Pharmaceuticals and Medical Devices Safety Information

No. 423 October 2025

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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 here

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Pharmaceuticals and Medical Devices Safety Information

No. 423 October 2025

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

[Outline of Information]

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

Abbreviations

BRAF	B-Raf proto-oncogene, serine/threonine kinase
CT	Computed Tomography
DIDPC	Department of Infectious Disease Prevention and Control
DLST	Drug-induced lymphocyte stimulation test
ICU	Intensive Care Unit
MAH	Marketing Authorization Holder
MHLW	Ministry of Health, Labour and Welfare
MPO-ANCA	Myeloperoxidase anti-neutrophil cytoplasmic antibody
TNM classification	tumor, node, metastasis classification
PD-L1	Programmed death-ligand 1
PMDA	Pharmaceuticals and Medical Devices Agency
PS	Performance Status
PSB	Pharmaceutical Safety Bureau

1

Suspected Adverse Reactions to Influenza Vaccines in the 2024 Season

1. Introduction

This section describes the status of instances of suspected adverse reactions to influenza vaccines [Note1)] reported from October 1, 2024 through March 31, 2025 (hereinafter referred to as the "2024 season").

Medical institutions are required to report to the MHLW when they encounter symptoms from influenza vaccines [Note1)] that they decide to meet the Suspected Adverse Reaction Reporting Criteria regardless of causality. Reports by medical institutions, together with those by the marketing authorization holders (MAHs), are compiled and evaluated by the PMDA. For serious cases, including fatal cases, the PMDA performs causality assessment and/or considers the necessity of safety measures in consultation with experts.

Joint meetings of the Side Effect Subcommittee of the Immunization and Vaccine Section Meeting in the Health Science Council and the Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs Council (hereinafter referred to as the "Joint Meeting") are convened periodically for the purpose of investigating and reviewing these reports of suspected adverse reactions to influenza vaccines and to discuss the necessity of safety measures[1)2)].

Note 1) Including intranasal live attenuated influenza vaccine

2. Reports of suspected adverse reactions to influenza vaccines (2024 season)

(1) Numbers and frequencies of suspected adverse reactions reported

Table 1 shows the numbers of reported suspected adverse reactions to the influenza vaccines and frequencies calculated from the estimated numbers of vaccinated persons based on the number of vaccines distributed to medical institutions.

Table 1 Numbers of suspected adverse reactions reported and estimated number of vaccinated persons

	Reports by MAHs (serious reports) *		Reports by medical institutions**		
Estimated number of vaccinated persons (number of vaccinations)	Number of serious cases reported (frequency)	Number of patient mortalities reported	Number of reports (frequency)	Number of serious cases reported (frequency)	Number of patient mortalities reported
45,474,335 (as of March 31, 2025)	33 (0.00073%)	3 (0.0000066%)	88 (0.00019%)	49 (0.00011%)	7 (0.0000154%)

* Reports by the MAHs were on cases determined to be "serious" under Article 68-10, Paragraph 1 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (PMD Act). Reports by the MAHs may duplicate some cases reported by medical institutions, and such duplicated cases are included in the number for reports by medical institutions.

** Reports by medical institutions were submitted under Article 12, Paragraph 1 of the Preventive Vaccination Law (PV Law) or Article 68-10, Paragraph 2 of the PMD Act.

(2) Reports of suspected adverse reactions by sex and age group

The numbers of reported suspected adverse reactions to influenza vaccines are shown by sex and age group in Table 2 and Table 3, respectively.

Table 2 Number of reports by sex

Sex	Number of Reports by MAHs (serious cases)	Number of Reports by medical institutions
Male	17	46
Female	16	42
Unknown	0	0
Total	33	88

Table 3 Number of reports by age group

Age group	Number of Reports by MAHs		Number of Reports by medical institutions		
	Number of serious cases reported		Number of reports	Number of serious cases reported	
		Number of patient mortalities reported			Number of patient mortalities reported
0-9	6	0	31	18	0
10-19	1	0	5	2	0
20-29	1	0	6	4	0
30-39	3	0	1	0	0
40-49	1	0	3	0	0
50-59	0	0	6	5	1
60-69	3	0	6	3	0
70-79	12	3	16	9	2
80 or older	4	0	12	8	4
Unknown	2	0	0	0	0
Total	33	3	88	49	7

(3) Details of reported symptoms

Suspected adverse reactions to influenza vaccines reported during the 2024 season are outlined by System Organ Class (SOC) in the right-hand side columns of Table 4. There was no increase in the number or frequency of reports compared to the details of the reports from October 1, 2023 to September 30, 2024 (hereinafter referred to as the "2023 season").

Furthermore, a total of 10 cases of post-vaccination deaths were reported for this season. The assessment by experts determined that the causality between the vaccination and death could not be assessed due to lack of information for these cases.

A total of 5 cases Note 2) of possible Guillain-Barré syndrome or acute disseminated encephalomyelitis (ADEM) were reported for this season. The assessment by experts determined that there was no cases for which a causal relationship between the respective diseases and vaccination was reasonably possible.

A total of 8 cases Note 3) were reported as possible anaphylaxis. Experts concluded that 4 cases (including 4 serious cases) were assessed as Level 3 or higher anaphylaxis using the Brighton Criteria. Regarding the number of reports from the MAHs by manufacturing lot, no distinct increases in the number of cases reported as possible anaphylaxis were attributed to any of the

specific lots.

At the Joint Meeting held in July 2025, it was concluded that there were no significant concerns regarding the safety of the reviewed vaccines based on the information including adverse reaction reports reported so far, including other reported symptoms than anaphylaxis, with no safety measures such as revision of package inserts required at present, but reporting of suspected adverse reactions and their details should be carefully monitored.

Note 2) Cases reported with the symptom name “Guillain-Barré syndrome” or “acute disseminated encephalomyelitis”
Note 3) Cases reported with the symptom name “anaphylaxis,” “anaphylactic reaction,” “anaphylactic shock,” “anaphylactoid reaction,” or “anaphylactoid shock”

Table 4 Comparison of the number of suspected adverse reaction reports between the 2023 and 2024 seasons (by SOC)

	2023 season *		2024 season **	
SOC of symptom	Reports by MAHs (serious cases)	Reports by medical institutions (serious cases)	Reports by MAHs (serious cases)	Reports by medical institutions (serious cases)
Gastrointestinal disorders	1	5	4	2
General disorders and administration site conditions	9	19	12	14
Infections and infestations	2	8	7	11
Haepatobiliary disorders	1	1	1	1
Eye disorders	1	6	0	0
Musculoskeletal and connective tissue disorders	7	2	4	5
Blood and lymphatic system disorders	1	5	1	1
Vascular disorders	1	4	1	2
Surgical and medical procedures	0	0	1	0
Respiratory, thoracic and mediastinal disorders	2	9	1	0
Injury, poisoning and procedural complications	1	0	0	2
Cardiac disorders	2	7	1	7
Nervous system disorder	7	19	5	18
Renal and urinary disorders	1	4	0	2
Mental disorder	1	0	0	0
Metabolic and nutritional disorders	1	3	3	6
Endocrine disorders	0	1	0	2
Skin and subcutaneous tissue disorders	0	4	6	4
Immune system disorders	3	8	2	6
Investigations	4	8	6	3
Total	45	113	55	86

* Reported from October 1, 2023 to September 30, 2024
** Reported from October 1, 2024 to March 31, 2025

3. Reports of suspected adverse reactions to intranasal live attenuated influenza vaccines (2024 season)

(1) Numbers and frequencies of suspected adverse reactions reported

Table 5 shows the numbers of reported suspected adverse reactions to the intranasal live attenuated influenza vaccines and frequencies calculated from the estimated numbers of vaccinated persons based on the number of vaccines distributed to medical institutions.

Table 5 Numbers of suspected adverse reactions reported and estimated number of vaccinated persons

	Reports by MAHs (Serious reports) *		Number of reports by medical institutions **		
Estimated number of vaccinated persons (number of vaccinations)	Number of serious cases reported (frequency)	Number of patient mortalities reported	Number of reports (frequency)	Number of serious cases reported (frequency)	Number of patient mortalities reported
371,660 (as of March 31, 2025)	16 (0.004305%)	0 (0.000000%)	4 (0.001076%)	3 (0.000807%)	0 (0.000000%)

* Reports by the MAHs were on cases determined to be “serious” under Article 68-10, Paragraph 1 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (PMD Act). Reports by the MAHs may duplicate some cases reported by medical institutions, and such duplicated cases are included in the number for reports by medical institutions.
** Reports by medical institutions were submitted under Article 12, Paragraph 1 of the Preventive Vaccination Law (PV Law) or Article 68-10, Paragraph 2 of the PMD Act.

(2) Reports of suspected adverse reactions by sex and age group

The numbers of reported suspected adverse reactions to intranasal live attenuated influenza vaccines are shown by sex and age group in Table 6 and Table 7, respectively.

Table 6 Number of reports by sex

Sex	Number of Reports by MAHs (serious cases)	Number of Reports by medical institutions
Male	9	3
Female	6	1
Unknown	1	0
Total	16	4

Table 7 Number of reports by age group

	Number of Reports by MAHs		Number of Reports by medical institutions		
Age group	Number of serious cases reported	Number of patient mortalities reported	Number of reports	Number of serious cases reported	Number of patient mortalities reported
0-9	14	0	4	3	0
10-19	2	0	0	0	0
20-29	0	0	0	0	0
30-39	0	0	0	0	0
40-49	0	0	0	0	0
50-59	0	0	0	0	0
60-69	0	0	0	0	0
70-79	0	0	0	0	0
80 or older	0	0	0	0	0

	Number of Reports by MAHs		Number of Reports by medical institutions		
Age group	Number of serious cases reported	Number of patient mortalities reported	Number of reports	Number of serious cases reported	Number of patient mortalities reported
Unknown	0	0	0	0	0
Total	16	0	4	3	0

(3) Details of reported symptoms

Suspected adverse reactions to intranasal live attenuated influenza vaccines reported during the 2024 season are outlined by System Organ Class (SOC) in Table 8.

No case of post-vaccination death was reported for this season.

One case [Note 4)] of possible Guillain-Barré syndrome was reported for this season. The assessment by experts determined that the causality between the vaccination and death could not be assessed due to lack of information for this case.

One case [Note 5)] was reported as possible anaphylaxis. Experts concluded that no case was assessed as Level 3 or higher anaphylaxis using the Brighton Criteria.

At the Joint Meeting held in July 2025, it was concluded that there were no significant concerns regarding the safety of the reviewed vaccines based on the information including adverse reaction reports reported so far, including reported symptoms other than anaphylaxis, with no safety measures such as revision of package inserts required at present, but reporting of suspected adverse reactions and their details should be carefully monitored.

Note 4) Cases reported with the symptom name “Guillain-Barré syndrome”
Note 5) Cases reported with the symptom name “anaphylaxis,” “anaphylactic reaction,” “anaphylactic shock,” “anaphylactoid reaction,” or “anaphylactoid shock”

Table 8 Number of suspected adverse reactions to intranasal live attenuated influenza vaccines reported during the 2024 season by System Organ Class (SOC) *

	2024 season **	
SOC of symptom	Reports by MAHs (serious cases)	Reports by medical institutions (serious cases)
General disorders and administration site conditions	3	1
Infections and infestations	5	2
Eye disorders	1	0
Musculoskeletal and connective tissue disorders	1	0
Vascular disorders	1	0
Respiratory, thoracic and mediastinal disorders	1	0
Nervous system disorder	7	2
Renal and urinary disorders	2	0
Mental disorder	0	1
Skin and subcutaneous tissue disorders	3	0
Immune system disorders	1	0
Investigations	6	0
Total	31	6

* Marketed in October in 2024
** Reported from October 1, 2024 to March 31, 2025

4. Future safety measures

As detailed in the “Reporting Suspected Adverse Reactions for Routine Vaccination, etc.” notification [3], medical institutions are urged to promptly report when they encounter symptoms that they believe meet the Suspected Adverse Reaction Reporting Criteria even if the causality is unclear.

In addition to the conventional reporting by fax, electronic reporting is available through the website since April 1, 2021.

[Report Reception Site (electronic report system)]
https://www.pmda.go.jp/safety/reports/hcp/0002.html (only in Japanese)

The MHLW/PMDA will continue their efforts to gather information concerning the safety of influenza vaccines including suspected adverse reaction reports, etc. and to implement safety measures based on such information. Continued cooperation is requested in alerting vaccine recipients to adverse reactions and reporting them when suspected.

[References]

1) MHLW: The Side Effect Subcommittee of the Immunization and Vaccine Section Meeting in the Health Science Council (the 107th meeting) and the 2025 Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs Council (the 3rd meeting) (Joint Meeting)
   - Material 2-31 Reports of Suspected Adverse Reactions to Influenza Vaccines
     https://www.mhlw.go.jp/content/11120000/001522665.pdf (only in Japanese)
   - Material 2-32 Reports of Suspected Adverse Reactions to Intranasal Live Attenuated Influenza Vaccines
     https://www.mhlw.go.jp/content/11120000/001522666.pdf (only in Japanese)
   - Material 2-37 List of reports of fatal cases after vaccination
     https://www.mhlw.go.jp/content/11120000/001522673.pdf (only in Japanese)
2) MHLW: The Side Effect Subcommittee of the Immunization and Vaccine Section Meeting in the Health Science Council (the 106th meeting) and the 2025 Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs Council (the 1st meeting) (Joint Meeting)
   - Material 2-36 List of reports of fatal cases after vaccination
     https://www.mhlw.go.jp/content/11120000/001475822.pdf (only in Japanese)
3) “Partial Amendment of Reporting Suspected Adverse Reactions for Routine Vaccination, etc.” notification dated March 31, 2025
   Joint DIDPC Notification No. 0331-12 and PSB Notification No. 0331-36 by the Director of the Department of Infectious Disease Prevention and Control and the Director-General of the Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare
   https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou20/hukuhannou_houkoku/kanrentuuti.html (only in Japanese)

   Report form
   https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou20/hukuhannou_houkoku/dl/r04youshiki_02.pdf (only in Japanese)

   Entry instructions
   https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou20/hukuhannou_houkoku/dl/r04youshiki_03.pdf (only in Japanese)

   Report entry application (National Institute of Infectious Diseases)
   https://id-info.jihs.go.jp/relevant/vaccine/topics/060/vaersapp.html (only in Japanese)

Reference: Suspected Adverse Reaction Reporting Criteria

<Routine vaccination>

Symptoms	Time to onset after inoculation
Anaphylaxis	4 hours
Hepatic impairment	28 days
Interstitial pneumonia	28 days
Acute disseminated encephalomyelitis (ADEM)	28 days
Acute generalised exanthematous pustulosis (AGEP)	28 days
Guillain-Barré syndrome	28 days
Convulsion	7 days
Vasculitis	28 days
Thrombocytopenic purpura	28 days
Optic neuritis	28 days
Myelitis	28 days
Asthmatic attack	24 hours
Nephrotic syndrome	28 days
Encephalitis or encephalopathy	28 days
Oculomucocutaneous syndrome	28 days
Other reactions (symptoms suspected to be associated with the vaccination and either (1) requiring hospital admission or (2) resulting in, or associated with a risk of death or persistent incapacity)	Time frame in which the event was considered by the physician to be associated with the vaccination

Except for “other reactions,” any event occurring within the specified time frame is subject to mandatory reporting to the MHLW regardless of causality under the PV Law and related rules.

<Voluntary vaccination>

Adverse reactions or infections associated with voluntary vaccinations should be reported when reporting is considered necessary to prevent the occurrence and spread of health hazards. Refer to the following for specific cases subject to reporting. Adverse reactions and infections for which causality with vaccinations is unclear may also be subject to reporting.

(1) Death
(2) Disability
(3) Events that may result in death
(4) Events that may result in disability
(5) Symptoms that require admission or prolonged hospitalization at medical institutions for treatment [excluding events in (3) and (4)]
(6) Serious events corresponding to those in items (1) to (5)
(7) Congenital diseases or anomalies in the next generation
(8) Onset of infections suspected of being caused by use of the applicable pharmaceutical
(9) Onset of unknown events which are not mild and could not be predicted based on the package insert, other than those listed in (1) to (8)

2

Important Safety Information

Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated August 28, September 9and17,2025, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.

1 Telmisartan

Brand name (name of company)	Micardis Tablets 20 mg, 40 mg, 80 mg, and the others (Boehringer Ingelheim Japan, Inc., and the others)
Therapeutic category	Antihypertensives
Indications	Hypertension

PRECAUTIONS (Revised language is underlined.)

11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Angioedema Cases of angioedema with swelling of the face, lip, pharynx/larynx, tongue, etc. have been reported, resulting in dyspnoea due to laryngeal oedema, etc. <u>Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.</u>
Reference information	Among the cases collected in the PMDA's safety database for drugs, those meeting the following conditions were retrieved: a) Cases that fell under MedDRA v28.0 PT “intestinal angioedema” or “gastrointestinal oedema” were retrieved. b) Among the cases that fell under “angioedema” in MedDRA v28.0 PT, those with symptoms such as abdominal pain and diarrhoea that may be related to intestinal angioedema were retrieved. c) Among the cases that fell under a) or b) above, cases for which the outcomes of the related events could not be identified from the information in the column of outcomes or clinical courses were excluded. Cases (for which a causal relationship between the drug and the event is reasonably possible) involving intestinal angioedema reported in Japan: 1 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 193,040 Japanese market launch: ［1］ Micardis Tablets 20 mg, 40 mg :Jannually 2005 ［2］ Micardis Tablets 80 mg :October 2010

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Male 40s	Hypertension (none)	Unknown for 38 days ↓ Discontinuation	**Angioedema, intestinal oedema, face oedema, acute kidney injury**	
				Day 1 of administration	Administration of telmisartan was initiated.
				Day 4 of administration	The patient repeatedly experienced enterocolitis symptoms, such as abdominal pain and diarrhoea several times, but they improved with antibiotics and probiotics.
				Day 36 of administration	The patient began to notice pain extending from the epigastric region to the umbilical region in the middle of the night. He visited Hospital A for abdominal pain. A contrast-enhanced CT revealed kidney enlargement, fluid retention in the anterior pararenal space, and oedema extending from the duodenum to the small intestine.
				Day 37 of administration	Due to the presence of renal impairment and prolongation of abdominal pain, the patient was transferred to Hospital B. He had a history of NASH (non-alcoholic steatohepatitis) and hypertension following appendectomy but no history of renal disorder.
				Day 38 of administration (day of discontinuation)	Telmisartan was discontinued, and the patient's clinical course was observed with fluid replacement.
				1 day after discontinuation	A kidney biopsy was performed for suspected rapidly progressive glomerulonephritis. Abdominal pain was alleviated.
				3 days after discontinuation	Abdominal pain nearly resolved spontaneously, and renal disorder improved. A kidney biopsy showed no significant findings in the glomeruli, and interstitial oedema was observed.
					DLST: Positive for telmisartan.

Laboratory test value

Test item (unit)	Day 1 of administration	Day 36 of administration	Day 37 of administration (first examination)	Day 37 of administration (second examination)
Urine protein	-	-	-	2+
Quantitative urine protein (g/gCr)	-	-	-	1.52
Urinary occult blood	-	-	-	+/-
BUN(mg/dL)	-	-	-	26.4
Cr(mg/dL)	0.86	3.34	4.68	5.03
eGFR(mL/min)	-	-	-	11
WBC (/μL)	-	-	-	8900
CRP(mg/dL)	-	-	-	5.5
PR3-ANCA(U/mL)	-	-	-	7.2
MPO-ANCA	-	-	-	Negative

Suspected concomitant drugs: Unknown
Concomitant drugs: Unknown

2 Perindopril erbumine

Brand name (name of company)	Perindopril erbumine Tablets 2 mg, 4 mg「sawai」 (Sawai Co. Ltd)
Therapeutic category	Antihypertensives
Indications	Hypertension

PRECAUTIONS (Revised language is underlined.)

11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Angioedema Angioedema accompanied by dyspnoea, with swelling of the face, tongue, glottis, and larynx, may occur. In such cases, administration should be discontinued immediately, and appropriate measures should be taken, such as administering adrenaline injections and maintaining the airway. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.
Reference information	Among the cases collected in the PMDA's safety database for drugs, those meeting the following conditions were retrieved: a) Cases that fell under MedDRA v28.0 PT “intestinal angioedema” or “gastrointestinal oedema” were retrieved. b) Among the cases that fell under “angioedema” in MedDRA v28.0 PT, those with symptoms such as abdominal pain and diarrhoea that may be related to intestinal angioedema were retrieved. c) Among the cases that fell under a) or b) above, cases for which the outcomes of the related events could not be identified from the information in the column of outcomes or clinical courses were excluded. Cases (for which a causal relationship between the drug and the event is reasonably possible) involving intestinal angioedema reported in Japan: 1 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 47,000 Japanese market launch: [1] Perindopril erbumine Tablets 2 mg, 4 mg「sawai」:July 2005

Case summary

<table>
<tr><th rowspan="2">No.</th><th colspan="2">Patient</th><th rowspan="2">Daily dose/
Administration duration</th><th colspan="2">Adverse reaction</th></tr>
<tr><th>Sex/
age</th><th>Reason for use
(complication)</th><th colspan="2">Clinical course and treatment</th></tr>
<tr><td rowspan="6">1</td><td rowspan="6">Female
60s</td><td rowspan="6">IgA nephropathy,
hypertension
(dyslipidaemia)</td><td rowspan="6">Unknown
for 4 years
↓
Discontinuation</td><td colspan="2">Small bowel angioedema</td></tr>
<tr><td>Day 1 of administration</td><td>Administration of perindopril erbumine was initiated.
Eyelid/lip oedema and abdominal pain began to appear after initiation of administration.
The patient repeatedly experienced abdominal pain. She underwent detailed examinations, such as blood tests, abdominal ultrasound, upper gastrointestinal tract endoscopy, and CT. However, the cause could not be identified, and her clinical course remained under observation.</td></tr>
<tr><td>4 years after administration (day of hospitalization)</td><td>The patient noticed sudden, intense abdominal pain, and visited the hospital because the symptom persisted. Mild tenderness was present in the lower abdomen.
A mild increase in the inflammatory reaction was observed with a white blood cell count of 15,000/μL and CRP of 1.92 mg/dL. A contrast-enhanced CT revealed fully circumferential edematous wall thickening affecting a wide area of the small intestine and a small amount of ascites. She was diagnosed with enteritis and was urgently admitted to the hospital.</td></tr>
<tr><td>Day 2 of hospitalization</td><td>Abdominal pain nearly resolved with treatment with fasting and fluid replacement alone.</td></tr>
<tr><td>Day 3 of hospitalization</td><td>An oral small intestinal endoscopy showed no abnormal findings. A random biopsy was also performed, but no abnormal pathological findings were found. The inflammatory reaction tended to improve with a white blood cell count of 6,300/μL and CRP of 1.86 mg/dL. A repeat CT showed marked improvement in small bowel oedema and disappearance of ascites. Since abdominal pain and CT findings improved within only 2 days, small bowel angioedema was suspected as the cause. Since C1 inhibitor and C4 levels were within the normal range and there was no family history, hereditary angioedema was considered unlikely.</td></tr>
<tr><td>Day of discontinuation</td><td>The patient was diagnosed with ACE inhibitor-induced small bowel angioedema, and administration of perindopril erbumine was discontinued.
Thereafter, there was no recurrence of abdominal pain or eyelid/lip oedema.</td></tr>
<tr><td colspan="6">Laboratory test value
<table>
<tr><th>Test item (unit)</th><th>4 years after administration (day of hospitalization)</th><th>Day 3 of hospitalization</th></tr>
<tr><td>White blood cell count (/μL)</td><td>15,000</td><td>6,300</td></tr>
<tr><td>CRP(mg/dL)</td><td>1.92</td><td>1.86</td></tr>
</table></td></tr>
<tr><td colspan="6">Concomitant drugs: Pitavastatin calcium</td></tr>
</table>

3 Mesalazine

Brand name (name of company)	Lialda Tablets 600 mg, 1200 mg (Mochida Pharmaceutical Co. Ltd.)
Therapeutic category	Other agents affecting digestive organs, Sulfonamide preparations
Indications	Ulcerative colitis (excluding severe cases)

PRECAUTIONS (Revised language is underlined.)

11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis General symptoms, such as pyrexia, malaise, arthralgia, and myalgia, and organ symptoms such as erythema, purpura (derma), bloody sputum (lung), haematuria, and proteinuria (kidney), may occur.
Reference information	Cases meeting both of the following conditions were retrieved from those collected in the PMDA's safety database for drugs: ・Cases that fell under MedDRA ver.28.0 SMQ “Vasculitis (broad)” ・Cases for which it was documented in the case report forms that the patient tested positive for anti-neutrophil cytoplasmic antibody (ANCA) Cases (for which a causal relationship between the drug and the event is reasonably possible) involving Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis reported in Japan: 4 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 91,000 Japanese market launch: ［1］ Lialda Tablets 600 mg:September 2025 ［2］ Lialda Tablets 1200 mg：November 2016

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
1	Female 40s	Ulcerative colitis (none)	Unknown ↓ Discontinuation	**ANCA-associated vasculitis**	
				Day 1 of administration	Administration of mesalazine was initiated, but the patient experienced repeated cycles of improvement and aggravation.
				Several years after administration	Pain in the left buttock pain developed and was accompanied by pyrexia, later extending to both buttocks as well as the upper and lower limbs. The patient visited a medical institution, and she was found to have an increased inflammatory reaction, bilateral sacroiliac joint sclerosis on pelvic X-ray, a nodular shadow in the right lower lobe on chest CT, and PR3-ANCA of 13.7 U/mL.
				Date unknown (day of discontinuation)	Two weeks after the visit, the right lower lobe nodule rapidly increased, and the patient was admitted to the hospital. A bronchoscopy lung biopsy revealed granuloma with multinucleated giant cells, and she was diagnosed with ANCA-associated vasculitis (AAV) and spondylarthritis (SpA). Mesalazine was discontinued because it was suspected to be involved in AAV, and steroid therapy was initiated.
				Date unknown	The symptoms promptly resolved, the pulmonary nodular shadow disappeared, and the patient was discharged from the hospital.
				Date unknown	AAV remained in remission even after tapering of steroids.
	Concomitant drugs: None				

4 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 ·Neoadjuvant therapy for non-small cell lung cancer ·Radically 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 ·Radically unresectable, advanced or recurrent oesophageal carcinoma ·Postoperative adjuvant therapy for oesophageal carcinoma ·Carcinoma of unknown primary ·Postoperative adjuvant therapy for urothelial carcinoma ·Radically unresectable urothelial carcinoma · Radically unresectable, advanced or recurrent epithelial skin malignancies ·Unresectable hepatocellular carcinoma

PRECAUTIONS (Revised language is underlined.)

8. IMPORTANT PRECAUTIONS (newly added)	<Common to all indications> <u>Tumour lysis syndrome may occur. Patients should be carefully monitored by checking serum electrolyte levels, renal function, etc.</u>
11. ADVERSE REACTIONS 11.1 Clinically Significant Adverse Reactions (newly added)	<u>Tumour lysis syndrome</u> <u>If any abnormalities are observed, administration of this drug should be discontinued, appropriate measures (e.g., administration of physiological saline solution and/or hyperuricaemia therapeutic agents, and dialysis) should be taken, and patients should be carefully monitored until recovery from such symptoms.</u>
Reference information	Among the cases collected in the PMDA's safety database for drugs, those for which blood test results for 2 or more of the following items (uric acid, potassium, phosphorus, and calcium) were documented in the case report forms were retrieved. Cases (for which a causal relationship between the drug and the event is reasonably possible) involving Tumour lysis syndrome reported in Japan: 4 (No patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 29,370 Japanese market launch:

［1］ Opdivo I.V. Infusion 20 mg, 100 mg: September 2014
［2］ Opdivo I.V. Infusion 120 mg: November 2020
［3］ Opdivo I.V. Infusion 240 mg: November 2018

Case summary

<table>
<tr><th rowspan="2">No.</th><th colspan="2">Patient</th><th rowspan="2">Daily dose/
Administration duration</th><th colspan="2">Adverse reaction</th></tr>
<tr><th>Sex/
age</th><th>Reason for use
(complication)</th><th colspan="2">Clinical course and treatment</th></tr>
<tr><td>1</td><td>Male
40s</td><td>Malignant melanoma (depression, metastases to left common ilium, metastases to left inguinal/external iliac lymph nodes, schizophrenia, dyslipidaemia, metastases to mesenteric lymph nodes, multiple metastases to intra-abdominal nodules)</td><td>80 mg
1 course every 3 weeks
↓
Discontinuation
↓
80 mg
1 course every 3 weeks</td><td colspan="2">Tumour lysis syndrome
The patient had a history of alcohol use, was a tobacco user, and had no abnormal renal function. His PS was 1.</td></tr>
<tr><td></td><td></td><td></td><td></td><td>Day 1 of administration</td><td>The patient received nivolumab (genetical recombination) (80 mg) and ipilimumab (genetical recombination) (3 mg/kg) as combination therapy for radically unresectable malignant melanoma (recurrence; disease type classification: Superficial spreading; stage 4; M stage: M1; BRAF mutation: Negative; PD-L1: <1%).</td></tr>
<tr><td></td><td></td><td></td><td></td><td>5 days after administration (day of discontinuation)</td><td>Hepatic function disorder and tumour lysis syndrome were observed. A slight increase in hepatic enzymes (lactate dehydrogenase) and renal disorder were observed as clinical symptoms of tumour lysis syndrome. No action was taken for hepatic function disorder. The patient received fluid for treatment of tumour lysis syndrome. Administration of nivolumab (genetical recombination) and ipilimumab (genetical recombination) was discontinued. He did not receive prophylactic treatment for tumour lysis syndrome.</td></tr>
<tr><td></td><td></td><td></td><td></td><td>8 days after administration</td><td>BUN, creatinine, and phosphorus levels increased.</td></tr>
<tr><td></td><td></td><td></td><td></td><td>11 days after administration</td><td>Rapid aggravation of renal function and a rapid increase in uric acid, BUN, and creatinine levels were observed. CT showed shrinkage of the intra-abdominal nodules and shrinkage of the left common iliac and mesenteric lymph nodes. The oncology department was consulted, and the patient was diagnosed with tumour lysis syndrome. Fluid replacement 2 L/day and administration of rasburicase (genetical recombination) (12.75 mg/day) were initiated as treatment.</td></tr>
<tr><td></td><td></td><td></td><td></td><td>17 days after administration</td><td>The renal function returned to the normal level. Administration of rasburicase (genetical recombination) was terminated.</td></tr>
<tr><td></td><td></td><td></td><td></td><td>25 days after administration (Day 1 of readministration)</td><td>Tumour lysis syndrome resolved. Administration of nivolumab (genetical recombination) (80 mg) and ipilimumab (genetical recombination) was restarted.</td></tr>
<tr><td colspan="6">Laboratory test value
<table>
<tr><th>Test item (unit)</th><th>1 day before administration</th><th>5 days after administration</th><th>8 days after administration</th><th>11 days after administration</th><th>12 days after administration</th><th>25 days after administration</th></tr>
<tr><td>Creatinine (mg/dL)</td><td>0.78</td><td>0.70</td><td>2.59</td><td>5.75</td><td>6.17</td><td>0.68</td></tr>
<tr><td>Uric acid (mg/dL)</td><td>2.5</td><td>-</td><td>6.7</td><td>14.3</td><td>14.3</td><td>1.4</td></tr>
<tr><td>BUN (mg/dL)</td><td>10.7</td><td>36.9</td><td>36.9</td><td>78.4</td><td>88.8</td><td>5.8</td></tr>
<tr><td>eGFR (mL/min/1.73 m^2)</td><td>83.8</td><td>94.4</td><td>-</td><td>-</td><td>8.7</td><td>97.4</td></tr>
<tr><td>K (mmol/L)</td><td>5.0</td><td>4.5</td><td>-</td><td>-</td><td>5.1</td><td>3.6</td></tr>
<tr><td>Ca (mg/dL)</td><td>7.7</td><td>7.8</td><td>-</td><td>-</td><td>7.1</td><td>7.3</td></tr>
<tr><td>P (mg/dL)</td><td>3.2</td><td>-</td><td>3.7</td><td>4.6</td><td>5.9</td><td>3.0</td></tr>
<tr><td>LDH (IU/L)</td><td>273</td><td>293</td><td>-</td><td>-</td><td>286</td><td>268</td></tr>
</table></td></tr>
<tr><td colspan="6">Suspected concomitant drugs: Ipilimumab (genetical recombination)
Concomitant drugs: Rosuvastatin calcium, Orengedokuto, Ninjinto</td></tr>
</table>

Case summary

<table>
<tr><th rowspan="2">No.</th><th colspan="2">Patient</th><th rowspan="2">Daily dose/
Administration duration</th><th colspan="2">Adverse reaction</th></tr>
<tr><th>Sex/
age</th><th>Reason for use
(complication)</th><th colspan="2">Clinical course and treatment</th></tr>
<tr><td rowspan="10">2</td><td rowspan="10">Male
50s</td><td rowspan="10">Metastatic renal cell carcinoma (metastases to lymph nodes, multiple metastases to lung, hepatic infiltration, metastases to pleura, peritoneal dissemination, diabetes mellitus)</td><td rowspan="10">240 mg
1 course every 3 weeks
↓
Discontinuation</td><td colspan="2">Tumour lysis syndrome
Past history: Large intestine carcinoma, PS: 1</td></tr>
<tr><td>Day 1 of administration</td><td>The patient received nivolumab (genetical recombination) (240 mg, every 3 weeks) and ipilimumab (genetical recombination) (72 mg, every 3 weeks) as combination therapy for radically unresectable or metastatic renal cell carcinoma (stage 4, TNM classification: T1bN1M1 [organs of metastasis: Lymph nodes, lung, pleura, peritoneal dissemination]).</td></tr>
<tr><td>3 hours after administration</td><td>Approximately 3 hours after administration, the patient experienced symptoms suggestive of tumour lysis syndrome (renal disorder, hypotension, cardiac failure).</td></tr>
<tr><td>6 hours after administration</td><td>Vital signs indicated shock, and the patient was transported to the ICU. CT revealed increased ascites/right pleural effusion and a leftward mediastinal shift including the heart, and he was diagnosed with cardiogenic shock. Noradrenaline and dobutamine were started for the treatment of cardiogenic shock. For the treatment of pleural effusion, a thoracic drain was inserted (2,000 mL), and methylprednisolone (500 mg) was administered. Non-invasive positive pressure ventilation was performed.</td></tr>
<tr><td>1 day after administration</td><td>The patient remained anuric and underwent continuous haemodiafiltration (CHDF) for the treatment of tumour lysis syndrome.</td></tr>
<tr><td>4 days after administration</td><td>The patient was being managed in the ICU.</td></tr>
<tr><td>5 days after administration</td><td>Renal function improved, and the patient was weaned from CHDF.</td></tr>
<tr><td>14 days after administration</td><td>Although catecholamine was required, the patient was transferred to a general ward because his vital signs had stabilized. Tumour lysis syndrome was resolving.</td></tr>
<tr><td>*Date unknown</td><td>The decision was made to discontinue nivolumab (genetical recombination) and ipilimumab (genetical recombination) due to the adverse event, although the date is unknown.</td></tr>
<tr><td colspan="6">Laboratory test value
<table>
<tr><th>Test item (unit)</th><th>1 day before administration</th><th>Day 1 of administration</th><th>1 day after administration</th><th>2 days after administration</th><th>7 days after administration</th><th>17 days after administration</th></tr>
<tr><td>Creatinine (mg/dL)</td><td>0.79</td><td>0.70</td><td>1.83</td><td>2.97</td><td>0.93</td><td>0.82</td></tr>
<tr><td>Uric acid (mg/dL)</td><td>8.0</td><td>8.3</td><td>-</td><td>8.3</td><td>5.0</td><td>-</td></tr>
<tr><td>BUN (mg/dL)</td><td>12</td><td>13</td><td>23</td><td>38</td><td>40</td><td>42</td></tr>
<tr><td>K (mmol/L)</td><td>4.8</td><td>4.5</td><td>6.3</td><td>5.7</td><td>4.9</td><td>5.6</td></tr>
<tr><td>Ca (mg/dL)</td><td>9.5</td><td>9.4</td><td>-</td><td>7.6</td><td>8.5</td><td>-</td></tr>
<tr><td>P (mg/dL)</td><td>-</td><td>3.8</td><td>-</td><td>5.1</td><td>-</td><td>-</td></tr>
<tr><td>LDH (IU/L)</td><td>389</td><td>577</td><td>8,713</td><td>16,274</td><td>702</td><td>890</td></tr>
</table></td></tr>
<tr><td colspan="6">Suspected concomitant drugs: Ipilimumab (genetical recombination)
Concomitant drugs: Tramadol hydrochloride, naldemedine tosilate, prochlorperazine maleate, vonoprazan fumarate, metformin hydrochloride</td></tr>
</table>

3

Revisions of PRECAUTIONS (No. 363)

This section presents details of revisions to the PRECAUTIONS and brand names of drugs that have been revised in accordance with the Notifications dated August 28, September 9 and 17, 2025.

1 Delandistrogene moxeparvovec

Brand name	Elevidys for Intravenous Infusion (Chugai Pharmaceutical Co., Ltd.)
8. IMPORTANT PRECAUTIONS	Hepatic function tests (clinical symptoms, hepatic enzymes (e.g., γ-GTP, ALT), total bilirubin, albumin, activated partial thromboplastin time, prothrombin time, prothrombin time/international normalized ratio, etc.) and imaging tests should be performed before administering this product. If any abnormalities are observed, appropriate measures, such as postponing the administration, should be taken. Patients should undergo hepatic function tests described above once a week for the first 3 months. If any abnormalities are observed, they should be monitored until the test results return to normal levels. Prednisolone should be administered before and after treatment with this product following the descriptions in Table 1 in Section 7. Administration of corticosteroids may induce infections. Therefore, patients should be closely monitored when they are administered this product, and attention should be paid to the occurrence or exacerbation of the infections.
9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS **9.1 Patients with Complication or History of Diseases, etc. (newly added)**	Patients complicated with infections Administration of corticosteroids may exacerbate infections. Therefore, administration of this product should be deferred until the patients recover from infections or the conditions become controllable.
11. DEFECTS/ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Hepatic impairment, acute hepatic failure Serious hepatic impairment accompanied by increases in hepatic enzymes (e.g., γ-GTP, ALT) and total bilirubin may occur. If any abnormalities are observed, appropriate measures, such as continuing the administration of prednisolone, should be taken. Cases of acute hepatic failure resulting in death after administration of this product have been reported overseas (in non-ambulatory patients).

2 Antihypertensives, vasodilators

[1] Azilsartan
[2] Azilsartan/amlodipine besilate
[3] Candesartan cilexetil
[4] Candesartan cilexetil/amlodipine besilate

[5] Candesartan cilexetil/hydrochlorothiazide

Brand name	[1] Azilva Tablets 10 mg, 20 mg, 40 mg, Azilva Granules 1%, and the others (Takeda Pharmaceutical Company Limited, and the others) [2] Zacras Combination Tablets LD, HD, and the others (Takeda Pharmaceutical Company Limited, and the others) [3] Blopress Tablets 2, 4, 8, 12, and the others (T's Seiyaku Co., Ltd., and the others) [4] Unisia Combination Tablets LD, HD, and the others (T's Seiyaku Co., Ltd., and the others) [5] Ecard Combination Tablets LD, HD, and the others (T's Seiyaku Co., Ltd., and the others)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Angioedema Angioedema with swelling of the face, lip, tongue, pharynx/larynx, etc. may occur. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

3 Antihypertensives

Alacepril

Brand name	Cetapril Tablets 25 mg, and the others (Sumitomo Pharma Co., Ltd., and the others)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Angioedema Angioedema accompanied by dyspnoea, with swelling of the face, tongue, glottis, and larynx, may occur. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

4 Antihypertensives

Aliskiren fumarate

Brand name	Rasilez Tablets 150 mg (OrphanPacific, Inc.)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Angioedema Symptoms such as dyspnoea, difficult swallowing, and swelling of the face, lip, pharynx, tongue, and limbs may occur. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

5 Antihypertensives

Imidapril hydrochloride

Brand name	Tanatril Tablets 2.5, 5, 10, and the others (Mitsubishi Tanabe Pharma Corporation, and the others)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Angioedema Angioedema accompanied by dyspnoea, with swelling of the face, tongue, glottis, and larynx, may occur. If any abnormalities are observed, administration should be discontinued immediately, and appropriate measures should be taken, such as administering antihistamines and/or corticosteroids and maintaining the airway. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

6 Antihypertensive

[1] Irbesartan
[2] Irbesartan/amlodipine besilate
[3] Irbesartan/trichlormethiazide

Brand name	[1] Avapro Tablets 50 mg, 100 mg, 200 mg, and the others (Sumitomo Pharma Co., Ltd. , and the others), Irbetan Tablets 50 mg, 100 mg, 200 mg, and the others (Shionogi Pharma Co., Ltd., and the others) [2] Aimix Combination Tablets LD, HD, and the others (Sumitomo Pharma Co., Ltd., and the others) [3] Irtra Combination Tablets LD, HD (Shionogi Pharma Co., Ltd.)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Angioedema Angioedema with swelling of the face, lip, pharynx, tongue, etc. may occur. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

7 Antihypertensives

[1] Olmesartan medoxomil
[2] Olmesartan medoxomil/azelnidipine
[3] Valsartan
[4] Valsartan/amlodipine besilate
[5] Valsartan/cilnidipine
[6] Valsartan/hydrochlorothiazide

Brand name	[1] Olmetec OD Tablets 5 mg, 10 mg, 20 mg, 40 mg, and the others (Daiichi Sankyo Co., Ltd., and the others) [2] Rezaltas Combination Tablets LD, HD (Daiichi Sankyo Co., Ltd.) [3] Diovan Tablets 20 mg, 40 mg, 80 mg, 160 mg, Diovan OD Tablets 20 mg, 40 mg, 80 mg, 160 mg, and the others (Novartis Pharma K.K., and the others) [4] Exforge Combination OD Tablets, Exforge Combination Tablets, and the others (Novartis Pharma K.K., and the others) [5] Atedio Combination Tablets (EA Pharma Co., Ltd.) [6] Co-Dio Combination Tablets MD, EX, and the others (Novartis Pharma K.K., and the others)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Angioedema Symptoms such as swelling of the face, lip, pharynx, and tongue may occur. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

8 Antihypertensives, other cardiovascular agents

Sacubitril valsartan sodium hydrate

Brand name	Entresto Tablets 50 mg, 100 mg, 200 mg, Entresto Granules for Pediatric 12.5 mg, 31.25 mg (Novartis Pharma K.K.)
11. ADVERSE REACTIONS	Angioedema Angioedema leading to airway obstruction may occur, with symptoms such as swelling of the tongue, glottis, and larynx. In such cases,

11.1 Clinically Significant Adverse Reactions	administration should be discontinued immediately, and appropriate measures should be taken, such as administering adrenaline injections and maintaining the airway. Administration of this drug should not be resumed even if angioedema resolves. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

9 Antihypertensives

Delapril hydrochloride

Brand name	Adecut 7.5 mg, 15 mg, 30 mg Tablets (T's Seiyaku Co., Ltd.)
11. ADVERSE REACTIONS	Angioedema
11.1 Clinically Significant Adverse Reactions	Angioedema accompanied by dyspnoea, with swelling of the face, tongue, glottis, and larynx, may occur. In such cases, administration should be discontinued immediately, and appropriate measures should be taken, such as administering adrenaline injections and maintaining the airway. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

10 Antihypertensives

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

Brand name	[1] Micardis Tablets 20 mg, 40 mg, 80 mg, and the others (Boehringer Ingelheim Japan, Inc., and the others) [2] Micamlo Combination Tablets AP, BP, and the other (Boehringer Ingelheim Japan, Inc., and the others) [3] Micatrio Combination Tablets (Boehringer Ingelheim Japan, Inc.) [4] Micombi Combination Tablets AP, BP, and the others (Boehringer Ingelheim Japan, Inc., and the others)
11. ADVERSE REACTIONS	Angioedema
11.1 Clinically Significant Adverse Reactions	Cases of angioedema with swelling of the face, lip, pharynx/larynx, tongue, etc. have been reported, resulting in dyspnoea due to laryngeal oedema, etc. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

11 Antihypertensives

Trandolapril

Brand name	Odric Tablets 0.5 mg, 1 mg, and the others and the others (Nippon Shinyaku Co., Ltd., and the others)
11. ADVERSE REACTIONS	Angioedema
11.1 Clinically Significant Adverse Reactions	Angioedema accompanied by dyspnoea, with swelling of the face, tongue, glottis, and larynx, may occur. If any abnormalities are observed, administration should be discontinued immediately, and appropriate measures should be taken, such as administering adrenaline injections and maintaining the airway. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

12 Antihypertensives

Perindopril erbumine

Brand name	Coversyl Tablets 2 mg, 4 mg, and the others (Kyowa Kirin Co., Ltd., and the others)
11. ADVERSE REACTIONS	Angioedema
11.1 Clinically Significant Adverse Reactions	Angioedema accompanied by dyspnoea, with swelling of the face, tongue, glottis, and larynx, may occur. In such cases, administration should be discontinued immediately, and appropriate measures should be taken, such as administering adrenaline injections and maintaining the airway. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

13 Antihypertensives

[1] Losartan potassium
[2] Losartan potassium/hydrochlorothiazide

Brand name	[1] Nu-Lotan Tablets 25 mg, 50 mg, 100 mg, and the others (Organon K.K., and the others) [2] Preminent Tablets LD, HD, and the others (Organon K.K., and the others)
11. ADVERSE REACTIONS	Angioedema
11.1 Clinically Significant Adverse Reactions	Swelling of the face, lip, pharynx, tongue, etc. may occur. Of note, intestinal angioedema accompanied by abdominal pain, queasy, vomiting, diarrhoea, etc. may occur.

14 Other agents affecting digestive organs, Sulfonamide preparations

[1] Mesalazine
[2] Salazosulfapyridine

Brand name	[1] Asacol tablets 400 mg, and the others (Zeria Pharmaceutical Co., Ltd., and the others), Pentasa Tablets 250 mg, 500 mg, Pentasa Granules 94%, Pentasa Suppositories 1 g, Pentasa Enema 1 g, and the others (Ferring Pharmaceuticals Co., Ltd., and the others), Lialda Tablets 600 mg, 1200 mg (Mochida Pharmaceutical Co. Ltd.) [2] Salazopyrin Tablets 500 mg, Salazopyrin Suppositories 500 mg (Pfizer Japan Inc.), Azulfidine EN tablets 250 mg, 500 mg, and the others (AYUMI Pharmaceutical Corporation, and the others)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis General symptoms, such as pyrexia, malaise, arthralgia, and myalgia, and organ symptoms such as erythema, purpura (derma), bloody sputum (lung), haematuria, and proteinuria (kidney), may occur.

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

[1] Adalimumab (genetical recombination)
[2] Adalimumab (genetical recombination) [adalimumab follow-on biologics 1]

[3] Adalimumab (genetical recombination) [adalimumab follow-on biologics 2]
[4] Adalimumab (genetical recombination) [adalimumab follow-on biologics 3]
[5] Adalimumab (genetical recombination) [adalimumab follow-on biologics 4]

Brand name	[1][2][3][4][5] Humira 20 mg for S.C. Injection Syringe 0.2 mL, Humira 40 mg for S.C. Injection Syringe 0.4 mL, Humira 80 mg for S.C. Injection Syringe 0.8 mL, Humira 40 mg for S.C. Injection Pen 0.4 mL, Humira 80 mg for S.C. Injection Pen 0.8 mL (AbbVie GK), and follow-on biologics (biosimilars)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Autoimmune hepatitis

16 Other antitumor agents

Ipilimumab (genetical recombination)

Brand name	Yervoy Injection 20 mg, 50 mg (Bristol-Myers Squibb K.K.)
8. IMPORTANT PRECAUTIONS (newly added)	Tumour lysis syndrome may occur. Patients should be carefully monitored by checking serum electrolyte levels, renal function, etc.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (nwly added)**	Tumour lysis syndrome If any abnormalities are observed, administration of this drug should be discontinued, appropriate measures (e.g., administration of physiological saline solution and/or hyperuricaemia therapeutic agents, and dialysis) should be taken, and patients should be carefully monitored until recovery from such symptoms.

17 Other antitumor agents

Nivolumab (genetical recombination)

Brand name	Opdivo I.V. Infusion 20 mg, 100 mg, 120 mg, 240 mg (Ono Pharmaceutical Co., Ltd.)
8. IMPORTANT PRECAUTIONS (newly added)	<Common to all indications> Tumour lysis syndrome may occur. Patients should be carefully monitored by checking serum electrolyte levels, renal function, etc.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Tumour lysis syndrome If any abnormalities are observed, administration of this drug should be discontinued, appropriate measures (e.g., administration of physiological saline solution and/or hyperuricaemia therapeutic agents, and dialysis) should be taken, and patients should be carefully monitored until recovery from such symptoms.

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

Meropenem hydrate

Brand name	Meropen For I.V. Infusion vial 0.25 g, 0.5 g, Meropen For I.V. Infusion kit 0.5 g (Sumitomo Pharma Co., Ltd.), and the others
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Toxic epidermal necrolysis (TEN), oculomucocutaneous syndrome (Stevens-Johnson syndrome), acute generalised exanthematous pustulosis

19 Other antitumor agents

Tarlatamab (genetical recombination)

Brand name	Imdelltra For I.V. Infusion 1mg, 10 mg (Amgen K.K.)
1. WARNINGS	Severe cytokine release syndrome and neurologic events (including immune effector cell-associated neurotoxicity syndrome) may occur. Since cases involving cytokine release syndrome that resulted in death have also been reported, caution should be exercised for the following: 1 This drug should be administered under appropriately arranged conditions, such as inpatient management, particularly during the initial phase of treatments. 2 Severe cytokine release syndrome may occur. In addition to taking preventive measures such as administration of premedication against cytokine release syndrome, patients should be carefully monitored. If any abnormalities are observed, appropriate measures should be taken in accordance with instructions, such as the guidance for management of cytokine release syndrome, provided by the marketing authorization holder. 3 Severe neurologic events (including immune effector cell-associated neurotoxicity syndrome) may occur. Patients should be carefully monitored, and if any abnormalities are observed, appropriate measures should be taken in accordance with instructions, such as the guidance for management of immune effector cell-associated neurotoxicity syndrome, provided by the marketing authorization holder.

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 August 31, 2025)
◎: Products for which EPPV was initiated after August 1, 2025

	Nonproprietary name / Brand name	Name of the MAH	Date of EPPV initiation
◎	Miglustat[*1] / 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）[*2] / 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
◎	Avatrombopag Maleate[*3] / 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
	Drospirenone[*4]	Aska Pharmaceutical	June 30, 2025

	Nonproprietary name Brand name	Name of the MAH	Date of EPPV initiation
	Slinda 28 Tablets	Co., Ltd.	
	Purified Vi polysaccharide typhoid vaccine Typhim Vi Syringe for Injection	Sanofi K.K.	June 30, 2025
	Guselkumab (genetical recombination)[*5] Tremfya Intravenous Infusion 200 mg, Tremfya Subcutaneous Injection Syringe 100 mg, 200 mg, Tremfya Subcutaneous Injection 200 mg Pen	Janssen Pharmaceutical K.K.	June 24, 2025
	Vutrisiran sodium[*6] Amvuttra Subcutaneous Injection 25 mg Syringe	Alnylam Japan K.K.	June 24, 2025
	pH4-Treated acidic normal human immunoglobulin (subcutaneous injection), vorhyaluronidase alfa (genetical recombination)[*7] HyQvia 10% S.C. Injection Set 5 g/50 mL, 10 g/100 mL, 20 g/200 mL	Takeda Pharmaceutical Company Limited	June 24, 2025
	IncobotulinumtoxinA Xeomin 50 units, 100 units, 200 units for Intramuscular injection	Teijin Pharma Limited	June 24, 2025
	Remimazolam besilate[*8] Anerem 50 mg for I.V. Injection	Mundipharma K.K.	June 24, 2025
	Maralixibat chloride Livmarli Oral Solution 10 mg/mL	Takeda Pharmaceutical Company Limited	June 12, 2025
	pH4-Treated acidic normal human immunoglobulin (subcutaneous injection), vorhyaluronidase alfa (genetical recombination) HyQvia 10% S.C. Injection Set 5 g/50 mL, 10 g/100 mL, 20 g/200 mL	Takeda Pharmaceutical Company Limited	June 12, 2025
	Ivosidenib Tibsovo Tablets 250 mg	Nihon Servier Co., Ltd.	June 2, 2025
	Amivantamab (genetical recombination)[*9] Rybrevant Intravenous Infusion 350 mg	Janssen Pharmaceutical K.K.	May 21, 2025
	Tisotumab vedotin (genetical recombination) Tivdak for Intravenous Infusion 40 mg	Genmab K.K.	May 21, 2025
	Lazertinib mesilate hydrate Lazcluze Tablets 80 mg, 240 mg	Janssen Pharmaceutical K.K.	May 21, 2025
	Guselkumab (genetical recombination)[*10] Tremfya Intravenous Infusion 200 mg, Tremfya Subcutaneous Injection 200 mg Syringe, 200 mg Pen, 100 mg Syringe	Janssen Pharmaceutical K.K.	May 21, 2025
	Mavacamten Camzyos capsules 5 mg, 2.5 mg, 1 mg	Bristol-Myers Squibb K.K.	May 21, 2025

Nonproprietary name Brand name		Name of the MAH	Date of EPPV initiation
	Acoramidis hydrochloride Beyonttra tablets 400 mg	Alexion Pharma Godo Kaisha	May 21, 2025
	Amivantamab (genetical recombination)*[11] Rybrevant Intravenous Infusion 350 mg	Janssen Pharmaceutical K.K.	May 19, 2025
	Iptacopan hydrochloride hydrate*[12] Fabhalta capsules 200 mg	Novartis Pharma K.K.	May 19, 2025
	Atropine sulfate hydrate*[13] Ryjusea Mini ophthalmic solution 0.025%	Santen Pharmaceutical Co., Ltd.	April 21, 2025
	Garadacimab (genetical recombination) Andembry S.C. Injection 200 mg Pens	CSL Behring K.K.	April 18, 2025
	Brivaracetam Briviact for I.V. injection 25 mg	UCB Japan Co. Ltd.	April 17, 2025
	Tarlatamab (genetical recombination) Imdelltra For I.V. Infusion 1 mg, 10 mg	Amgen K.K.	April 16, 2025
	Tirzepatide*[14] Zepbound Subcutaneous Injection Ateos 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg	Eli Lilly Japan K.K.	April 11,2025
	Letermovir*[15] Prevymis Tablets 240 mg, Prevymis Intravenous Infusion 240 mg	MSD K.K.	March 27, 2025
	Marstacimab (genetical recombination) Hympavzi S.C. Injection 150 mg Pen	Pfizer Japan Inc.	March 24, 2025
	Teclistamab (genetical recombination) Tecvayli Subcutaneous Injection 153 mg, 30 mg	Janssen Pharmaceutical K.K.	March 19, 2025
	Mosunetuzumab (genetical recombination) Lunsumio for Intravenous Infusion 1 mg, 30 mg	Chugai Pharmaceutical Co., Ltd.	March19, 2025
	Datopotamab deruxtecan (genetical recombination) Datroway for Intravenous Drip Infusion 100 mg	Daiichi Sankyo Co., Ltd.	March 19, 2025
	Selexipag Uptravi Tablets for Pediatric 0.05 mg	Nippon Shinyaku Co., Ltd.	March 19, 2025
	Ozanimod hydrochloride Zeposia capsules 0.92 mg, Zeposia capsules starter pack	Bristol-Myers Squibb K.K.	March 19, 2025
	Tofersen Qalsody Intrathecal injection 100 mg	Biogen Japan Ltd	March 19, 2025
	Zanubrutinib Brukinsa capsules 80 mg	BeOne Medicines Japan	March 19, 2025
	Patiromer sorbitex calcium Veltassa 8.4 g powder for suspension (single-dose package)	Zeria Pharmaceutical Co., Ltd.	March 17, 2025
	Flortaucipir (^{18}F) Tauvid Injection	PDRadiopharma Inc.	March 3, 2025

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

*2 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)

*3 Persistent and chronic immune thrombocytopenia

*4 Contraception

*5 Treatment of moderate to severe active Crohn's disease (only in patients who have had an inadequate response to conventional treatments)

*6 Transthyretin cardiac amyloidosis (wild type and mutant type)

*7 Slowing the progression of motor function decline in chronic inflammatory demyelinating polyradiculoneuritis and multifocal motor neuropathy (when improvement in muscle weakness is observed)

*8 Sedation during gastrointestinal endoscopy

*9 Coadministration with lazertinib mesilate hydrate for unresectable, advanced or recurrent *EGFR* mutation-positive non-small cell lung cancer

*10 Maintenance therapy for moderate to severe ulcerative colitis (only in patients who have had an inadequate response to conventional treatments)

*11 Coadministration with carboplatin and pemetrexed sodium hydrate for unresectable, advanced or recurrent *EGFR* mutation-positive non-small cell lung cancer

*12 C3 nephropathy

*13 Slowing the progression of myopia

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

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