Pharmaceuticals and Medical Devices Safety Information

No. 378 December 2020

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) Medical Product Information web page (http://www.pmda.go.jp/english/index.html) and on the MHLW website (https://www.mhlw.go.jp, only in Japanese).

Available information is listed here

Your cooperation with the survey on the PMDA Medi-navi utilization and others is encouraged.

From November 26 (Thu) to December 13 (Sun), 2020, utilization of the PMDA Medi-navi will be surveyed in the medical professionals who use the service.

The survey can be answered in the page accessed from the URL in the delivered Medi-navi mails or the QR code below.

Register and answer the survey here.

Published by
Ministry of Health, Labour and Welfare

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No. 378 December 2020

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

[Outline of Information]

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
Al-P	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AST	Aspartate Transaminase
CD	Cluster of Differentiation
CT	Computed Tomography
EPPV	Early Post-marketing Phase Vigilance
FY	Fiscal year
γ-GTP	γ-Glutamyl Transpeptidase
MAH	Marketing authorization holder
MHLW	Ministry of Health, Labour and Welfare
PD-1	Programmed cell death 1
PMDA	Pharmaceuticals and Medical Devices Agency
PMDSI	Pharmaceuticals and Medical Devices Safety Information
PT	Prothrombin Time
QR	Quick Response

1

Utilization of Risk Management Plan (RMP) of Drugs and Request for Participation in a Survey Investigating Utilization of Safety Information through PMDA Medi-navi

1. Introduction

The Risk Management Plan (RMP) of a drug is a document prepared by the marketing authorization holder (MAH) of the drug. It compiles the risks associated with the drug as well as the activities to be done by its MAH to minimize the risks. PMDA confirms the contents of RMP. RMP lists information that the package insert of the drug does not contain such as risks of adverse events that potentially occur with the subject drug. It is important therefore, for medical professionals to acknowledge the information contained in the RMP in addition to those in the package insert for promoting proper use of the drug and to minimize the risks associated.

This section introduces the initiatives taken by the MHLW and PMDA for promoting utilization of RMP as well as the materials prepared and provided by MAHs as additional activities to minimize risks associated with drugs (hereinafter referred to as RMP materials). The online survey conducted by PMDA to understand the utilization status of the safety information on drugs including RMP as well as the utilization of the PMDA Medi-navi will also be introduced for medical professionals to look through and participate in the survey.

2. Awareness and Utilization of RMP

(1) What are RMP and RMP materials?

RMP is a document that sorts out the risk information including adverse drug reactions (ADRs) of a drug collected from its preapproval through the post-marketing stages and formulates the information into what activities are required to minimize the identified risks or what types of investigation should be carried out to obtain missing information.

RMP lists already confirmed ADRs (identified risks). It also lists adverse events for which a relationship to the administered drug is suspected but not thoroughly verified (potential risks) and identifies the information considered insufficient (missing information) for predicting the post-marketing safety of the drug. In addition, to address these risks or missing information, post-marketing activities such as information provision for risk minimization (the risk minimization activities) or collection of the missing information (the pharmacovigilance activities) are described. In the risk minimization activities, besides the routine risk minimization activities such as providing information through package inserts, materials (the RMP Materials) may be prepared intended for medical professionals and patients as additional risk minimization activities. Such materials are prepared for drugs for which additional information provided by materials and other means was considered necessary in the process of marketing authorization review. Contents of RMP and RMP Materials were confirmed at PMDA and the RMP Marking is affixed to these materials to indicate that they are materials prepared in line with RMP.

(2) Awareness and Utilization of RMP

As many as 596 RMPs have been published on the PMDA website as of September 30, 2020 in the hope of encouraging active use in clinical settings.

The awareness and understanding of RMP in clinical settings are not very high. As described in the Pharmaceuticals and Medical Devices Safety Information (PMDSI) No. 358*, only 48.2% of the hospital respondents and 17.4% of the pharmacy respondents understood the contents of RMP according to the survey PMDA conducted in Fiscal Year (FY) 2017. Similarly, only 50.6% of the hospital respondents and 39.4% of the pharmacy respondents among the facilities that responded as understanding the contents of RMP to the preceding question had actually utilized it. These

figures are not very encouraging.

Acknowledging this situation, PMDA has made efforts to promote utilization of RMP and RMP Materials in clinical settings. RMP and RMP Materials have been posted on the PMDA website, information has been provided through the PMDA Medi-navi, and “Learn about RMP in 3 Minutes,” an RMP made-easy material, as well as “Simple Enough to Start Today! How to use RMP” have been prepared and released.

3. Simple Enough to Start Today! How to use RMP

PMDA in collaboration with the Japanese Society of Drug Informatics and with the intention of enhancing the promotion of utilization of RMP in clinical settings, has developed an e-learning video set titled “Simple Enough to Start today! How to use RMP” as an easy-to-understand guide. The set has been available since March 2020 on the PMDA’s YouTube channel and on its website.

There are 2 videos in the set. One video is "What’s RMP?” which describes RMP as well as RMP Materials and the basics of RMP. The other is “Let’s Try RMP!” which identifies specific scenes in clinical settings where RMP can be actually utilized or specific parts of RMP to look at in such scenes, citing actual cases encountered in hospitals and pharmacies. The “Let’s Try RMP!” part in particular was prepared based on the actual interviews conducted by PMDA with pharmacists who actually utilized RMP. The part therefore contains examples of practices for users to adopt right away, even today. The slides used in the videos are also separately posted for reference.

The videos can be viewed with the QR code below, on the Pmda Channel, the agency’s YouTube channel, and on its website for free. Medical professionals are strongly encouraged to view the videos to deepen their understanding of RMP and RMP Materials for active use in clinical settings.

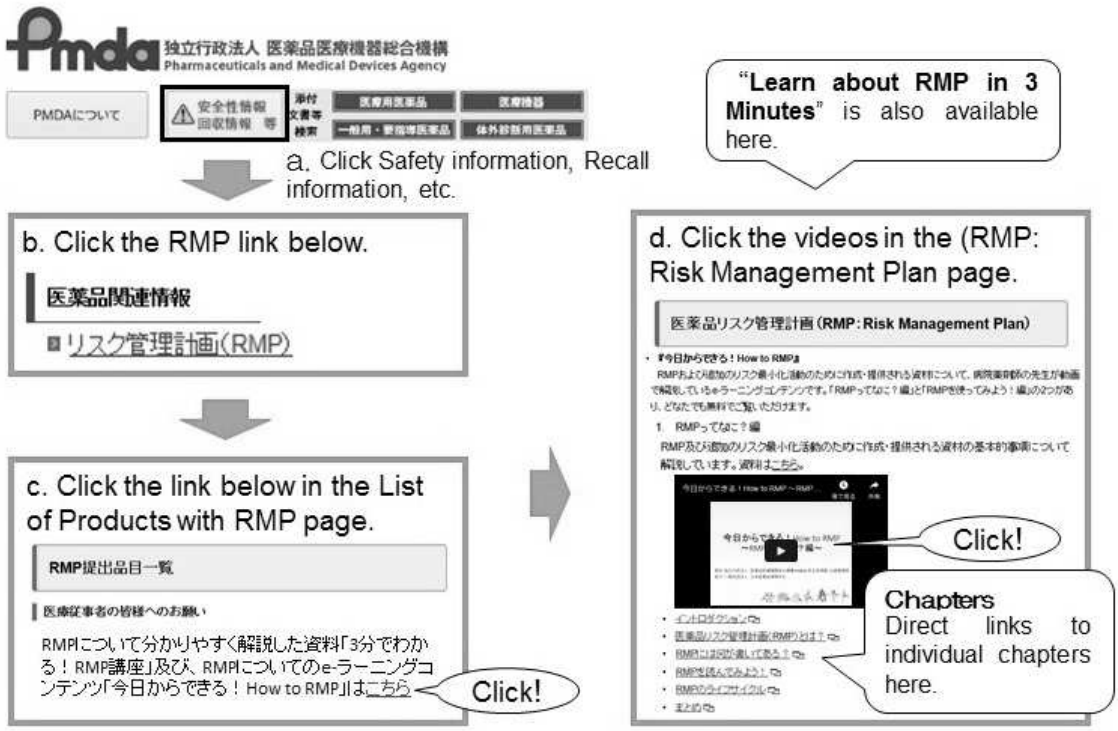
≪How to view the e-learning videos≫(only on the Japanese site)

(1) The YouTube videos are available directly from the QR code below.

(2) The videos can be viewed directly on the PMDA website as follows:
   a. Click “Safety information, recall information, etc.” on the front page of the PMDA website.
   b. Click “Risk Management Plan (RMP)” under “Drug related information”
   c. Click “Click here to access the e-learning content for RMP.”
   d. Play the listed videos in the RMP: Risk Management Plan page.

< e-learning content page > (only in Japanese)
https://www.pmda.go.jp/safety/info-services/drugs/items-information/rmp/0002.html

Figure 1 Viewing via the PMDA website



4. Request for participation in an online survey investigating utilization of safety information by the PMDA Medi-navi

From Thursday, November 26 to Sunday, December 13, 2020, PMDA will run a survey for those who belong to medical institutions among the PMDA Medi-navi users, to understand the status of their utilization of the safety information of drugs, etc., including RMP as well as to solicit requests for the improvement of usability of the PMDA Medi-navi (hereinafter referred to as Medi-navi Survey). Participation in the survey would be much appreciated. It contains mainly set-choice questions and takes around 5 minutes to complete. Users who are not registered in the PMDA Medi-navi themselves and receive Medi-navi information through a mailing list and other indirect means are also invited to participate in the survey.

The online survey page can be accessed from the URL in the delivered Medi-navi e-mail or from the PMDA website (Figure 2). The survey page is available only on the Japanese site.

Results of the Medi-navi Survey will be used as important data for the discussion towards more active use of safety information including RMP and RMP Materials in clinical settings and for the promotion of the safe use of drugs among others. To reflect more opinions from clinical settings in our future safety measures, the participation of medical professionals is requested.
Collected answers will not be used for any purposes other than those mentioned above.

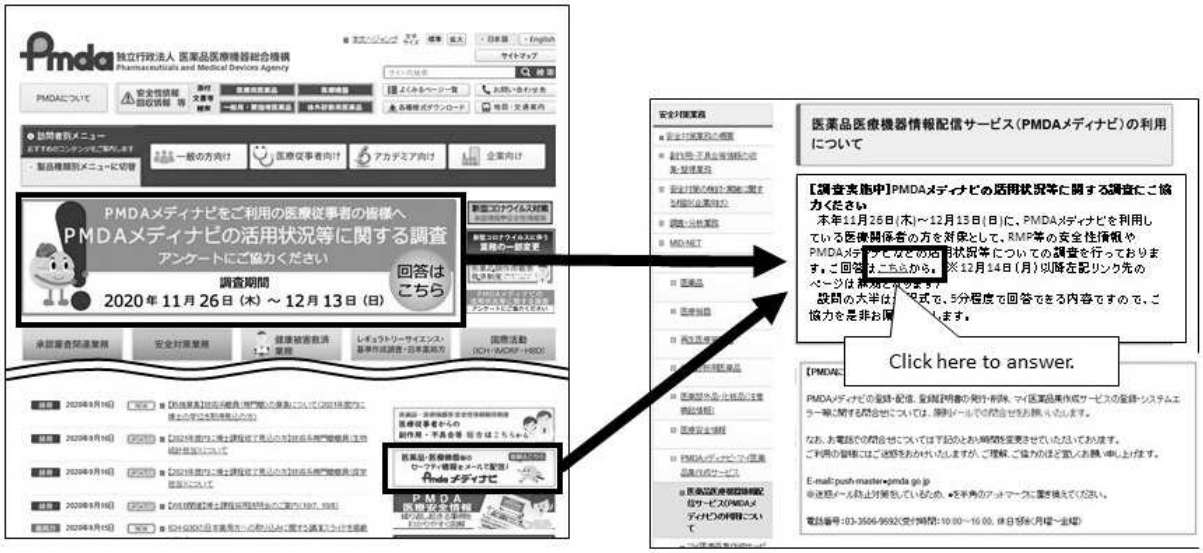


Figure 2 Answering the Medi-navi Survey from the PMDA website
(Language or format may differ in part from the actual site.)

5. Closing remarks

RMP is a document that compiles how the risk management of a drug is performed by the MAH of the drug. Use by medical professionals of the e-leaning content “Simple Enough to Start Today! How to use RMP” and others is encouraged to deepen medical professionals’ understanding of RMP thereby increasing their use of RMP as well as RMP Materials.

PMDA has taken various measures to promote the use of RMP and safety information on drugs and others. Such measures include publishing RMP and RMP materials on the agency’s website and enhancing the content of the PMDA Medi-navi newsletters.

Considering the opinions that will be collected by the Medi-Navi Survey, PMDA will continue these efforts to improve the tools to be more convenient to adopt in clinical settings, with cooperation from medical professionals.

6. Reference

Results of a Survey Investigating Access, Communication, and Utilization of Drug Safety Information at Hospitals and Pharmacies and Desirable Directions, Pharmaceuticals and Medical Devices Safety Information (No. 358, published November 2018)
https://www.pmda.go.jp/files/000226850.pdf

2

Important Safety Information

Regarding the revision of the Precautions of package inserts of drugs in accordance with the Notification dated November 5, 2020, this section will present the details of important revisions as well as the case summaries serving as the basis for these revisions.

1 Nivolumab (genetical recombination)

Branded name (name of company)	Opdivo Intravenous 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 Unresectable or metastatic renal cell carcinoma Relapsed or refractory classical Hodgkin lymphoma Relapsed or metastatic head and neck cancer Unresectable, advanced or recurrent gastric cancer that has progressed after cancer chemotherapy Unresectable, advanced or recurrent malignant pleural mesothelioma that has progressed after cancer chemotherapy Microsatellite instability high (MSI-High) unresectable advanced or recurrent colorectal cancer that has progressed after chemotherapy Unresectable advanced or recurrent esophageal cancer that has progressed after chemotherapy

PRECAUTIONS (revised language is underlined)

[Under new instructions]

8. IMPORTANT PRECAUTIONS (newly added)	<u>Fulminant hepatitis, hepatic failure, hepatic impairment, hepatitis, and sclerosing cholangitis may occur. Patients should be carefully monitored through periodic liver function tests.</u>
11. ADVERSE REACTIONS	<u>Fulminant hepatitis</u>, hepatic failure, hepatic impairment, hepatitis, and sclerosing cholangitis
11.1 Clinically Significant Adverse Reaction	<u>Fulminant hepatitis</u>, hepatic failure, hepatic impairment accompanied by increased levels of AST, ALT, γ-GTP, Al-P as well as bilirubin, etc., hepatitis, and sclerosing cholangitis may occur.
Reference information	Number of cases (for which a causal relationship between the drug and event is reasonably possible) reported during the previous approximately 41-month period (April 2017 to August 2020) Cases involving fulminant hepatitis: 3 (3 patient mortalities) Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 19 000 Japanese market launch: September 2014

Case

No.	Patient		Daily dose/ administration duration	Adverse reaction
	Sex/ age	Reason for use (complication)		No.
1	Female 80s	Renal cell carcinoma (metastases to lymph nodes (N2), multiple metastases to lung, metastasis to left adrenal gland)	140 mg 2 courses at 2-week intervals ↓ 240 mg 2 courses at 2-week intervals	**Hepatitis fulminant** Anorexia nervosa, abdominal distension, decreased weight, smoking history Day 1 of administration: Administration of nivolumab (140 mg/day) was initiated for the treatment of unresectable or metastatic renal cell carcinoma (histologic type: Chromophobe renal cell carcinoma, stage 4, TNM Classification: T3bN2M1) 32 days after administration: Nivolumab was increased to 240 mg/day. 46 days after administration (day of discontinuation): The patient received the 4th dose of nivolumab. Hepatic impairment (grade 2) was noted. Ursodeoxycholic acid was administered for treatment. 14 days after discontinuation: Hepatic impairment (grade 3) was observed. Mild malaise was noted as a clinical condition. It was observed that right adrenal metastases had appeared at this point. 20 days after discontinuation: The patient had experienced abdominal pain and general malaise for 3 days before she visited the emergency department. Marked jaundice was noted. Hepatic impairment (grade 4) was observed and prednisolone sodium succinate (80 mg/day) was administered for treatment. The patient was immediately admitted to the hospital. 21 days after discontinuation: Disturbing behavior, elevated serum ammonia levels (103 μg/dL) and hepatic encephalopathy were noted. A CT scan identified hepatic atrophy. The patient was diagnosed with hepatitis fulminant and started to receive prednisolone sodium succinate (1000 mg/day, 4 days) for treatment. Date unknown: Liver disorder, level of consciousness, and general condition did not resolve. 24 days after discontinuation: Hepatic failure was noted. The patient died of hepatitis fulminant and hepatic failure. [Autopsy findings] Massive necrosis and loss of hepatocytes and inflammatory cell infiltration were noted. The findings were considered consistent with conditions for drug-induced hepatitis fulminant. Image of submassive hepatic necrosis centered around the central veins and the canals of Herring-like structures around the portal tracts with neutrophil infiltration were noted. Numerous inflammations, portal vein endotheliitis, and central venous endotheliitis in the portal tracts and lobule were observed. In immunohistochemistry, PD-1 and CD 8-positive T cells dominated the inflammatory cells, mixed with CD 4-positive T cells and histiocytes. On the other hand, few B-cells and plasma cells were observed.

Laboratory test values:

	Day before administration	32 days after administration	46 days after administration	14 days after discontinuation	20 days after discontinuation	21 days after discontinuation	23 days after discontinuation
PT (%)	—	—	—	—	13	10	11
PT (second)	—	—	—	—	39.3	48.6	43.3
AST (IU/L)	17	37	125	723	—	324	166
ALT (IU/L)	4	12	39	178	—	208	144
ALT (IU/L)	231	287	514	1 628	—	1 065	968
γ-GTP (IU/L)	94	132	336	778	—	418	414
T-Bil (mg/dL)	0.51	0.49	0.77	3.73	—	11.81	15.28

Concomitant drugs: Unknown

3
Revision of Precautions (No.318)

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 November 5, 2020.

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

Branded name	Copaxone S.C. Injection 20 mg Syringe (Takeda Pharmaceutical Company Limited.)
[Under Old instructions]	
Important Precaution (newly added)	Hepatic impairment may occur. Liver function tests should be performed prior to the initiation of, and periodically during, the administration of this drug.
Adverse Reactions Clinically Significant Adverse Reactions (newly added)	Hepatic impairment: Hepatic impairment accompanied by increased levels of AST and ALT, etc., may occur. If any abnormalities are observed, appropriate measures should be taken such as discontinuing administration of this drug.
[Under New instructions]	
8. IMPORTANT PRECAUTIONS (newly added)	Hepatic impairment may occur. Liver function tests should be performed prior to the initiation of, and periodically during, the administration of this drug.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Hepatic impairment Hepatic impairment accompanied by increased levels of AST and ALT, etc., may occur.

2 Other antitumor agents
Nivolumab (genetical recombination)

Branded name	Opdivo Intravenous Infusion 20 mg, 100 mg, 120 mg, 240 mg (Ono Pharmaceutical Co., Ltd.)
[Under New instructions]	
8. IMPORTANT PRECAUTIONS (newly added)	Fulminant hepatitis, hepatic failure, hepatic impairment, hepatitis, and sclerosing cholangitis may occur. Patients should be carefully monitored through periodic liver function tests.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions**	Fulminant hepatitis, hepatic failure, hepatic impairment, hepatitis, and sclerosing cholangitis Fulminant hepatitis, hepatic failure, hepatic impairment accompanied by increased levels of AST, ALT, γ-GTP, Al-P as well as bilirubin, etc., hepatitis, and sclerosing cholangitis may occur.

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 October 2020)

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

	Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
◎	Oxycodone hydrochloride hydrate*1 OxyContin TR Tablets 5 mg, 10 mg, 20 mg, 40 mg	Shionogi Pharma Co., Ltd.	October 29, 2020
◎	Glucagon Baqsimi Nasal Powder 3 mg	Eli Lilly Japan K.K.	October 2, 2020
	Trastuzumab deruxtecan (genetical recombination) *2 Enhertu For Intravenous Drip Infusion 100 mg	Daiichi Sankyo Co., Ltd.	September 25, 2020
	Ravulizumab (genetical recombination) *3 Ultomiris for Intravenous Infusion 300 mg	Alexion Pharmaceuticals, Inc.	September 25, 2020
	Tildrakizumab (genetical recombination) Ilumya Subcutaneous Injection 100 mg Syringe	Sun Pharma Japan Limited	September 23, 2020
	Siponimod fumaric acid Mayzent tablets 0.25 mg, 2 mg	Novartis Pharma K.K.	September 14, 2020
	Ferric carboxymaltose Ferinject solution for injection/infusion 500 mg	Zeria Pharmaceutical Co., Ltd.	September 1, 2020
	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	Novartis Pharma K.K.	August 26, 2020

Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
hard capsules		
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*4 Velexbru Tablets 80 mg	Ono Pharmaceutical Co., Ltd.	August 21, 2020
Vonicog alfa (genetical recombination) Vonvendi Intravenous 1300	Shire Japan KK	August 17, 2020
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*5 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*6 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
Lurasidone hydrochloride	Sumitomo Dainippon	June 11,

	Nonproprietary name Branded name on	Name of the MAH	Date of EPPV initiate
	Latuda tablets 20 mg, 40 mg, 60 mg, 80 mg	Pharma Co., Ltd.	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*7 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
	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

*1 Relief of moderate to severe chronic pain difficult to manage with non-opioid analgesics or other opioid analgesics

*2 HER2 positive unresectable advanced or recurrent gastric cancer that has progressed after chemotherapy

*3 Atypical hemolytic uremic syndrome

*4 Primary macroglobulinaemia and lymphoplasmacytic type lymphoma

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

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

*7 Progressive fibrosing interstitial lung disease

＜List of corrections in the PMDSI No.373-No.377＞

"Date of EPPV initiate" for "Latuda tablets 20 mg, 40 mg, 60 mg, 80 mg" in the List of Products Subject to Early Post-marketing Phase Vigilance

Original : April 22, 2020
Revised : June 11, 2020