitis] 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 safety database
Cases involving vasculitis reported in Japan:
6 patients (No patient mortalities)
Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 27,900
Japanese market launch: Opdivo I.V. Infusion 20 mg, 100 mg: September 2014
Opdivo I.V. Infusion 120 mg: November 2020
Opdivo I.V. Infusion 240 mg: November, 2018

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Male 40s	Combination therapy for unresectable advanced or recurrent non-small cell lung cancer (metastases to lymph nodes, metastases to spine, metastases to pleura)	Unknown Approximately for 10 months ↓ Discontinuation	Polyarteritis nodosa	
				Day 1 of administration	Administration of nivolumab (genetical recombination) (dose unknown), ipilimumab (genetical recombination) (dose unknown), pemetrexed sodium hydrate, and carboplatin was started as first-line treatment. After that, treatment with nivolumab (genetical recombination) and ipilimumab (genetical recombination) was continued. As a result, the patient responded well to the treatment and achieved complete remission.
				Around Month 10 of administration	Multiple necrotic ulcers were noted in the limbs. Circulatory disorder peripheral accompanied by black-colored necrosis was

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				(day of discontinuation)	noted on the left second finger, right second and third toes, and left second toe, and multiple skin ulcers and livedo reticularis were observed in the area from the anterior aspect of both lower legs to the dorsum pedis (the lower limbs were more affected compared to the upper limbs). Treatment with nivolumab (genetical recombination) and ipilimumab (genetical recombination) was discontinued. [Blood test] CRP: 2.07 mg/dL [Antibody test] Antinuclear antibody, MPO-ANCA and PR3-ANCA: All of these values were within the normal range Anticardiolipin IgG antibody: 38.2 U/mL (reference value ≤ 12.3 U/mL), Lupus anticoagulant: Increased titer Anti-beta2-GPI antibody and anti-PS/PT antibody: Both negative [Histological examination (biopsy)] Around medium blood vessels (arteries): Infiltration of many lymphocytes and neutrophils, extravasation of nuclear dusts and red blood cells, and fibrinoid degeneration of the vascular wall were observed. [CT scanning] No other organ disorder associated with vasculitis was identified. [Contrast-enhanced CT scanning] No other vascular lesion was identified. [Head MRI scanning] Changes after infarction related to thrombosis were identified (subacute to chronic infarct lesions from the right basal ganglia to corona radiata). A diagnosis of cutaneous arteritis (cutaneous polyarteritis nodosa) with potential antiphospholipid syndrome (APS) that may have been induced by nivolumab (genetical recombination) and ipilimumab (genetical recombination) was made.
				Date unknown	Administration of oral prednisolone 45 mg (1.0 mg/kg) per day was started.
				Date unknown	The area of necrosis that had developed on the fingers and toes had extended, and black-colored necrosis in the left fifth finger had progressed. Alprostadil alfadex, warfarin, and sarpogrelate hydrochloride were added in this order.
				Date unknown	Near-infrared ray irradiation on the stellate ganglion was provided concomitantly to reduce angiospasm, which gradually led to reduction and epithelization of ulcers and resolution of livedo reticularis. After that, black-colored necrosis in the peripheral portion of the limbs did not extend, and multiple ulcers were decreasing.
				Date unknown	Tapering of steroids did not lead to relapse, and the patient was discharged from the hospital.
				Date unknown	Three months after the start of prednisolone, APS was diagnosed because laboratory tests revealed an increased lupus anticoagulant level.
				Date unknown	Polyarteritis nodosa and APS were resolving. Treatment with steroids, anticoagulant, and vasodilator avoided amputation of fingers and contributed to a tendency toward improvement in pain and ulcer. After that, ulcers in the lower limbs completely epithelized and the necrotic ulcer on the fingers and toes disappeared.
			Concomitant suspect drug: Ipilimumab (genetical recombination) Concomitant drugs: Pemetrexed sodium hydrate, carboplatin		

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
2	Male 60s	Recurrent or metastatic head and neck cancer (metastases to lymph nodes, hypopharyngeal cancer, gastric cancer, esophageal cancer)	Unknown Unknown ↓ Discontinuation	Aortitis	
				Date unknown	Squamous cell carcinoma of the lower gum (stage 4a, TNM classification: cT4aN1M0) was diagnosed. After 2 cycles of preoperative chemotherapy with docetaxel, cisplatin, and fluorouracil, radical surgery containing segmental mandibulectomy and reconstructive surgery using free fibular flap and rectus abdominis muscle flap was performed.
				Day 1 of administration	Local recurrence was noted 4 months after the surgery, and administration of nivolumab (genetical recombination) (dose unknown) was thus started.
				Month 23 of administration	Chest compression was noted.

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				Date unknown	Although an electrocardiogram showed no abnormal findings, a syncopal attack occurred and the patient was urgently admitted to the hospital on the following day. Severe sinus tachycardia (200/min), pyrexia (38.6 degrees C.), and CRP increased (20.73 mg/dL) were observed. Whole-body contrast-enhanced CT scanning revealed circumferential diffuse wall thickening of the thoracic aorta in the area from the distal aortic arch to the descending aorta. Infection and other autoimmune diseases were ruled out, and eventually, acute aortitis induced by nivolumab (genetical recombination) was diagnosed.
				Date unknown	Prednisolone 50 mg (1 mg/kg) was administered, leading to prompt alleviation of chest compression and pyrexia.
				Date unknown	CT scanning showed improvement in aortic thickening.
				Date unknown (day of discontinuation)	The patient was discharged from the hospital on hospital day 61, and the dose of oral prednisolone was tapered thereafter. Nivolumab (genetical recombination) was discontinued because it involved a risk of worsening of aortitis.
				Date unknown	The dose of prednisolone was reduced to 10 mg.
				11 months after discontinuation	The patient again presented to the emergency room with chest pain and syncope. As contrast-enhanced chest CT scanning showed irregular protrusion of contrast medium and hemorrhagic pericardial effusion from the aortic arch, thoracic aortic aneurysm rupture was diagnosed. Emergency stent-graft insertion was performed, and the patient was saved with thoracic endovascular aortic repair.
				Date unknown	At 4 months after the onset of aortic rupture, metastases to cervical lymph nodes were observed. The patient refused salvage therapy, and the treatment was shifted to supportive care (BSC). The outcomes of acute aortitis and thoracic aortic aneurysm rupture were unknown.
				Concomitant drugs: None	

6 Nivolumab (genetical recombination)

Brand name (name of company)	Opdivo I.V. Infusion 20 mg, 100 mg, 120 mg, 240 mg (Ono Pharmaceutical Co., Ltd.)
Therapeutic category	Other antitumor agents
Indications	○ Malignant melanoma ○ Unresectable advanced or recurrent non-small cell lung cancer ○ Preoperative adjuvant treatment for non-small-cell lung cancer ○ Unresectable or metastatic renal cell carcinoma ○ Relapsed or refractory classical Hodgkin lymphoma ○ Recurrent or metastatic head and neck cancer ○ Unresectable advanced or recurrent gastric cancer ○ Unresectable advanced or recurrent malignant pleural mesothelioma ○ Malignant mesothelioma (excluding malignant pleural mesothelioma) ○ Unresectable advanced or recurrent microsatellite instability-high (MSI-High) colorectal cancer ○ Unresectable advanced or recurrent esophageal cancer ○ Postoperative adjuvant therapy for esophageal cancer ○ Carcinoma of unknown primary ○ Postoperative adjuvant therapy for urothelial carcinoma ○ Unresectable urothelial carcinoma ○ Unresectable advanced or recurrent epithelial skin malignancies ○ Unresectable hepatocellular carcinoma

PRECAUTIONS (A revised description is underlined.)

11. ADVERSE REACTIONS

Thrombotic microangiopathy

11.1 Clinically Significant Adverse Reactions (newly added)

Thrombotic microangiopathy including thrombotic thrombocytopenic purpura may occur. If anaemia accompanied by schizocytes, thrombocytopenia, renal impairment, etc. are observed, appropriate measures should be taken.

Reference information

Number of cases (for which a causal relationship between the drug and the event is reasonably possible) collected in the PMDA's safety database
Cases involving thrombotic microangiopathy reported in Japan:
4 patients (No patient mortalities)
Number of patients using the drug as estimated by the MAH during the previous 1-year period: approximately 27,900
Japanese market launch: Opdivo I.V. Infusion 20 mg, 100 mg: September 2014
Opdivo I.V. Infusion 120 mg: November 2020
Opdivo I.V. Infusion 240 mg: November, 2018

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Male 70s	Unresectable advanced or recurrent gastric cancer that has progressed after cancer chemotherapy (none)	240 mg every 2 weeks for 15 cycles ↓ Discontinuation	Thrombotic thrombocytopenic purpura Medical history: Middle thoracic esophageal cancer	
				8 months before administration	Medical checkup led to a diagnosis of advanced gastric tube cancer (reconstructed gastric tube, poorly differentiated adenocarcinoma, HER2-negative, PD-L1 composite positive score: 0).
				Day 1 of administration	Administration of nivolumab (genetical recombination) (240 mg) was started.
				Date unknown	The 15th dose of nivolumab (genetical recombination) was administered. No adverse events or progression of cancer was identified.
				Date unknown (day of discontinuation)	A blood test on the scheduled day of the 16th dose of nivolumab (genetical recombination) showed platelet count decreased (30,000/mcL). Fatigue, oral mucosa bleeding, and purpura on the extremities were noted. Administration of nivolumab (genetical recombination) was discontinued.
				6 days after discontinuation	A blood test showed a decrease in platelet count. Furthermore, findings suggestive of haemolytic anaemia were identified, including red blood cell count decreased, haptoglobin decreased, an increase in reticulocyte rate, indirect bilirubin increased, and lactate dehydrogenase increased. Pyrexia and malaise were noted, and platelets decreased was aggravated. Thus, the patient was admitted to the hospital for detailed examination and treatment. PLASMIC score of thrombotic thrombocytopenic purpura (TTP) based on the blood test data on admission indicated intermediate risk (5 out of 7 points). A peripheral blood picture showed haemolytic anaemia accompanied by the appearance of schistocytes, and bone marrow examination showed normocellular marrow without megakaryocytes increased. [Blood test] Ht: 24.5%, Hb: 7.9 g/dL, MCV: 90.4 fL, PLT: 10,000/mcL, RET: 9.6%, schistocytes: 3.2%, PT-INR: 1.07, T-Bil: 2.7 mg/dL, D-Bil: 0.3 mg/dL, LDH: 646 U/L, Cr: 10.5 mg/dL, Hp: 1.9 mg/dL, ADAMTS13 activity: < 0.01 IU/mL [Antibody test] ADAMTS13 inhibitor: 2.7 BU/mL
				7 days after discontinuation	Because TTP was strongly suspected based on the clinical features, ADAMTS13 activity test was performed, and administration of prednisolone 50 mg/day was started as a treatment for TTP.
				8 days after discontinuation	Administration of prednisolone was completed. As a result of consultation with the department of hematology, steroid pulse therapy (methylprednisolone 1,000 mg/day for 3 days) was performed.
				10 days after discontinuation	On the day of completion of steroid pulse therapy, plasma exchange therapy was performed. Steroid pulse therapy was

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					switched to administration of prednisolone 50 mg/day, and the dose was tapered by 10 mg/day every week.
				13 days after discontinuation	The patient responded well to steroids and plasma exchange, and platelet count improved to 230,000/mcL. Based on the result of ADAMTS13 test on hospital admission, acquired thrombotic thrombocytopenic purpura (aTTP) was diagnosed.
				14 days after discontinuation	Plasma exchange therapy was performed.
				24 days after discontinuation	Platelet count decreased (95,000/mcL) and ADAMTS13 activity decreased relapsed. Since exacerbation of aTTP was suspected, the dose of prednisolone was increased from 30 mg/day to 40 mg/day, and administration of fresh frozen plasma was started.
				27 days after discontinuation	ADAMTS13 activity was 0.21 IU/mL. Administration of rituximab was started at the department of hematology.
				31 days after discontinuation	Platelet count had recovered.
				32 days after discontinuation	Rituximab (the second dose) was administered.
				34 days after discontinuation	The dose of prednisolone was reduced to 30 mg/day. After these treatments, platelets decreased did not occur, and no decrease in ADAMTS13 activity was observed.
				37 days after discontinuation	Platelet count did not decrease in the subsequent course, and the patient was discharged from the hospital. On discharge, improvements in creatinine (0.6 to 0.7 mg/dL) and haemoglobin (10 to 11 g/dL) were noted, and TTP had resolved.
				135 days after discontinuation	The dose of prednisolone was reduced to 5 mg/day.
				198 days after discontinuation	Supportive care (BSC) was continued without readministration of nivolumab (genetical recombination). No relapse of TTP was observed.
				Concomitant suspect drugs: None Concomitant drugs: Levothyroxine sodium hydrate, celecoxib, pregabalin, vonoprazan fumarate	

4.

Revisions of PRECAUTIONS (No. 371)

This section provides details of the revisions to the PRECAUTIONS and brand names of drugs that were subject to the revisions in accordance with the Notifications dated June 30 and July 14, 2026.

1 Antibiotic preparations acting mainly on gram-positive and gram-negative bacteria **Cefcapene pivoxil hydrochloride hydrate (for pediatric use)**

Brand name Flomox Fine Granules for Pediatric 100 mg (Shionogi & Co., Ltd.), and the others
8. IMPORTANT PRECAUTIONS (newly added) < Children >

In children (especially infants), serious hypoglycaemia, convulsions, encephalopathy, etc. associated with hypocarnitinaemia may occur after administration of antibacterials with a pivoxil group including this drug (cefcapene pivoxil hydrochloride hydrate, cefditoren pivoxil, ceftaram pivoxil, tebipenem pivoxil). When selecting drugs, including a process of considering the necessity of this drug, and determining treatment duration, refer to the latest guidelines, etc. Patients' families, etc. should be instructed to immediately seek medical attention if any hypoglycemic symptoms such as convulsions and consciousness disturbed are observed.

2 Antibiotic preparations acting mainly on gram-positive and gram-negative bacteria **Cefditoren pivoxil (for pediatric use)**

Brand name Meiact MS Fine Granules 10% for Pediatric (Meiji Seika Pharma Co., Ltd.), and the others
8. IMPORTANT PRECAUTIONS (newly added) < Children >

In children (especially infants), serious hypoglycaemia, convulsions, encephalopathy, etc. associated with hypocarnitinaemia may occur after administration of antibacterials with a pivoxil group including this drug (cefditoren pivoxil, cefcapene pivoxil hydrochloride hydrate, ceftaram pivoxil, tebipenem pivoxil). When selecting drugs, including a process of considering the necessity of this drug, and determining treatment duration, refer to the latest guidelines, etc. Patients' families, etc. should be instructed to immediately seek medical attention if any hypoglycemic symptoms such as convulsions and consciousness disturbed are observed.

3 Antibiotic preparations acting mainly on gram-positive and gram-negative bacteria **Ceftaram pivoxil (for pediatric use)**

Brand name Tomiron Fine granules 20% for pediatric (FUJIFILM Toyama Chemical Co., Ltd.)
8. IMPORTANT PRECAUTIONS (newly added) < Children >

In children (especially infants), serious hypoglycaemia, convulsions, encephalopathy, etc. associated with hypocarnitinaemia may occur after administration of antibacterials with a pivoxil group including this drug (ceftaram pivoxil, cefditoren pivoxil, cefcapene pivoxil hydrochloride hydrate, tebipenem pivoxil). When selecting drugs, including a process of considering the necessity of this drug, and determining treatment duration, refer to the latest guidelines, etc. Patients' families, etc. should be instructed to immediately seek medical attention if any

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hypoglycemic symptoms such as convulsions and consciousness disturbed are observed.

4 Antibiotic preparations acting mainly on gram-positive and gram-negative bacteria

Tebipenem pivoxil

Brand name

Orapenem Fine Granules 10% For Pediatric (Meiji Seika Pharma Co., Ltd.)

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

In children (especially infants), serious hypoglycaemia, convulsions, encephalopathy, etc. associated with hypocarnitinaemia may occur after administration of antibacterials with a pivoxil group including this drug (tebipenem pivoxil, cefditoren pivoxil, cefcapene pivoxil hydrochloride hydrate, cefteram pivoxil). When selecting drugs, including a process of considering the necessity of this drug, and determining treatment duration, refer to the latest guidelines, etc. Patients' families, etc. should be instructed to immediately seek medical attention if any hypoglycemic symptoms such as convulsions and consciousness disturbed are observed.

5 Agents for peptic ulcer

[1] Esomeprazole magnesium hydrate

[2] Omeprazole

[3] Vonoprazan fumarate

[4] Rabeprazole sodium

[5] Lansoprazole (oral dosage form)

Brand name

- [1] Nexium Capsules 10 mg, 20 mg, Nexium Granules for Suspension 10 mg, 20 mg, and the others (AstraZeneca K.K., and the others)
- [2] Omepral Tablets 10, 20, and the others (TAIYO Pharma Co., Ltd., and the others), Omeprazon Tablets 10 mg, 20 mg, and the others (Tanabe Pharma Corporation, and the others)
- [3] Takecab OD Tablets 10 mg, 20 mg, Takecab Tablets 10 mg, 20 mg (Takeda Pharmaceutical Company Limited)
- [4] Pariet tablets 5 mg, 10 mg, 20 mg, and the others (Eisai Co., Ltd., and the others)
- [5] Takepron OD Tablets 15, 30, Takepron capsules 15, 30, and the others (T's Seiyaku Co., Ltd., and the others)

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

Prolonged use of this drug may cause hypomagnesaemia. Blood magnesium levels should be periodically measured when long-term treatment with this drug is deemed necessary.

**11. ADVERSE
REACTIONS**

Hypomagnesaemia

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

Prolonged use of this drug may cause hypomagnesaemia accompanied by symptoms such as prolonged QT, convulsion, and numbness. Electrolyte abnormalities such as hypocalcaemia and hypokalaemia caused by hypomagnesaemia may also occur. If any symptoms suggestive of these electrolyte abnormalities occur, blood magnesium levels should be measured. If any abnormality is observed, appropriate measures should be taken such as magnesium replacement.

6 Agents for peptic ulcer

[1] Omeprazole sodium

[2] Lansoprazole (injection)

Brand name

- [1] Omeprazole for Injection 20 mg "Nichi-iko" (Nichi-Iko Pharmaceutical Co., Ltd.), Omeprazole for Injection 20 mg "NP" (NIPRO CORPORATION), Omeprazole for Injection 20 mg "TYK" (T's Seiyaku Co., Ltd.)
- [2] Takepron Intravenous 30 mg, and the others (T's Seiyaku Co., Ltd., and the others)

8. IMPORTANT PRECAUTIONS (newly added)
11. ADVERSE REACTIONS
11.1 Clinically Significant Adverse Reactions (newly added)

Prolonged use of proton pump inhibitors may cause hypomagnesaemia. Blood magnesium levels should be periodically measured when long-term treatment with proton pump inhibitors is deemed necessary.

Hypomagnesaemia

Prolonged use of proton pump inhibitors may cause hypomagnesaemia accompanied by symptoms such as prolonged QT, convulsion, and numbness. Electrolyte abnormalities such as hypocalcaemia and hypokalaemia caused by hypomagnesaemia may also occur. If any symptoms suggestive of these electrolyte abnormalities occur, blood magnesium levels should be measured. If any abnormality is observed, appropriate measures should be taken such as magnesium replacement.

7 Other hormone preparations

Insulin aspart (genetical recombination) (Fiasp Injection 100 U/mL)

Brand name

Fiasp Injection 100 U/mL (Novo Nordisk Pharma Ltd.)

8. IMPORTANT PRECAUTIONS (newly added)

Gelling of this drug may occur when exposed to high temperatures exceeding 37 degrees C. Use of a portable insulin pump at high temperature may cause gelling of insulin to cause occlusion in the insulin pump, which may prevent the pump from appropriately delivering this drug and consequently serious hyperglycaemia, diabetic ketoacidosis, etc. may occur. Patients should be instructed as follows:

- Avoid use of a portable insulin pump in an environment of high temperature exceeding 37 degrees C.
- Check the inside of the insulin pump, and if there is any change in the appearance of the injection solution, do not use it.

8 Other agents relating to blood and body fluids

Aspirin/vonoprazan fumarate

Brand name

Cabpirin Combination Tablets (Takeda Pharmaceutical Company Limited)

8. IMPORTANT PRECAUTIONS (newly added)

Prolonged use of vonoprazan may cause hypomagnesaemia. Blood magnesium levels should be periodically measured when long-term treatment with this drug is deemed necessary.

11. ADVERSE REACTIONS

Hypomagnesaemia

11.1 Clinically Significant Adverse Reactions (newly added)

Prolonged use of vonoprazan may cause hypomagnesaemia accompanied by symptoms such as prolonged QT, convulsion, and numbness. Electrolyte abnormalities such as hypocalcaemia and hypokalaemia caused by hypomagnesaemia may also occur. If any symptoms suggestive of these electrolyte abnormalities occur, blood magnesium levels should be measured. If any abnormality is observed, appropriate measures should be taken such as magnesium replacement.

9 Other agents relating to blood and body fluids

Aspirin/lansoprazole

Brand name

Takelda Combination Tablets (T's Seiyaku Co., Ltd.)

8. IMPORTANT PRECAUTIONS (newly added)

Prolonged use of lansoprazole may cause hypomagnesaemia. Blood magnesium levels should be periodically measured when long-term treatment with this drug is deemed necessary.

11. ADVERSE REACTIONS

Hypomagnesaemia

11.1 Clinically Significant Adverse Reactions (newly added)

Prolonged use of lansoprazole may cause hypomagnesaemia accompanied by symptoms such as prolonged QT, convulsion, and numbness. Electrolyte abnormalities such as hypocalcaemia and hypokalaemia caused by hypomagnesaemia may also occur. If any symptoms suggestive of these electrolyte abnormalities occur, blood magnesium levels should be measured. If any abnormality is observed, appropriate measures should be taken such as magnesium replacement.

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

Guselkumab (genetical recombination)

Brand name	Tremfya Subcutaneous Injection 100 mg syringe, 200 mg syringe, Tremfya Subcutaneous Injection 200 mg pen, Tremfya Intravenous Infusion 200 mg (Janssen Pharmaceutical K.K.)
8. IMPORTANT PRECAUTIONS (newly added)	<u>Hepatic impairment including autoimmune hepatitis may occur. Patients should be carefully monitored for their condition through such methods as periodic liver function tests.</u>
11. ADVERSE REACTIONS	<u>Hepatic impairment</u>
11.1 Clinically Significant Adverse Reactions (newly added)	<u>Hepatic impairment including autoimmune hepatitis may occur.</u>

11 Antitumor antibiotics and preparations

Doxorubicin hydrochloride (liposome formulations)

Brand name	Doxil Injection 20 mg (Baxter Japan K.K.)
8. IMPORTANT PRECAUTIONS (newly added)	<u>Renal-limited thrombotic microangiopathy may occur. Patients should be carefully monitored through such methods as periodic blood tests, renal function tests, and urine tests.</u>
11. ADVERSE REACTIONS	<u>Renal-limited thrombotic microangiopathy</u>
11.1 Clinically Significant Adverse Reactions (newly added)	

12 Other antitumor agents

- [1] Atezolizumab (genetical recombination)
- [2] Avelumab (genetical recombination)
- [3] Ipilimumab (genetical recombination)
- [4] Cemiplimab (genetical recombination)
- [5] Tislelizumab (genetical recombination)
- [6] Durvalumab (genetical recombination)
- [7] Tremelimumab (genetical recombination)
- [8] Nivolumab (genetical recombination)
- [9] Retifanlimab (genetical recombination)

Brand name	[1] Tecentriq for Intravenous Infusion 840 mg, 1200 mg (Chugai Pharmaceutical Co., Ltd.) [2] Bavencio intravenous infusion 200 mg (Merck Biopharma Co., Ltd) [3] Yervoy Injection 20 mg, 50 mg (Bristol-Myers Squibb K.K.) [4] Libtayo I.V. Infusion 350 mg (Regeneron Japan KK) [5] Tevimbra I.V. Infusion 100 mg (BeOne Medicines Japan) [6] Imfinzi Injection 120 mg, 500 mg (AstraZeneca K.K.) [7] Imjudo Injection 25mg, 300mg (AstraZeneca K.K.) [8] Opdivo I.V. Infusion 20 mg, 100 mg, 120 mg, 240 mg (Ono Pharmaceutical Co., Ltd.) [9] Zynyz for Intravenous Infusion 500 mg (Incyte Biosciences Japan G.K.)
11. ADVERSE REACTIONS	<u>Vasculitis</u>
11.1 Clinically Significant Adverse Reactions (newly added)	<u>Large vessel vasculitis, medium vessel vasculitis, and small vessel vasculitis [including antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, IgA vasculitis, and cutaneous vasculitis] may occur.</u>

13 Other antitumor agents**Ixazomib citrate**

Brand name	[1] Ninlaro capsules 0.5 mg, [2] 2.3 mg, [3] 3 mg, [4] 4 mg (Takeda Pharmaceutical Company Limited)
11. ADVERSE REACTIONS	<u>Thrombotic microangiopathy</u>
11.1 Clinically Significant Adverse Reactions (newly added)	<u>Thrombotic microangiopathy including thrombotic thrombocytopenic purpura and haemolytic uraemic syndrome may occur. If anaemia accompanied by schizocytes, thrombocytopenia, renal impairment, etc. are observed, appropriate measures should be taken.</u>

14 Other antitumor agents**Carboplatin**

Brand name	Paraplatin injection 50 mg, 150 mg, 450 mg (CHEPLAPHARM K.K.) and the others
11. ADVERSE REACTIONS	<u>Syndrome of inappropriate antidiuretic hormone secretion (SIADH)</u>
11.1 Clinically Significant Adverse Reactions (newly added)	

15 Other antitumor agents**Nivolumab (genetical recombination)**

Brand name	Opdivo I.V. Infusion 20 mg, 100 mg, 120 mg, 240 mg (Ono Pharmaceutical Co., Ltd.)
11. ADVERSE REACTIONS	<u>Thrombotic microangiopathy</u>
11.1 Clinically Significant Adverse Reactions (newly added)	<u>Thrombotic microangiopathy including thrombotic thrombocytopenic purpura may occur. If anaemia accompanied by schizocytes, thrombocytopenia, renal impairment, etc. are observed, appropriate measures should be taken.</u>

16 Other antibiotic preparations**[1] Vonoprazan fumarate/amoxicillin hydrate/clarithromycin****[2] Vonoprazan fumarate/amoxicillin hydrate/metronidazole**

Brand name	[1] Vonosap Pack 400, 800 (Takeda Pharmaceutical Company Limited) [2] Vonopion Pack (Takeda Pharmaceutical Company Limited)
8. IMPORTANT PRECAUTIONS (newly added)	(Vonoprazan fumarate) <u>Prolonged use of proton pump inhibitors may cause hypomagnesaemia. Blood magnesium levels should be periodically measured when long-term treatment with proton pump inhibitors is deemed necessary.</u>
11. ADVERSE REACTIONS	(Vonoprazan fumarate) <u>Hypomagnesaemia</u>
11.1 Clinically Significant Adverse Reactions (newly added)	<u>Prolonged use of proton pump inhibitors may cause hypomagnesaemia accompanied by symptoms such as prolonged QT, convulsion, and numbness. Electrolyte abnormalities such as hypocalcaemia and hypokalaemia caused by hypomagnesaemia may also occur. If any symptoms suggestive of these electrolyte abnormalities occur, blood magnesium levels should be measured. If any abnormality is observed, appropriate measures should be taken such as magnesium replacement.</u>

17 Vaccines**Recombinant RS virus vaccine**

Brand name	[1] Abrysvo intramuscular injection (Pfizer Japan Inc.) [2] Arexvy Intramuscular Injection (GlaxoSmithKline K.K.)
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11. ADVERSE REACTIONS
11.1 Clinically Significant Adverse Reactions (newly added)

Guillain-Barre syndrome
Symptoms such as flaccid paralysis starting from the distal limbs and decreased or absent tendon reflexes may occur.

18 Other biological preparations

Anti-human thymocyte immunoglobulin, rabbit

Brand name Thymoglobuline I.V. Infusion (Sanofi K.K.)

11. ADVERSE REACTIONS Thrombotic microangiopathy

11.1 Clinically Significant Adverse Reactions (newly added) Anaemia accompanied by schizocytes, thrombocytopenia, renal impairment, etc. may occur.

19 Gastrointestinal medicine

Preparations containing omeprazole (guidance-mandatory drugs)

Brand name Omepral S (Sato Pharmaceutical Co., Ltd.)

CONSULTATION

If the following symptoms are observed after taking this drug, they may be adverse reactions, so immediately discontinue the use of this drug, and show this document to your physician, pharmacist, or registered salesperson for a consultation.

Relevant region	Symptoms
Neuropsychiatric system	Headache, drowsiness, abnormal sensations such as numbness, dizziness, trembling, insomnia, depression
Others	Blurred vision, fever, swelling, gynecomastia (male breasts becoming enlarged like a female's), hair loss, general fatigue, joint pain, abnormal taste, menstrual irregularities, muscle pain, sweating, muscle weakness

(newly added)

The following serious symptoms may occur in rare cases. In such cases, immediately seek medical aid:

Name of symptom	Symptoms
<u>Hypomagnesaemia</u>	<u>Symptoms such as nausea, vomiting, loss of appetite, feeling of weariness, muscle twitching in the face and limbs, temporary drowsiness, decreased consciousness, stiffening of the limbs and trembling, numbness, dizziness, palpitations, loss of consciousness may occur.</u>

20 Gastrointestinal medicine

Preparations containing rabeprazole sodium (guidance-mandatory drugs)

Brand name Pariet S (Eisai Co., Ltd.)

CONSULTATION

If the following symptoms are observed after taking this drug, they may be adverse reactions, so immediately discontinue the use of this drug, and show this document to your physician or pharmacist for a consultation.

Relevant region	Symptoms
Neuropsychiatric system	Headache, dizziness, light-headedness, sleepiness, weakness of limbs, hypoesthesia (reduced sensation), grip strength decreased, slurred speech, disorientation (being confused)

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	about the place, time, name, etc.), delirium (mild clouding of consciousness with illusion or hallucinations), coma (complete loss of consciousness)
Others	Anemia, blurred/flickering vision, edema, malaise, fever, alopecia, numbness, arthralgia, myalgia, gynecomastia

(newly added)

The following serious symptoms may occur in rare cases. In such cases, immediately seek medical aid:

Name of symptom	Symptoms
<u>Hypomagnesaemia</u>	<u>Symptoms such as nausea, vomiting, loss of appetite, feeling of weariness, muscle twitching in the face and limbs, temporary drowsiness, decreased consciousness, stiffening of the limbs and trembling, numbness, dizziness, palpitations, loss of consciousness may occur.</u>

21 Gastrointestinal medicine

Preparations containing lansoprazole (guidance-mandatory drugs)

Brand name

CONSULTATION

Takepron s (Alinamin Pharmaceutical Co., Ltd.)

If the following symptoms are observed after taking this drug, they may be adverse reactions, so immediately discontinue the use of this drug, and show this document to your physician or pharmacist for a consultation.

Relevant region	Symptoms
Neuropsychiatric system	Headache, depressed state, sleeplessness, dizziness, sleepiness, tremor, convulsion, decreased consciousness
Others	Pyrexia, gynecomastia, oedema, listlessness, numbness of tongue and lips, numbness of limbs, myalgia, alopecia, weakness, arthralgia, blurred vision

(newly added)

(Deleted)

The following serious symptoms may occur in rare cases. In such cases, immediately seek medical aid:

Name of symptom	Symptoms
<u>Hypomagnesaemia</u>	<u>Symptoms such as nausea, vomiting, loss of appetite, feeling of weariness, muscle twitching in the face and limbs, temporary drowsiness, decreased consciousness, stiffening of the limbs and trembling, numbness, dizziness, palpitations, loss of consciousness may occur.</u>

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 June 30, 2026)

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

Nonproprietary name		Name of the MAH	Date of EPPV initiation
Brand name			
◎	Tafasitamab (genetical recombination) * ¹	Incyte Biosciences Japan G.K.	June 19, 2026
	Minjuvi for intravenous infusion 200 mg		
◎	Ivosidenib * ²	NIHON SERVIER CO., LTD	June 19, 2026
	Tibsovo Tablets 250 mg		
◎	Incobotulinumtoxin A * ³	Teijin Pharma Limited	June 19, 2026
	Xeomin 50 units for injection, 100 units, 200 units		
◎	Lomitapide mesilate	Recordati Rare Diseases Japan K.K.	June 19, 2026
	Juxtapid Capsules 5 mg, 10 mg, 20 mg		
◎	Semaglutide (genetical recombination) * ⁴	Novo Nordisk Pharma Ltd.	June 19, 2026
	Wegovy Subcutaneous Injection 0.25 mg SD, 0.5 mg SD, 1.0 mg SD, 1.7 mg SD, 2.4 mg SD, Wegovy Subcutaneous Injection 0.25 mg pen 1.0 MD, 0.5 mg pen 2.0 MD, 1.0 mg pen 4.0 MD, 1.7 mg pen 6.8 MD, 2.4 mg pen 9.6 MD		
◎	Fedratinib hydrochloride hydrate	Recordati Rare Diseases Japan K.K.	June 1, 2026
	Inrebic capsules 100 mg		
	Gadoquatrane hydrate	Bayer Yakuhin, Ltd.	May 26, 2026
	Ambelvist iv injection 2 mL, Ambelvist iv injection syringes 5 mL, 7.5 mL, 10 mL		
	Triheptanoin	Ultragenyx Japan K.K.	May 21, 2026
	Dojolvi oral liquid 100%		
	Tirzepatide * ⁵	Eli Lilly Japan K.K.	May 18, 2026
	Zepbound Subcutaneous Injection 2.5 mg Ateos, 5 mg Ateos, 7.5 mg Ateos, 10 mg Ateos, 12.5 mg Ateos, 15 mg Ateos		
	Benralizumab (genetical recombination) * ⁶	AstraZeneca K.K.	May 18, 2026
	Fasenra Subcutaneous Injection 30 mg Syringe, Fasenra Subcutaneous Iniection 30 mg Pen		

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Nonproprietary name		Name of the MAH	Date of EPPV initiation
Brand name			
	Deucravacitinib ^{*7} ----- Sotyktu tablets 6 mg	Bristol-Myers Squibb K.K.	May 18, 2026
	Oxymetazoline hydrochloride ^{*8} ----- Upneeq Mini ophthalmic solution 0.1%	Santen Pharmaceutical Co., Ltd.	May 15, 2026
	Freeze-dried live attenuated measles and rubella combined vaccine ----- MearubikII 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
	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 1.1g/mL	OrphanPacific, Inc.	April 15, 2026
	Motugivatrep ----- Avarept Ophthalmic Suspension 0.3%	Senju Pharmaceutical Co.,Ltd.	April 6, 2026
	Vorasidenib citric acid hydrate ----- Vorango Tablets 10 mg, 40 mg	NIHON SERVIER CO., LTD	March 30, 2026
	Luseogliflozin hydrate ----- Lusefi OD film 2.5mg, Lusefi tablets 2.5mg, 5 mg	Taisho Pharmaceutical Co., Ltd.	March 23, 2026
	Linzagolix choline ----- Ysely Tablets 100mg	KISSEI PHARMACEUTICAL CO., LTD.	March 19, 2026
	Zuranolone ----- Zurzuvae Capsules 30mg	Shionogi & Co., Ltd.	March 19, 2026
	Sebetralstat ----- Ekterly Tablets 300mg	KalVista Pharmaceuticals Ltd.	March 18, 2026

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Nonproprietary name		Name of the MAH	Date of EPPV initiation
Brand name			
	Tafasitamab (genetical recombination)	Incyte Biosciences Japan G.K.	March 18, 2026
	Minjuvi for intravenous infusion 200 mg		
	Tagraxofusp (genetical recombination)	Nippon Shinyaku Co., Ltd.	March 18, 2026
	Elzonris I.V. Injection 1000 µg		
	Retifanlimab (genetical recombination)	Incyte Biosciences Japan G.K.	March 18, 2026
	Zynyz for Intravenous Infusion 500mg		
	Sepiapterin	PTC Therapeutics K.K.	March 18, 2026
	Sephience Granules 250 mg, 1000 mg		
	Amivantamab (genetical recombination)/vorhyaluronidase alfa (genetical recombination)	Janssen Pharmaceutical K.K.	March 18, 2026
	Rybrofaz Combination Subcutaneous Injection		
	Mosunetuzumab (genetical recombination)	Chugai Pharmaceutical Co., Ltd.	March 18, 2026
	Lunsumio for Subcutaneous Injection 5 mg, 45 mg		
	Belantamab mafodotin (genetical recombination)	GlaxoSmithKline K.K.	March 18, 2026
	Blenrep for I.V. infusion 100 mg		
	Vonicog alfa (genetical recombination)	Takeda Pharmaceutical Company Limited	February 19, 2026
	Vonvendi Intravenous 1300		
	Tezepelumab (genetical recombination) * ⁹	AstraZeneca K.K.	February 19, 2026
	Tezspire Subcutaneous Injection 210mg Syringe, Tezspire Subcutaneous Injection 210mg Pen		
	Adrenaline	Alfresa Pharma Corporation	February 12, 2026
	neffy nasal spray 1mg, 2mg		
	Cantharidin	Torii Pharmaceutical CO., LTD.	February 9, 2026
	Ycath topical solution 0.71%		

*1 Relapsed or refractory diffuse large B-cell lymphoma

*2 Unresectable biliary tract cancer with IDH1 gene mutation positive exacerbated after cancer chemotherapy

*3 Cervical dystonia and blepharospasm

*4 Metabolic dysfunction-associated steatohepatitis without hepatic cirrhosis (only for patients with moderate-severe fibrosis)

*5 Moderate or more severe obstructive sleep apnoea syndrome, for only patients with BMI of ≥ 27 kg/m²

*6 Eosinophilia

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

*8 Acquired blepharoptosis

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

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