Pharmaceuticals and Medical Devices Safety Information

No. 376 October 2020

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Available information is listed here

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

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No. 376 October 2020

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

[Outline of Information]

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2	**Important Safety Information**	*P* *C*	Relugolix: Regarding the revision of the precautions in package inserts of drugs in accordance with the Notification dated September 8, 2020, this section will present the details of an important revision as well as the case summaries serving as the basis for these revision.	10
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E: Distribution of Dear Healthcare Professional Letters of Emergency Communication R: Distribution of Dear Healthcare Professional Letters of Rapid Communications P: Revision of Precautions C: Case Summaries

Reporting of safety information such as adverse reactions to the Minister of Health, Labour and Welfare is a duty of providers of medical care and pharmaceutical products.

If providers of medical care and pharmaceutical products such as physicians, dentists, and pharmacists detect adverse reactions, infections associated with drugs or medical devices, or medical device adverse events, it is mandatory for such providers to report them to the Minister of Health, Labour and Welfare directly or through the marketing authorization holder. As providers of medical care and pharmaceutical products, drugstore and pharmacy personnel are also required to report safety issues related to drugs and medical devices.

Abbreviations

ADR	Adverse drug reaction
ADEM	Acute Disseminated Encephalomyelitis
AGEP	Acute Generalised Exanthematous Pustulosis
CA	Calcium
CEA	Carcinoembryonic antigen
EPPV	Early Post-marketing Phase Vigilance
FY	Fiscal year
Hb	Hemoglobin
LDH	Lactate Dehydrogenase
MAH	Marketing authorization holder
MHLW	Ministry of Health, Labour and Welfare
MRI	Magnetic Resonance Imaging
NILM	Negative for intraepithelial lesion or malignancy
SpO_2	Percutaneous oxygen saturation
PMDA	Pharmaceuticals and Medical Devices Agency
PMDSI	Pharmaceuticals and Medical Devices Safety Information
PSEHB	Pharmaceutical Safety and Environmental Health Bureau
PMD Act	Act on Securing Quality, Efficacy and Safety of Pharmaceuticals and Medical Devices
SOC	System Organ Class
PV Law	Preventative Vaccination Law

1
Suspected Adverse Reactions to Influenza vaccines in the 2019 Season

1. Introduction

This section describes the status of instances of suspected adverse reactions to influenza vaccines reported from October 1, 2019 through April 30, 2020 (hereinafter referred to as the "2019 season").

Medical institutions are required to report to MHLW when they encounter symptoms they decide meet the Suspected Adverse Reaction Reporting Criteria for influenza vaccines regardless of causality. Reports by medical institutions, together with those by MAHs, are compiled and evaluated by PMDA. For serious cases including patient mortalities, PMDA performs causality assessment and/or considers 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 and Food Sanitation 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)].

2. Reports of Suspected Adverse Reactions to Influenza Vaccines (2019 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 amount of vaccines distributed to medical institutions.

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

	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 mortality reported	Number of reports (frequency)	Number of serious cases reported (frequency)	Number of patient mortality reported
56 496 152 (as of April 30, 2020)	55 (0.000097%)	1 (0.0000018%)	278 (0.00049%)	93 (0.00016%)	5 (0.0000089%)

* Reports by MAHs were of cases determined to be "serious" in accordance with Article 68-10-1 of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals and Medical Devices (PMD Act). Reports by MAHs may duplicate some cases reported by medical institutions, and duplicated cases were added up as reported by medical institutions.

** Reports by medical institutions were submitted in accordance with Article 12-1 of the Preventative Vaccination Law (PV Law) or Article 68-10-2 of the PMD Act. (* and ** also apply to Tables 2 to 4.)

(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	Number of reports by medical institutions
Male	25	118
Female	25	160
Unknown	5	0
Total	55	278

Table 3 Number of reports by age group

	Reports by MAHs		Reports by medical institutions		
Age group	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	10	0	72	31	1
10 - 19	8	0	21	4	1
20 - 29	4	0	32	8	0
30 - 39	1	0	27	6	0
40 - 49	2	0	38	11	0
50 - 59	3	0	18	3	0
60 - 69	7	0	21	6	0
70 - 79	9	0	34	18	2
80 or older	8	1	15	6	1
Unknown	3	0	0	0	0
Total	55	1	278	93	5

(3) Details of reported symptoms

Suspected adverse reactions to influenza vaccines reported during the 2019 season are outlined by System Organ Class (SOC) in the right columns of Table 4. There were no major changes compared with the 2018 season (October 1, 2018 to September 30, 2019).

A total of 6 cases of post-vaccination deaths were reported for this season. The assessment by experts determined the causality between the vaccination and the death unclear for 4 cases and unlikely for the other 2 cases. For 1 additional case reported after the season, It was decided that the causal relationship between the vaccination and the death could not be assessed due to lack of information.

A total of 10 cases (Note 1) were reported as possible Guillain-Barre syndrome or acute disseminated encephalomyelitis (ADEM) within the season. Of these, 1 case and 4 cases, respectively were determined to be of Guillain-Barre syndrome, and of ADEM for which a causal relationship between the respective disease and the influenza vaccine was reasonably possible, according to expert opinions.

A total of 22 cases (Note 2) were reported as possible anaphylaxis. Of these, 8 cases were assessed as Level 3 or higher anaphylaxis using the Brighton Criteria (including 6 serious cases). Regarding the number of reports from MAHs by manufacturing lot, there were no distinct concentration of reports of anaphylaxis found on specific lots.

At the Joint Meeting, it was concluded that there were no new concerns regarding safety of vaccines, 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 1) Cases reported with the symptom name terminology “Guillain-Barre syndrome” or “ADEM,” and those which are suspected to be Guillain-Barre syndrome or ADEM based on their clinical courses.

Note 2) Cases reported with the symptom name terminology “anaphylactic reaction,” “anaphylactic shock,” “anaphylactoid reaction,” or “anaphylactoid shock.”

Table 4 Comparison of the number of suspected adverse reaction reports between the 2018 and 2019 seasons (by SOC)

	2018 season†		2019 season††	
SOC of symptom	Reports by MAHs	Reports by medical institutions (serious cases)	Reports by MAHs	Reports by medical institutions (serious cases)
Gastrointestinal disorders	4	7	1	8
General disorders and administration site conditions	20	28	18	53
Infections and infestations	9	9	7	15
Hepatobiliary disorders	3	3	6	4
Eye disorders	3	1	0	1
Musculoskeletal and connective tissue disorders	3	14	6	7
Blood and lymphatic system disorders	3	2	0	6
Vascular disorders	2	3	0	2
Respiratory, thoracic and mediastinal disorders	2	8	5	12
Ear and labyrinth disorders	0	0	1	2
Injury, poisoning and procedural complications	1	1	0	4
Cardiac disorders	1	4	0	3
Nervous system disorders	28	30	22	27
Renal and urinary disorders	2	3	0	1
Psychiatric disorders	1	0	0	1
Metabolic and nutritional disorders	5	0	0	2
Skin and subcutaneous tissue disorders	11	16	7	12
Immune system disorders	3	7	5	15
Investigations	2	4	4	1
Total	103	140	82	176

† reported from October 1, 2018 to September 30, 2019

†† reported from October 1, 2019 to April 30, 2020

3. Future safety measures

As detailed in the Reporting Suspected Adverse Reactions for Routine Vaccination[3)] notification, 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.

MHLW/PMDA will continue their efforts to gather information concerning the safety of influenza vaccines including suspected adverse reaction reports 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: Distributed Material 12 for the Side Effect Subcommittee of the Immunization and Vaccine Section Meeting in the Health Science Council (the 48th meeting) and the 2020 Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs and Food Sanitation Council (the 4th meeting) (Joint Meeting), Reports of Suspected Adverse Reactions to Influenza Vaccines
https://www.mhlw.go.jp/content/10906000/000675622.pdf (only in Japanese)

2) MHLW: Distributed Material 15-1 for the Side Effect Subcommittee of the Immunization and Vaccine Section Meeting in the Health Science Council (the 49th meeting) and the 2020 Subcommittee on Drug Safety of the Committee on Drug Safety in the Pharmaceutical Affairs and Food Sanitation Council (the 6th meeting) (Joint Meeting), Reports of Post-Influenza HA Vaccination Deaths for 2019-2020 Season
https://www.mhlw.go.jp/content/10601000/000675088.pdf (only in Japanese)

3) Partial Amendment of Reporting Suspected Adverse Reactions for Routine Vaccinations, etc. dated September 24, 2020, Joint HSB Notification No. 0924-1 and No.0924-2, by the Director-General of Health Service Bureau and by the Director-General of Pharmaceutical and Food Safety Bureau, Ministry of Health, Labor 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/r01youshiki_02.pdf (only in Japanese)
Entry instructions
https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou20/hukuhannou_houkoku/dl/r01youshiki_03.pdf (only in Japanese)
Report entry application (National Institute of Infectious Diseases)
http://www.nih.go.jp/niid/ja/vaccine-j/6366-vaers-app.html (only in Japanese)

Reference: Suspected Adverse Reaction Reporting Criteria
<Routine vaccination>

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-Barre 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 strongly associated with the vaccination

Except for “other reactions,” any event occurring within the specified time frame is subject to mandatory reporting to MHLW regardless of causality according to the PV Act 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 September 8, 2020, this section will present the details of important revisions as well as the case summaries serving as the basis for these revisions.

1 Relugolix

Branded name (name of company)	Relumina Tablets 40 mg (Aska Pharmaceutical. Co., Ltd.)
Therapeutic category	Other hormone preparations (including antihormone preparations)
Indications	Relief of the following symptoms associated with uterine fibroids: menorrhagia, lower abdominal pain, lumbar pain, and anemia

PRECAUTIONS (revised language is underlined)

[Under old instructions]

Careful Administration (newly added)

Careful Administration
Patients with submucosal fibroid

Important Precaution (newly added)

Important Precautions
When administering this drug to patients with submucosal fibroid severe abnormal uterine bleeding may occur. Patients should be carefully monitored and if any abnormalities are observed, appropriate measures should be taken. Patients should be instructed to immediately contact medical institutions if they experience heavy bleeding at one time.

Reference information

Number of cases (for which a causal relationship between the drug and event is reasonably possible) reported during the previous approximately 16-month period (March 2019 to June 2020)
Cases involving severe abnormal uterine bleeding: 10 (No patient mortalities)
Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 17 000
Japanese market launch: March 2019

Case

No.	Patient		Daily dose/ administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		No.	
1	Female 50s	Submucosal fibroid (hypertension, hyperlipidaemia, reflux oesophagitis, abnormal uterine bleeding)	40 mg 35 days	Heavy genital bleeding, myoma expulsion	
				2 years and 10 months before administration	Submucosal fibroid (22×14mm) was noted at her previous hospital.
				5 months before administration	Abnormal genital bleeding ocurred. Submucosal fibroid grew to 59×45 mm with a tendency for expulsion into the cervical canal.
				1 month before administration	Abnormal genital bleeding recurred.
				Day 1 of administration	Ptosis of submucosal fibroid progressed further. Oral administration of relugolix was started to go through the transition into menopause to avoid surgery.
				35 days after administration (day of discontinuation)	Sudden heavy genital bleeding occurred. Relugolix was discontinued.
				1 day after dis-continuation	The patient was referred to this hospital for emergency treatment by her previous doctor. Conditions at the time of visiting: Height: 158.9 cm, body weight: 72.4 kg, BMI 30.2, body temperature 36.1 °C, blood pressure 122/93 mmHg, pulse rate: 141 beats/min, SpO_2 96%, the abdomen was soft but the patient complained of no pain. The patient's bleeding was prolonged and heavier than the gauze inserted into the vagina could hold. A speculum exam revealed a myoma expulsion of 5 cm in size. On pelvic exam, the uterus was about the size of a fist. Transvaginal ultrasonography and MRI: Uterine fibroids prolapsed or expelled into and out of the vagina were observed. Blood test: The patient had no anemia (Hb 14.2 g/dL) and no increased tumour marker (LDH 217 U/L, neuron-specific enolase 8.2 g/mL, CEA 1.9 ng/mL, CA19-9 10 U/mL, CA125 8 U/mL). Pathological exam: No findings suggesting malignancy were observed (endometrial cytology (1 year and 6 months before): Negative, cervical cytology (6 months before): NILM)
				2 days after discontinuation	Total hysterectomy with abdominal upper vaginal amputation was performed due to continuous active bleeding.
				9 days after discontinuation	A transvaginal ultrasound identified no ascites or haematoma in the pelvis. Residual fragments of the cervix were identified.
				10 days after discontinuation	The patient was discharged from the hospital based on her favorable clinical course.
	Concomitant drugs: Olmesartan medoxomil, vonoprazan fumarate, celecoxib, rosuvastatin calcium				

3
Revision of Precautions (No.316)

This section presents details of revisions to the Precautions of package inserts and brand names of drugs that have been revised in accordance with the Notifications dated September 8, 2020.

1 Other hormone preparations (including antihormone preparations)

Relugolix

Branded name [Under Old instructions]	Relumina Tablets 40 mg (Aska Pharmaceutical. Co., Ltd.)
Careful Administration (newly added)	Patients with submucosal fibroid
Important Precaution (newly added)	When administering this drug to patients with submucosal fibroid, severe abnormal uterine bleeding may occur. Patients should be carefully monitored and if any abnormalities are observed, appropriate measures should be taken. Patients should be instructed to immediately contact medical institutions if they experience heavy bleeding at one time.

2 Other agents affecting metabolism

Hydroxychloroquine sulfate

Branded name [Under Old instructions]	Plaquenil 200 mg Tablets (Sanofi K.K.)
Adverse Reactions (Clinically Significant	**Prolonged QT, ventricular tachycardia (including torsades de pointes)**:
Adverse Reactions) (newly added)	Prolonged QT and ventricular tachycardia (including torsades de pointes) may occur. Patients should be carefully monitored. If any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be taken.

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 31 August, 2020)

◎: Products for which EPPV was initiated after August 1, 2020

	Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
◎	Isatuximab (genetical recombination) Sarclisa 100 mg I.V. Infusion, Sarclisa 500 mg I.V. Infusion	Sanofi K.K.	August 31, 2020
◎	Indacaterol acetate/glycopyrronium bromide/ mometasone furoate Enerzair medium dose inhalation powder with hard capsules, Enerzair high dose inhalation powder with hard capsules	Novartis Pharma K.K.	August 26, 2020
◎	Indacaterol acetate/mometasone furoate Atectura low dose inhalation powder with hard capsules, Atectura medium dose inhalation powder with hard capsules, Atectura high dose inhalation powder with hard capsules	Novartis Pharma K.K.	August 26, 2020
◎	Sacubitril valsartan sodium hydrate Entresto Tablets 50 mg, 100 mg, 200 mg	Novartis Pharma K.K.	August 26, 2020
◎	Capmatinib hydrochloride hydrate Tabrecta tablets 150 mg, 200 mg	Novartis Pharma K.K.	August 26, 2020
◎	Satralizumab (genetical recombination) Enspryng Syringes for Subcutaneous Injection 120 mg	Chugai Pharmaceutical Co., Ltd.	August 26, 2020
◎	Daprodustat Duvroq Tablets 1 mg, 2 mg, 4 mg, 6 mg	GlaxoSmithKline K.K.	August 26, 2020
◎	Vadadustat Vafseo Tablets 150 mg, 300 mg	Mitsubishi Tanabe Pharma Corporation	August 26, 2020
◎	Opicapone Ongentys Tablets 25 mg	Ono Pharmaceutical Co., Ltd.	August 26, 2020
◎	Tirabrutinib hydrochloride*1 Velexbru Tablets 80 mg	Ono Pharmaceutical Co., Ltd.	August 21, 2020
◎	Vonicog alfa (genetical recombination) Vonvendi Intravenous 1300	Shire Japan KK	August 17, 2020

	Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
◎	Remimazolam besilate Anerem 50 mg for I.V. Injection	Mundipharma K.K.	August 7, 2020
	Posaconazole Noxafil for Intravenous Infusion 300 mg	MSD K.K.	July 21, 2020
	Lemborexant Dayvigo Tablets 2.5 mg, 5mg, 10 mg	Eisai Co., Ltd.	July 6, 2020
	Fluticasone propionate/formoterol fumarate hydrate Flutiform 50 Aerosol 56 puffs, 120 puffs	Kyorin Pharmaceutical Co.,Ltd.	June 29, 2020
	Semaglutide (genetical recombination) Ozempic Subcutaneous Injection 0.25 mg SD, 0.5 mg SD, 1.0 mg SD	Novo Nordisk Pharma Ltd.	June 29, 2020
	Tolvaptan*2 Samsca tablets 7.5 mg, 15 mg, 30 mg, Samsca OD tablets 7.5 mg, 15 mg, 30 mg, Samsca granules 1%	Otsuka Pharmaceutical Co., Ltd.	June 29, 2020
	Landiolol hydrochloride*3 Onoact for I. V. Infusion 50 mg, 150 mg	Ono Pharmaceutical Co., Ltd.	June 29, 2020
	Levothyroxine sodium hydrate Thyradin-S I.V. Injection 200 μg	Aska Pharmaceutical. Co., Ltd.	June 29, 2020
	Delgocitinib Corectim Ointment 0.5%	Japan Tabacco Inc.	June 24, 2020
	Melatonin Melatobel granules 0.2% for pediatric	Nobelpharma Co., Ltd.	June 23, 2020
	Insulin lispro (genetical recombination) Lyumjev Injection Cart, Lyumjev Injection MirioPen, Lyumjev Injection MirioPen HD Lyumjev Injection 100 U/mL	Eli Lilly Japan K.K.	June 17, 2020
	Insulin glargine (genetical recombination)/lixisenatide Soliqua Injection SoloStar	Sanofi K.K.	June 8, 2020
	Tepotinib hydrochloride hydrate Tepmetko Tablets 250 mg	Merck Biopharma Co., Ltd	June 1, 2020
	Nintedanib ethanesulfonate*4 Ofev capsules 100 mg, 150 mg	Boehringer Ingelheim Japan, Inc.	May 29, 2020
	Darolutamide Nubeqa tablets 300 mg	Bayer Yakuhin Ltd	May 26, 2020
	Trastuzumab deruxtecan (genetical recombination) Enhertu for intravenous drip infusion 100 mg	Daiichi Sankyo Co., Ltd.	May 25, 2020
	Brolucizumab (genetical recombination) Beovu kit for intravitreal injection 120 mg/mL	Novartis Pharma K.K.	May 25, 2020
	Dotinurad Urece Tablets 0.5 mg, 1 mg, 2 mg	FUJIYAKUHIN Co., Ltd.	May 25, 2020
	Cabozantinib malate Cabometyx tablets 20 mg, 60 mg	Takeda Pharmaceutical Company Limited.	May 22, 2020
	Borofalan (^{10}B) Steboronine 9000 mg/300 mL for infusion	STELLA PHARMA CORPORATION	May 20, 2020

Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
Tirabrutinib hydrochloride Velexbru Tablets 80 mg	Ono Pharmaceutical Co., Ltd.	May 20, 2020
Viltolarsen Viltepso Injection 250 mg	Nippon Shinyaku Co., Ltd.	May 20, 2020
Sodium zirconium cyclosilicate hydrate Lokelma 5 g/10 g powder for suspension (single-dose package)	AstraZeneca K.K.	May 20, 2020
Remdesivir Veklury for Intravenous Injection 100 mg	Gilead Sciences Inc.	May 11, 2020
Upadacitinib hydrate Rinvoq Tablets 7.5 mg, 15 mg	AbbVie GK	April 24, 2020
Posaconazole Noxafil Tablets 100 mg	MSD K.K.	April 24, 2020
Lurasidone hydrochloride Latuda tablets 20 mg, 40 mg, 60 mg, 80 mg	Sumitomo Dainippon Pharma Co., Ltd.	April 22, 2020
Dinoprostone Propess vaginal inserts 10 mg	Ferring Pharmaceuticals Co., Ltd.	April 2, 2020
Mepolizumab (genetical recombination) Nucala for s.c. injection 100 mg	Glaxo Smith Kline K.K.	March 25, 2020
Dupilumab (genetical recombination) *5 Dupixent 300 mg Syringe for S.C. Injection	Sanofi K.K.	March 25, 2020

*1 Primary macroglobulinaemia and lymphoplasmacytic type lymphoma

*2 Improvement of hyponatraemia secondary to the syndrome of inappropriate antidiuretic hormone secretion (SIADH)

*3 Tachyarrhythmia (atrial fibrillation, atrial flutter and sinus tachycardia) associated with sepsis

*4 Progressive fibrosing interstitial lung disease

*5 Chronic rhinosinusitis with nasal polyps (only in patients not adequately controlled with existing therapies)