Pharmaceuticals and Medical Devices Safety Information

No. 326 September 2015

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This *Pharmaceuticals and Medical Devices Safety Information (PMDSI)* is issued based on 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 (http://www.mhlw.go.jp/, only available in Japanese language).

Available information is listed here

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Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare
1-2-2 Kasumigaseki, Chiyoda-ku, Tokyo
100-8916 Japan

Translated by
Pharmaceuticals and Medical Devices Agency

Office of Safety I,
Pharmaceuticals and Medical Devices Agency
3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo
100-0013 Japan E-mail: safety.info@pmda.go.jp

Pharmaceuticals and Medical Devices Safety Information

No. 326 September 2015

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

[Outline of Information]

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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 medical and pharmaceutical providers.

If medical and pharmaceutical providers 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 medical and pharmaceutical providers, drugstore and pharmacy personnel are also required to report safety issues related to drugs and medical devices.

Abbreviations

ADR	Adverse drug reaction
CRP	C-reactive protein
CT	Computed tomography
EPPV	Early Post-marketing Phase Vigilance
FOLFOX	Folinic acid, Fluorouracil, and Oxaliplatin
KL-6	Krebs von den Lunge-6
LDH	Lactate dehydrogenase
MAH	Marketing authorization holder
MHLW	Ministry of Health, Labour and Welfare
SIDS	Sudden infant death syndrome
SP-D	Surfactant protein D
SpO_2	Oxygen saturation
TEN	Toxic epidermal necrolysis
WBC	White blood cell

1

Epidemiological Survey on Vaccination and Sudden Death of Infants

1. Introduction

In order to investigate the relationship between vaccination and sudden death of infants, the Ministry of Health, Labour and Welfare (MHLW) has been conducting a national epidemiological survey since December 2012 with the cooperation of institutions certified as training facilities for those wishing to become a Certified Board Pediatrician of the Japan Pediatric Society and related institutions.

This section presents an overview of the survey.

2. Objectives of the survey

It was determined that this epidemiological survey should be conducted based on a statement made at the joint meeting of the Subcommittee on Drug Safety of Committee on Drug Safety and the Vaccine Adverse Reaction Review Committee for Carcinoma of the Uterine Cervix. The statement was “A system should be established that will allow a positive epidemiological survey to be conducted in the future by obtaining the cooperation of related parties in order to verify if a relationship exists between fatalities or serious adverse events and vaccines.”

During infancy, there are many opportunities to receive vaccinations and sudden death from an unknown cause. Thus, vaccination and death may incidentally coincide at a certain frequency. However, many parents with small children cannot eliminate their anxiety regarding vaccination even if a direct and clear causality has been ruled out in case of death after vaccination based on a subsequent examination because there are no data to epidemiologically verify this in Japan. The MHLW has been conducting this epidemiological survey in order to provide more accurate information on the safety of vaccination.

3. Survey methods

As shown in **Figure 1**, this survey has been conducted as a prospective case-control study by a research group in which the National Institute of Infectious Diseases, requested by the MHLW, plays a central role. The group requests institutions certified as training facilities for those wishing to become a Certified Board Pediatrician of the Japan Pediatric Society and related institutions to provide information on cases of sudden death of infants from an unknown cause and control infants.

When sudden death of infants from an unknown cause occurs, the “Interview and Checklist for Diagnosis of Sudden Infant Death Syndrome (SIDS)” (**Figure 2**) in the “Diagnostic Guideline on SIDS (second edition)” will be utilized in order to properly diagnose SIDS. When sudden death of infants from an unknown cause occurs in medical institutions participating in the research, the institutions are requested to submit a copy of the checklist obtained from the medical records of the case. In addition, the institutions are requested to submit the Control Group Questionnaire (**Figure 3**) separately prepared for this survey after entering the required information for 2 matched control infants.

Collected information will be epidemiologically and statistically analyzed at the National Institute of Infectious Diseases. Survey results will be published in review meetings, etc.

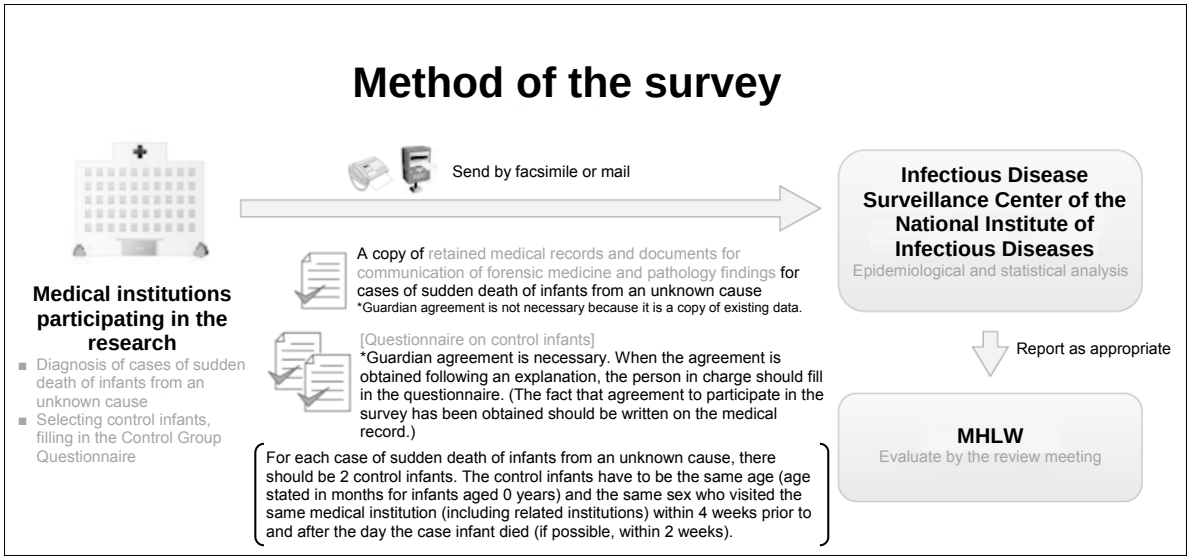

Figure 1　Method used in the epidemiological survey

Figure 2　Interview and Checklist for Diagnosis of SIDS

突然死の症例を診断された前後４週間（できれば前後２週間）で、年齢（0歳の場合は月齢）、性別が同じお子さん２名についてご記入ください。
なお、２名のお子様は、実医療機関小児科を受診したお子様の中から、無作為に選んでください（死亡例を診断後受診順等）。

ワクチン接種と乳幼児の突然死に関する疫学調査
（対照例用問診・チェックリスト）

登録及びカルテ保存用紙　　医療機関名（　　）
※　死亡「症例」の　ID-No.（　　）　担当医（　　）
直近1ヶ月間のワクチン歴は、母子手帳あるいはカルテからの転載をお願いいたします。

記載年月日	年　月　日	調査実施前日までの様子	
医療機関用 No.		鼻汁症状	①なし　②あり（　　）
		発熱	①なし　②あり（最高体温　℃）
年齢・性別	歳　ヶ月　男・女	嘔吐	①なし　②あり（　　）
普段の健康時体位	①あおむけ　②うつぶせ　③その他（　）	直近1ヶ月間のワクチン歴	ここに、書ききれない場合は、左下の欄をご活用いただき、ご記入をお願いいたします。
普段の健康時の泣い様の有無	①いつもする ②どちらかといえばする ③どちらかといえばしない ④しない		あり（同時接種　有　無）　なし ありの場合、各々のワクチン名と接種年月日： ワクチン名：　接種日　年　月　日 ワクチン名：　接種日　年　月　日
寝返りの有無	①あおむけからうつぶせに自由に出来る（おおよそ生後　ヶ月頃より出来た） ②うつぶせからあおむけに自由に出来る（おおよそ生後　ヶ月頃より出来た） ③まだ寝返りは一人で出来ていない	出生体重	g　在胎　週　日
		分娩中の異常	①なし　②あり（　）
		第何子	子（同胎　人）
		栄養方法（現在）	①母乳　②ミルク　③都乳食　④普通食
受診時の臨床診断	（　）	普段の睡眠中の着衣	①薄着　②普通　③厚着
個人の特定には施設名・担当医名・医療機関用 No. は外し、連結不能とします。 この用紙をコピーしてカルテ保存用紙としてお使い下さい。 ALTE: Apparent life threatening event; 突発性危急事態		発育発達の遅れ	①なし　②あり（　）
		基礎疾患の有無	①なし　②あり（　）
直近１ヶ月間のワクチン歴が右上欄に書ききれなかった場合は、この欄をご利用ください。		主な既往歴	①なし　②あり（　）
		原因不明のALTE（突発性危急事態）歴の有無	①なし　②あり
		これまでに無呼吸やチアノーゼ発作の既往	①なし　②あり（病名　）
		母親・父親の年齢	母親　歳　／　父親　歳
		母親の仕事	①なし　②あり（　）
		母親の喫煙	①なし　②あり（　本/日）
		父親の喫煙	①なし　②あり（　本/日）
		同胞のSIDS（乳幼児突然死症候群）又はSIDS疑い、原因不明のALTE（突発性危急事態）の有無	①なし ②あり（SIDS・原因不明のALTE）

ご協力いただき、どうもありがとうございました。

Figure 3　Control Group Questionnaire

4. Request for cooperation in the survey

This survey involves collecting as many cases as possible because it targets sudden death of infants from an unknown cause, which is an event that occurs very rarely.

Therefore, the concerned medical institutions were requested to utilize the “Interview and Checklist for Diagnosis of SIDS” included in the “Diagnostic Guideline on SIDS (second edition)” as advised in a notification dated October 24, 2012. The documents are encouraged to be used for communicating the diagnosis, findings of the forensic investigation, and pathology findings for sudden death of infants of unknown cause. The notification also outlined the aim of the survey and requested the cooperation of institutions in the collection of case information.

[References]

1. Website for the epidemiological survey on vaccination and sudden death of infants (available only in Japanese): http://www.nih.go.jp/niid/ja/vaccine-j/3047-vaccine-d.html
2. Press release at the start of this survey (only available in Japanese): http://www.mhlw.go.jp/stf/houdou/2r9852000002q33r.html
3. Epidemiological survey review meeting on vaccination and sudden death of infants (available only in Japanese): http://www.mhlw.go.jp/stf/shingi/other-iyaku.html?tid=128769
4. Diagnostic Guideline on SIDS (second edition) (available only in Japanese): http://www.mhlw.go.jp/bunya/kodomo/sids_guideline.html

2

Important Safety Information

Regarding the revision of the Precautions section of package inserts of drugs in accordance with the Notification dated August 6, 2015, the contents of important revisions and case summaries that served as the basis for these revisions are provided in this section.

1 Sterile Talc

Brand name (name of company)	Unitalc Intrapleural Suspensions 4 g (Nobelpharma Co., Ltd.)
Therapeutic category	Antineoplastics-Miscellaneous
Indications	Prevention of recurrent malignant pleural effusion

PRECAUTIONS (underlined parts are revised)

Careful administration	Patients with interstitial lung disease
Adverse reactions (clinically significant adverse reactions)	**Interstitial lung disease**: Interstitial lung disease may occur. Patients should be carefully monitored for clinical symptoms such as cough, dyspnoea, and pyrexia. If any abnormalities are observed, tests such as chest X-rays or chest computed tomography (CT) scans should be conducted. If interstitial lung disease is suspected, appropriate measures such as the administration of adrenal corticosteroids should be adopted.
Reference information	The number of reported adverse reactions (for which a causal relationship to the drug could not be ruled out) for the past 1 year and 7 months (from initial marketing to June 2015) Cases of adverse events associated with interstitial lung disease: 4 cases (no fatal case) Number of patients using this drug estimated by the marketing authorization holder (MAH): Approximately 8 000 (from June 2014 to May 2015) Launched in Japan: December 2013

Case summary

No.	Patient		Daily dose/ Treatment duration	Adverse reactions
	Sex/ Age	Reason for use (complications)		Clinical course and therapeutic measures
1	Female 60s	Pleurodesis (breast cancer, pleurisy)	4 g, once	Drug-induced lung disorder (left) Day 1 of administration Sterile talc at a dose of 4 g was intrapleurally administered to the pleural adhesion from 16:30 to 16:45. 1 day after administration Body temperature was 38.0°C at 6:30. The patient had dyspnoea and hypoxaemia and received oxygen at a rate of 2 L/min, and oxygen saturation (SpO_2) was reduced from 98% to 88%. Left ground-glass opacity was observed on her X-ray image. After the oxygen level was increased, dyspnoea was resolving. 2 days after administration No remarkable change in the ground-glass opacity was visible on her X-ray image.

				7 days after administration The administration of 125 mg/day of methylprednisolone was started (for 3 days). The ground-glass opacity was resolving slightly. Oxygenation was resolving. 13 days after administration The administration of oxygen at the rate of 1 L/min improved SpO_2 to 94%. 32 days after administration The administration of oxygen was discontinued. The drug-induced lung disorder was resolving.

Laboratory examination

	24 days before administration	2 days after administration	4 days after administration	48 days after administration
WBC count (/μL)	10 400	8 500	8 300	10 700
LDH (IU/L)	-	159	177	677
CRP (mg/dL)	0.29	28.41	16.5	1.65
KL-6 (U/L)	-	-	1 651	1 098

Concomitant drugs: none

Case summary

No.	Patient		Daily dose/ Treatment duration	Adverse reactions
	Sex/ Age	Reason for use (complications)		Clinical course and therapeutic measures
2	Male 60s	Malignant pleural effusion (gastric cancer)	4 g, once	Interstitial pneumonia Approximately 1 year before administration The patient underwent pylorogastrectomy for Borrmann type II gastric cancer. 5 days before administration The patient visited the hospital with the chief complaint of a feeling of dyspnoea. Imaging revealed a large amount of right pleural effusion. This was a malignant pleural effusion caused by the dissemination of gastric cancer to pleura. Day 1 of administration The pleural effusion was drained using a trocar tube, and 4 g of sterile talc was injected into the right pleural cavity to prevent adhesion of the pleural. 13 days after administration The patient had dyspnoea when walking stairs. No abnormality was found in the sputum test. 14 days after administration Feeling of dyspnoea worsened, and chest CT showed the appearance of an interstitial opacity in the middle and lower right lung field. Both Krebs von den Lunge-6 (KL-6) and surfactant protein D (SP-D) were increased, and the patient was diagnosed as having interstitial pneumonia. The patient also presented with respiratory failure. The administration of oxygen and steroid mini-pulse therapy were started. Bronchoalveolar lavage was performed on the same day, and *Streptococcus* was detected; however, this was not considered to be a significant infection. The administration of sulbactam sodium/ampicillin

				sodium for intravenous injection was started (for 4 days). From that point, responsiveness to steroids was favorable, and the respiratory status was resolving. 36 days after administration The patient was discharged from the hospital. At the time of discharge, 30 mg of prednisolone was administered for maintenance.

Laboratory examination

	8 days before administration	1 day after administration	13 days after administration	16 days after administration	28 days after administration	39 days after administration
WBC count (/μL)	8 700	10 200	11 600	20 500	22 500	15 600
LDH (IU/L)	271	267	613	431	474	449
CRP (mg/dL)	5.85	11.29	11.05	10.10	8.90	7.50
KL-6 (U/L)	-	-	2 510	-	5 510	-
SP-D (ng/mL)	-	-	118.8	-	59.4	-

Concomitant drugs: none

2 Panitumumab (Genetical Recombination)

Brand name (name of company)	Vectibix Intravenous Infusions 100 mg, 400 mg (Takeda Pharmaceutical Company Limited)
Therapeutic category	Antineoplastics-Miscellaneous
Indications	*KRAS* wild-type, incurable, unresectable, advanced/recurrent colorectal cancer

PRECAUTIONS (underlined parts are revised)

Adverse reactions (clinically significant adverse reactions)

Toxic epidermal necrolysis (TEN) and oculomucocutaneous syndrome (Stevens–Johnson syndrome): Toxic epidermal necrolysis or oculomucocutaneous syndrome may occur. Patients should be carefully monitored. If any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be adopted.

Reference information

Number of reported adverse reactions (for which a causal relationship to the drug could not be ruled out) for the past 3 years (from April 2012 to May 2015)
TEN: 1 case (1 fatal case)
Number of patients using this drug estimated by MAH: approximately 9 374 (from October 2013 to September 2014)
Launched in Japan: June 2010

Case summary

No.	Patient		Daily dose/ Treatment duration	Adverse reactions
	Sex/ Age	Reason for use (complications)		Clinical course and therapeutic measures
1	Female 60s	Colon cancer (metastases to the liver, peripheral neuropathy, gastritis, hypertension, hyperlipidaemia, diarrhoea, insomnia, pruritus)	6 mg/kg every 2 weeks, a total of 25 doses	**TEN** 36 days before administration At another hospital, the patient had been diagnosed with large intestine carcinoma and multiple metastases to the liver and visited our hospital. 23 days before administration The primary lesion was laparoscopically resected, and a stoma was formed. 5 days before administration Chemotherapy was planned due to an increase in the number of metastases to the liver. Day 1 of administration Combination therapy with Folinic acid, fluorouracil, and oxaliplatin (FOLFOX) and panitumumab (first dose) was started as the first-line therapy (*KRAS* wild-type). 139 days after administration FOLFOX and panitumumab (ninth dose) were administered. 155 days after administration Panitumumab alone (10th dose) was administered (6 mg/kg) as the second-line therapy. 369 days after administration (day of completion) Panitumumab (25th dose) was administered. No serious skin disorder caused by panitumumab was observed before the 25th administration. Appropriately 3 days after completion (day of onset) Erythema with an erosion appeared on the abdomen, upper back, and upper extremities. 7 days after completion

				The patient was diagnosed as having a skin disorder caused by panitumumab. Olopatadine hydrochloride was orally administered, and topical steroids (difluprednate and mometasone furoate) were prescribed. 14 days after completion The erosive area expanded. The patient was diagnosed as having severe erythema multiforme and was admitted to hospital on the same day. An oral steroid (betamethasone/*d*-chlorpheniramine maleate) and topical clobetasol propionate were started. 20 days after completion Although epithelialization was partially observed on the erosive surface, the erosive surface occupied 30% or more of the body on a body surface basis. Therefore, the disease was judged to have advanced to become TEN. Transfusion was started. 21 days after completion Blood pressure decreased, and vital signs rapidly worsened. Death was confirmed thereafter (cause of death, TEN; autopsy was not performed.)
	Concomitant drugs: fluorouracil, calcium folinate, oxaliplatin, mecobalamin, telmisartan, amlodipine besilate, clopidogrel sulfate, aspirin, ethyl icosapentate, combination drug containing *Clostridium butyricum*, zolpidem tartrate, fexofenadine hydrochloride, lansoprazole			

3

Revision of Precautions (No. 267)

This section presents details of revisions to the Precautions section of package inserts and brand names of drugs that have been revised in accordance with the Notifications dated August 6, 2015.

1

Psychotropics

(1) Hydroxyzine hydrochloride
(2) Hydroxyzine pamoate

Brand name	a. Atarax Tablets 10 mg and 25 mg and Atarax-P Parenteral Solution 25 mg/mL and 50 mg/mL (Pfizer Japan Inc.) b. Atarax-P Powder 10%, Atarax-P Capsules 25 mg and 50 mg, Atarax-P Syrup 0.5%, Atarax-P Dry Syrup 2.5% (Pfizer Japan Inc. and others)
Careful administration	Patients with prolonged QT interval (including those with congenital long QT interval syndrome), patients being administered drugs known to prolong QT interval, and patients with significant bradycardia or hypokalaemia
Adverse reactions (clinically significant adverse reactions	**QT interval prolongation and ventricular tachycardia (including torsades de pointes)**: QT interval prolongation or 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 adopted.

2

Central nervous system agents-Miscellaneous

Memantine hydrochloride

Brand name	Memary Tablets 5 mg, 10 mg, and 20 mg, and Memary OD Tablets 5 mg, 10 mg, and 20 mg (Daiichi Sankyo Company, Limited)
Adverse reactions (clinically significant adverse reactions	**Rhabdomyolysis**: Rhabdomyolysis may occur. Patients should be carefully monitored. If symptoms including myalgia, feelings of weakness, increased creatine kinase (creatine phosphokinase), or increased myoglobin in blood and urine are observed, administration of this drug should be discontinued, and appropriate measures should be adopted. In addition, caution should be exercised for development of acute renal failure due to rhabdomyolysis.

3

Antidotes

Deferasirox

Brand name	Exjade Dispersible Tablets 125 mg and 500 mg (Novartis Pharma K.K.)
Adverse reactions (clinically significant	**Gastrointestinal perforations, gastric ulcers (including multiple ulcers), duodenal ulcers, and gastrointestinal haemorrhage**:

adverse reactions	Gastrointestinal perforations, gastric ulcers (including multiple ulcers), duodenal ulcers, or gastrointestinal haemorrhage may occur. Patients should be carefully monitored. If any abnormalities are observed, appropriate measures such as drug suspension should be adopted.

4 **Antineoplastics-Miscellaneous**

Pomalidomide

Brand name	Pomalyst Capsules 1 mg, 2 mg, 3 mg, and 4 mg (Celgene K.K.)
Adverse reactions (clinically significant adverse reactions	**Hepatic function disorder and jaundice:** Hepatic function disorder or jaundice associated with elevated AST (GOT), ALT (GPT), γ-GTP, or bilirubin levels may occur. Patients should be carefully monitored through periodic testing, etc. If any abnormalities are observed, appropriate measures such as dose reduction, drug suspension, or discontinuation of administration should be adopted.

5 **Antivirals**

(1) Zanamivir hydrate
(2) Laninamivir octanoate hydrate

Brand name	a. Relenza (GlaxoSmithKline K.K.) b. Inavir Dry Powder Inhalers 20 mg (Daiichi Sankyo Company, Limited)
Careful administration	Patients with a history of hypersensitivity to milk products
Important precautions	This drug is using the lactose hydrate that contains milk proteins. There have been reports of anaphylaxis on the administration of this drug to patients with a history of hypersensitivity to milk products. Therefore, caution should be exercised when administering this drug to such patients.

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 new drugs refers to any safety assurance activities that are conducted within a period of 6 months just after marketing of a new drug. It is imposed that its MAH is responsible for collecting the ADR (Adverse drug reaction) from all of the medical institutions where the drugs are used and taking safety measures. The aim of the EPPV is to promote the rational proper use of drugs in medical treatments, and to promptly take actions for prevention of the serious ADR. EPPV is specified as a condition of approval.

(As of August 31, 2015)
◎: Products for which EPPV was initiated after July 1, 2015

	Nonproprietary name Brand name on	Name of the MAH	Date of EPPV initiate
◎	nintedanib ethanesulfonate Ofev Capsules 100 mg, 150 mg	Nippon Boehringer Ingelheim Co., Ltd.	August 31, 2015
◎	panobinostat lactate Farydak Capsules 10 mg, 15 mg	Novartis Pharma K.K.	August 31, 2015
◎	ipilimumab (genetical recombination) Yervoy Injection 50 mg	Bristol-Myers K.K.	August 31, 2015
◎	asfotase alfa (genetical recombination) Strensiq Subcutaneous Injection 12 mg/0.3 mL, 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/1 mL, 80 mg/0.8 mL	Alexion Pharma G.K.	August 31, 2015
◎	catridecacog (genetical recombination) NovoThirteen Intraveous Injections 2500	Novo Nordisk Pharma Ltd.	August 27, 2015
◎	nitric oxide INOflo for Inhalation 800 ppm[*1]	Air Water Inc.	August 24, 2015
◎	bosentan hydrate Tracleer Tablets 62.5 mg[*2]	Actelion Pharmaceuticals Japan Ltd.	August 24, 2015
◎	ribavirin Rebetol Capsules 200 mg[*3]	MSD K.K.	July 29, 2015
◎	clindamycin phosphate hydrate/benzoyl peroxide Duac Combination Gel	GlaxoSmithKline K.K.	July 17, 2015
	gadobutrol Gadovist IV Injection 1.0 mol/L Syringe 5 mL, 1.0 mol/L Syringe 7.5 mL, 1.0 mol/L Syringe 10 mL	Bayer Yakuhin, Ltd.	June 30, 2015
	bortezomib Velcade Injection 3 mg[*4]	Janssen Pharmaceutical K.K.	June 26, 2015
	lidocaine/propitocaine EMLA Cream[*5]	Sato Pharmaceutical Co., Ltd.	June 26, 2015

Nonproprietary name Brand name on	Name of the MAH	Date of EPPV initiate
edaravone Radicut Injection 30 mg, Radicut Bag for I.V. Infusion 30 mg[*6]	Mitsubishi Tanabe Pharma Corporation	June 26, 2015
botulinum toxin type A Botox for Injection 50 units, 100 units[*7]	GlaxoSmithKline K.K.	June 26, 2015
tazobactam/piperacillin hydrate Zosyn IV Injection 2.25 and 4.5, Zosyn Fixed-dose Bag for I.V. Infusion 4.5[*8]	Taiho Pharmaceutical Co., Ltd.	June 26, 2015
pitavastatin calcium hydrate Livalo Tablets 1 mg and 2 mg, Livalo OD Tablets 1 mg and 2 mg[*9]	Kowa Company, Ltd.	June 26, 2015
ramucirumab (genetical recombination) Cyramza Injection 100 mg, 500 mg	Eli Lilly Japan K.K.	June 22, 2015
macitentan Opsumit Tablet 10 mg	Actelion Pharmaceuticals Japan Ltd.	June 9, 2015
tramadol hydrochloride Onetram Tablets 100 mg	Nippon Shinyaku Co., Ltd.	June 2, 2015
trelagliptin succinate Zafatek Tablets 50 mg, 100 mg	Takeda Pharmaceutical Company Limited	May 28, 2015
peginterferon alfa-2b (genetical recombination) Peginteron Powder for Injection 50 μg/0.5 mL, 100 μg/0.5 mL, 150 μg/0.5 mL[*10]	MSD K.K.	May 26, 2015
ramosetron hydrochloride Irribow Tablets 2.5 μg and 5 μg[*11], Irribow OD Tablets 2.5 μg and 5 μg[*11]	Astellas Pharma Inc.	May 26, 2015
duloxetine hydrochloride Cymbalta Capsules 20 mg, 30 mg[*12]	Shionogi & Co., Ltd.	May 26, 2015
nalfurafine hydrochloride Nopicor Capsules 2.5 μg[*13]	Toray Medical Co., Ltd.	May 26, 2015
aripiprazole hydrate Abilify prolonged release aqueous suspension for IM injection 300 mg and 400 mg, Abilify prolonged release aqueous suspension for IM injection 300 mg Syringe and 400 mg Syringe	Otsuka Pharmaceutical Co., Ltd.	May 25, 2015
colistin sodium methanesulfonate Aldreb for Injection 150 mg	GlaxoSmithKline K.K.	May 25, 2015
(1) sofosbuvir, (2) ribavirin (1) Sovaldi Tablets 400 mg, (2) Copegus Tablets 200 mg[*14]	(1) Gilead Sciences, Inc. (2) Chugai Pharmaceutical Co., Ltd.	May 25, 2015
pomalidomide Pomalyst Capsules 1 mg, 2 mg, 3 mg, 4 mg	Celgene K.K.	May 21, 2015
nalfurafine hydrochloride Remitch Capsules 2.5 μg	Toray Industries, Inc.	May 20, 2015
lenvatinib mesilate Lenvima Capsules 4 mg, 10 mg	Eisai Co., Ltd.	May 20, 2015

Nonproprietary name Brand name on	Name of the MAH	Date of EPPV initiate
aclidinium bromide Eklira 400 µg Genuair 30, 400 µg Genuair 60	Kyorin Pharmaceutical Co., Ltd.	May 20, 2015
4-strain meningococcal vaccine (diphtheria toxoid conjugate) Menactra intramuscular injection	Sanofi K.K.	May 18, 2015
metronidazole Rozex Gel 0.75%	Galderma S.A.	May 11, 2015
elosulfase alfa (genetical recombination) Vimizim I.V. Infusion 5 mg	BioMarin Pharmaceutical Japan Inc.	April 23, 2015
N/A Allergen Extract Mites Subcutaneous Injections for Treatment “Torii” 10,000 JAU/mL, 100 000 JAU/mL	Torii Pharmaceutical Co., Ltd.	April 21, 2015
nitisinone Orfadin Capsules 2 mg, 5 mg, 10 mg	Astellas Pharma Inc.	April 14, 2015
dolutegravir sodium/lamivudine/abacavir sulfate Triumeq Combination Tablets	ViiV Healthcare K.K.	April 10, 2015
benzoyl peroxide Bepio Gel 2.5%	Maruho Co., Ltd.	April 1, 2015
efraloctocog alfa (genetical recombination) Eloctate Intravenous 250, 500, 750, 1000, 1500, 2000, 3000	Biogen Idec Japan Ltd.	March 9, 2015

*1 Improvement of pulmonary hypertension in the perioperative period of cardiac surgery
*2 Suppress development of digital ulcers in systemic sclerosis (scleroderma)
*3 Improvement of viraemia in patients with serogroup 2 chronic hepatitis C or compensated cirrhosis type C in combination therapy with sofosbuvir
*4 Mantle cell lymphoma
*5 Pediatric dose for pain relief during skin laser therapy and indications for pain relief during pricking injection of an intravenous indwelling needle
*6 Suppress progression of functional disorders associated to amyotrophic lateral sclerosis (ALS)
*7 Strabismus
*8 Febrile neutropenia (new pediatric dose)
*9 Familial hypercholesterolaemia (new pediatric dose)
*10 Postoperative adjuvant therapy for malignant melanoma
*11 Irritable bowel syndrome with diarrhea in females
*12 Pain associated with fibromyalgia
*13 Improvement of pruritus in patients with chronic liver disease
*14 Improvement of viraemia in patients with serogroup 2 chronic hepatitis C or compensated cirrhosis type C in combination therapy with sofosbuvir