Pharmaceuticals and Medical Devices Safety Information

No. 418 April 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

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

The PMDA Medi-navi is an e-mail mailing list service that serves to provide essential safety information released by the MHLW and PMDA. Subscribing to the Medi-navi will allow you to receive this information on the day of its release.
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Pharmaceuticals and Medical Devices Safety Information

No. 418 April 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

This English version of PMDSI is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Abbreviations

ADR	Adverse Drug Reaction
CTCAE	Common Terminology Criteria for Adverse Events
DLST	Drug-induced Lymphocyte Stimulation Test
EPPV	Early Post-marketing Phase Vigilance
FY	Fiscal Year
JJSEM	Journal of Japanese Society for Emergency Medicine
MAH	Marketing Authorization Holder
MHLW	Ministry of Health, Labour and Welfare
MRCP	Magnetic Resonance Cholangiopancreatography
OD	Overdose
OTC	Over-the-Counter Drugs
PMDA	Pharmaceuticals and Medical Devices Agency
WG	Working Group

1

Initiatives Against Abuse of Over-the-Counter Drugs

1. Introduction

In recent years, there has been a rapid increase in cases of abuse of over-the-counter (OTC) drugs such as antitussive and expectorant drugs, leading to emergency transportation or drug dependence, mainly in young people in their teens and twenties. Therefore, it is required to raise awareness for prevention and to establish a system for consultation/support for young people. Accordingly, in FY 2024, the MHLW implemented the "Project for Measures to Prevent Abuse of OTC Drugs by Utilizing the Societies of School Pharmacists and Regional Pharmacists" (hereinafter referred to as the "Project"), and prepared awareness-raising materials and guidance manuals for those involved in pharmaceutical sales. In addition, seminars using these materials were held. Details are presented below.

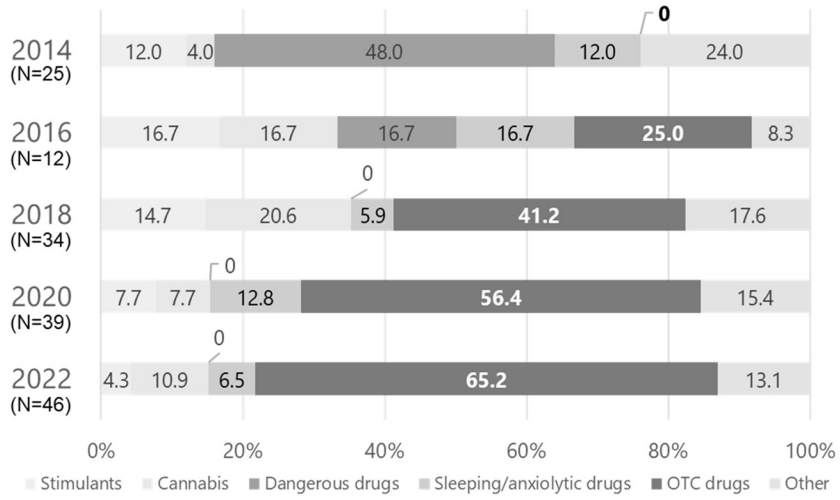
2. Background

Conventional measures against drug abuse have been focused on illegal drugs such as stimulants, cannabis, and dangerous drugs. Possession or use of these drugs is an illegal act and has been strictly clamped down on.

Thereafter, after the enforcement of the Pharmaceuticals and Medical Devices Act (in 2014), which prohibits possession and use of designated drugs, it has been reported that the number of cases being transported to a hospital associated with OTC drugs tends to increase[1)], and a survey conducted in high school students attending full-day school reported that the rate of experiencing abuse of OTC drugs (within the past 1 year) was 1.6% (1.2% in males and 1.7% in females), which was approximately 10 times higher than that of cannabis, which is the most abused drug among illicit drugs[2)]. Thus, the main ingredient of abused drugs in young people is shifting to OTC drugs (Figure 1). However, existing awareness-raising materials mainly focused on illegal drugs such as stimulants, cannabis, and dangerous drugs, lacking information related to abuse, especially overdose (OD), of OTC drugs.

Moreover, unlike prohibited drugs such as narcotics/stimulants and dangerous drugs, OTC drugs can be purchased at pharmacies, drug stores, etc., and it is difficult to prevent their abuse only by restrictions on selling the "drugs that may cause abuse, etc." In addition to measures to prevent abuse through sales regulations and raising awareness of proper use of drugs, it was necessary to take comprehensive measures to prevent abuse such as publicizing the risk of abuse, bridging to consultation/support facilities, and publicizing the methods of consultation in sales and school settings.

Figure. 1 "Changes in major drugs" in teenage patients treated for drug dependence at psychiatric medical institutions nationwide



Source: Survey on the Actual State of Drug-related Psychiatric Diseases at Psychiatric Medical Facilities Nationwide (2022) (National Center of Neurology and Psychiatry)
(FY 2022 Health, Labour and Welfare Policy Research Grants [Research on Regulatory Science of Pharmaceuticals and Medical Devices])

3. Contents of the project

Therefore, in this project, the following matters were implemented for the purpose of conducting comprehensive educational activities related to drug abuse prevention.

- Preparation of materials for education of young people on prevention of abuse of OTC drugs
- Preparation of a guidance manual for salespersons of OTC drugs (pharmacists, registered salespersons) and school pharmacists
- Holding seminars for young people and their families
- Holding seminars for salespersons of OTC drugs (pharmacists, registered salespersons) and school pharmacists

In addition, for the implementation of this project, a working group (WG) was established for the purpose of obtaining advice, etc. to raise awareness of prevention of abuse of OTC drugs, and opinions were sought from the following experts.

- Experts who can provide advice from a medical point of view
- Pharmacists who can give advice from the viewpoint of selling OTC drugs
- Pharmacists who can give advice from the viewpoint of raising awareness of prevention of drug abuse at schools and pharmacies
- A person who can give advice on the psychological state of individuals with drug dependence

Based on the discussion at the WG, deliverables including the following elements were prepared.

(1) Educational brochure (for elementary school students, junior and senior high school students)
In order to make it easy for young people of the target age group to read, cartoons were utilized for elementary school students and illustrations of characters matching the generations of the targeted readers were utilized for junior and senior high school students giving a sense of familiarity. In addition, the content of the educational brochure was narrowed down to avoid including too much information so that it becomes easy to try reading. Furthermore, the contact information that can be used when consultation is actually needed is described. We prepared a brochure for elementary school children conveying the importance of proper use of drugs, and a

brochure for junior and senior high school students conveying the background information on overdose.

(2) Educational videos (for elementary school students, junior and senior high school students)

We created educational brochures and videos so that illustrations in the brochures and the videos become correlated, making it easier to be used in raising-awareness activities, etc. by combining both materials. Young people with experience of abuse are interviewed by the counseling/support facilities about their experiences of overcoming abuse, with the expectation that hearing about psychological conflicts and experiences will convey the reality of abuse.

In the videos, in addition to an introduction of the consultation service, supporters and psychiatrists who are actually engaged in the consultation appear to communicate the atmosphere of the consultation and to make them feel more approachable.

(3) Guidance manual

A manual was prepared to explain in an easy-to-understand manner how pharmacists, registered salespersons who sell OTC drugs, and school pharmacists can guide individuals with OTC drug dependence to consultation services. The background of overdose of OTC drugs is described, and the process for handling consultations is explained using a figure. We also retrieved cases at drug stores, etc., where individuals with OTC drug dependence are frequently encountered, and described specific examples to make it easy to use the manual.

(4) Seminars (for the general public and for experts)

For the correct understanding of overdose of OTC drugs, experts explained the background of abuse of OTC drugs, and people with experience of overdose explained their experience of overcoming overdose to share the actual situation.

At the seminar for the general public, an explanation was given about actions to be taken and the mental attitude to have when encountering a person who experiences an overdose around them. In addition, lecturers actually engaged in consultation services made a presentation for the audience to deepen their understanding of these services.

At the seminar for experts, how to use educational materials, etc. described in (1) to (3) above, and points to consider, etc. when school pharmacists give classes on overdose of OTC drugs at schools, etc., were explained. In addition, questions were answered by the experts.

Educational brochures, videos, and guidance manuals created were published on the website of the MHLW on February 20, 2025. The seminars for young people and their families and those for salespersons of OTC drugs and school pharmacists were held online on March 2, 2025 via YouTube.

The contents of the seminars are scheduled to be disclosed at a later date on the official MHLW YouTube channel and the website of the MHLW.

Brochure for elementary school students

Brochure for junior and senior high school students

4. Conclusion

The educational brochure, educational videos, and guidance manuals created in this project are available on the website of the MHLW (https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/index_00033.html (only in Japanese)). We would appreciate it if those involved in pharmacies and retail distributors and school pharmacists use these materials in awareness-raising activities for young people for prevention of abuse of OTC drugs and for consultation services in the sales field of OTC drugs. Continued cooperation in raising awareness of preventing drug abuse is appreciated.

[References]

1) Current status and countermeasures for patients with poisoning caused by OTC drugs. Masayuki Hirose, et al.: Journal of Japanese Society for Emergency Medicine (JJSEM), 2020; 23: 702-6
2) Research Project on Drug Dependence by the MHLW National Survey for High School Student on Drug Use and Life (Issue No. 202204) Research Report on FY2022
National Survey for High School Student on Drug Use and Life (2021)
https://www.ncnp.go.jp/nimh/yakubutsu/report/pdf/highschool2021_ver2.pdf (only in Japanese)

(Reference information)

- Abuse of OTC drugs (overdose)
  https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/index_00010.html (only in Japanese)
- Abuse of OTC drugs (overdose) (for pharmacists and registered salespersons)
  https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/index_00033.html (only in Japanese)
- Information on drug abuse prevention
  https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iyakuhin/yakubuturanyou/index.html (only in Japanese)
- The 2nd Review Meeting on Drug Sales System, Material 2
  https://www.mhlw.go.jp/content/11121000/001062520.pdf (only in Japanese)

- The 15th Administrative Evaluation and Review Committee for Drugs, etc. Material 1. Initiatives Against Abuse of OTC Drugs (materials prepared by the Pharmaceutical Safety Bureau) https://www.mhlw.go.jp/content/10601000/001230826.pdf (only in Japanese)
- The 177th municipal seminar (Material 2) Administrative explanation 2 "Initiatives against abuse of OTC drugs in the government" https://www.mhlw.go.jp/content/12602000/001375020.pdf (only in Japanese)
- Do you know about Overdose (OD)? Press Release by Shogakukan-Shueisha Productions Co., Ltd. https://prtimes.jp/main/html/rd/p/000001450.000002610.html (only in Japanese)
- Release of educational materials intended to prevent abuse of marketed drugs (press release). https://www.mhlw.go.jp/stf/newpage_50612.html (only in Japanese)
- Disclosure of deliverables of "Project for Countermeasures to Prevent Abuse of OTC Drugs by Utilizing the Societies of School Pharmacists and Regional Pharmacists" (Administrative Notice dated February 20, 2025) https://www.mhlw.go.jp/content/001418016.pdf (only in Japanese)

2

Important Safety Information

Regarding the revision of the PRECAUTIONS of package inserts of drugs in accordance with the Notification dated March 5, 2025, this section will present the details of important revisions as well as the case summary serving as the basis for these revisions.

1 Dulaglutide (genetical recombination)

Brand name (name of company)	Trulicity Subcutaneous Injection 0.75 mg Ateos, 1.5 mg Ateos (Eli Lilly Japan K.K.)
Therapeutic category	Other hormone preparations (including antihormone preparations)
Indications	Type 2 diabetes mellitus

PRECAUTIONS (Revised language is underlined.)

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

<u>Hepatic impairment</u>

Reference information

Number of cases (for which a causal relationship between the drug and event is reasonably possible) collected in the PMDA's database for adverse drug reactions, etc. reports
Cases involving hepatic impairment reported in Japan[*1]: 4 (No patient mortalities)
Cases involving hepatic impairment reported overseas[*2]: 1 (No patient mortalities)
*1 Cases meeting both of the following conditions were retrieved from those collected in the PMDA's database for adverse drug reactions, etc. reports:
・Cases that fell under MedDRA ver.27.0 SMQ "Hepatic disorders (broad)"
・Cases in which the hepatic function test value (either of ALT, AST, ALP, γ-GTP, or T-Bil) was classified as grade 3 or higher according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0
*2 Cases meeting all of the following conditions were retrieved from those collected in the PMDA's database for adverse drug reactions, etc. reports:
・Cases that fell under MedDRA ver.27.0 SMQ "Hepatic disorders (broad)"
・Cases in which the hepatic function test value (either of ALT, AST, ALP, γ-GTP, or T-Bil) was classified as grade 3 or higher according to CTCAE version 5.0
・Cases that included descriptions of hepatic function-related test values at 3 time points (before administration and after discontinuation of dulaglutide (genetical recombination), and at the onset of the event)

Number of patients using the drug as estimated by the MAH during the previous 1-year period: Approximately 134,200
Japanese market launch:
Trulicity Subcutaneous Injection 0.75 mg Ateos: September 2015
Trulicity Subcutaneous Injection 1.5 mg Ateos: Before market launch

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">1</td><td rowspan="10">Male
60s</td><td rowspan="10">Type 2 diabetes mellitus
(chronic kidney disease, hyperuricaemia, dyslipidaemia)</td><td rowspan="10">0.75 mg/week
for 56 days
↓
discontinuation</td><td colspan="2">Hepatic impairment
Medical history: Fatty liver</td></tr>
<tr><td>7 days before administration</td><td>Blood tests were performed.</td></tr>
<tr><td>Day 1 of administration</td><td>Administration of dulaglutide (genetical recombination) was initiated.</td></tr>
<tr><td>56 days after administration (day of discontinuation)</td><td>Increases in liver function test values were observed (T.Bil: 7.4 mg/dL, AST: 204 IU/L, ALT: 355 IU/L, γ-GTP: 1,002 IU/L, ALP: 823 IU/L). The patient was assessed to have hepatic impairment. He had malaise as a subjective symptom. Administration of dulaglutide (genetical recombination) was discontinued.</td></tr>
<tr><td>6 days after discontinuation</td><td>The patient was admitted to the hospital for a detailed examination to determine the cause of the increased liver function test values. Imaging tests revealed no significant findings.</td></tr>
<tr><td>9 days after discontinuation</td><td>Blood tests were performed.</td></tr>
<tr><td>20 days after discontinuation</td><td>Improvement in hepatic function was noted (T-Bil: 1.5 mg/dL, AST: 44 IU/L, ALT: 50 IU/L, γ-GTP: 159 IU/L, ALP: 474 IU/L, LDH: 240 IU/L).</td></tr>
<tr><td>21 days after discontinuation</td><td>The patient was discharged from the hospital.</td></tr>
<tr><td>49 days after discontinuation</td><td>The symptoms were resolving. Dulaglutide (genetical recombination) was not readministered to the patient.</td></tr>
<tr><td colspan="6">Laboratory test value
<table>
<tr><th>Test item (unit)</th><th>7 days before administration</th><th>Day 1 of administration</th><th>56 days after administration</th><th>6 days after discontinuation</th><th>9 days after discontinuation</th><th>20 days after discontinuation</th></tr>
<tr><td>AST (IU/L)</td><td>17</td><td>17</td><td>204</td><td>29</td><td>35</td><td>44</td></tr>
<tr><td>ALT (IU/L)</td><td>19</td><td>19</td><td>355</td><td>81</td><td>50</td><td>50</td></tr>
<tr><td>γ-GTP (IU/L)</td><td>182</td><td>−</td><td>1002</td><td>600</td><td>364</td><td>159</td></tr>
<tr><td>ALP (IU/L)</td><td>−</td><td>−</td><td>823</td><td>928</td><td>689</td><td>474</td></tr>
<tr><td>LDH (IU/L)</td><td>−</td><td>−</td><td>385</td><td>312</td><td>275</td><td>240</td></tr>
<tr><td>TG (IU/L)</td><td>736</td><td>−</td><td>643</td><td>−</td><td>−</td><td>−</td></tr>
<tr><td>T-Bil (mg/dL)</td><td>−</td><td>−</td><td>7.4</td><td>6.1</td><td>3.2</td><td>1.5</td></tr>
<tr><td>BUN (mg/dL)</td><td>25.5</td><td>−</td><td>27.1</td><td>35.0</td><td>40.3</td><td>50.1</td></tr>
<tr><td>e-GFR (mL/min/1.73m^2)</td><td>25.2</td><td>−</td><td>23.1</td><td>23.3</td><td>25.8</td><td>23.7</td></tr>
<tr><td>Blood glucose (mg/dL)</td><td>280</td><td>−</td><td>250</td><td>−</td><td>−</td><td>−</td></tr>
<tr><td>HbA1c (%)</td><td>9.7</td><td>9.7</td><td>7.9</td><td>−</td><td>−</td><td>−</td></tr>
</table></td></tr>
<tr><td colspan="6">Concomitant drugs: Glimepiride, pioglitazone, febuxostat, ezetimibe, amlodipine besilate</td></tr>
</table>

Case summary

No.	Patient		Daily dose/ Administration duration	Adverse reaction	
	Sex/ age	Reason for use (complication)		Clinical course and treatment	
2	Male 50s	Type 2 diabetes mellitus (cerebral infarction)	0.75 mg/week for 116 days ↓ discontinuation	**Drug-induced liver disorder** Medical history: Cerebral infarction	
				Day 1 of administration	The patient started receiving dulaglutide (genetical recombination).
				81 days after administration	The dose of glimepiride (2 mg/day) was changed to 1 mg/day.
				116 days after administration (day of discontinuation)	An increase in AST and ALT to 10 times or more of the facility's reference range was noted. The patient consulted the gastroenterological medicine department. The presence or absence of structural and functional abnormalities in the liver and the biliary tract was examined, revealing no abnormalities. His blood glucose level was slightly elevated. He was admitted to the hospital for glycaemic control and a detailed examination. Dulaglutide (genetical recombination) and all concomitant drugs other than rivaroxaban were withdrawn, and the blood glucose was controlled with insulin.
				1 day after discontinuation	A blood test was performed.
				2 days after discontinuation	Magnetic resonance cholangiopancreatography (MRCP) was conducted, and it revealed no significant findings.
				3 days after discontinuation	Since the values of liver function tests decreased and viral liver disorder was excluded by the tests, a drug-induced liver disorder caused by dulaglutide (genetical recombination) was strongly suspected.
				4 days after discontinuation	A blood test was performed.
				7 days after discontinuation	A blood test was performed.
				12 days after discontinuation	Laboratory test values improved as follows: AST 49 IU/L; ALT 143 IU/L; γ-GTP 517 IU/L; ALP 811 IU/L, T-Bil 0.74 mg/dL. The patient's glycaemic control also improved. Therefore, he was discharged from the hospital.
				74 days after discontinuation	The results of the drug-induced lymphocyte stimulation test (DLST) were positive only for dulaglutide (genetical recombination) and negative for all other drugs taken at the time of onset. Oral administration of drugs other than glimepiride that the patient was taking at the onset of liver disorder (ipragliflozin L-proline, metformin hydrochloride, rosuvastatin calcium, suvorexant, esomeprazole magnesium hydrate, linagliptin) was resumed. No increase in AST and ALT was noted at the periodic blood tests thereafter.

Laboratory test value

Test item (unit)	Day 1 of administ-ration	81 days after administ-ration	116 days after administ-ration	1 day after discontin-uation	2 days after discontin-uation	4 days after discontin-uation	7 days after discontin-uation	12 days after discontin-uation
AST (IU/L)	20	14	587	976	863	300	11	49
ALT (IU/L)	20	16	767	1259	1387	784	350	143
γ-GTP (IU/L)	41	25	199	261	303	—	—	517
LDH (IU/L)	160	138	496	719	605	—	—	185
ALP (IU/L)	303	248	540	—	—	—	—	811
T-BiL (mg/dL)	0.36	0.37	0.46	0.66	0.62	—	—	0.74

Concomitant drugs: Ipragliflozin L-proline, glimepiride, metformin hydrochloride, rosuvastatin calcium, rivaroxaban, suvorexant, esomeprazole magnesium hydrate

3

Revisions of PRECAUTIONS (No. 358)

This section presents details of revisions to the PRECAUTIONS and brand names of drugs that have been revised in accordance with the Notifications dated March 5, 2025.

1 Other hormone preparations (including antihormone preparations)

Dulaglutide (genetical recombination)

Brand name	Trulicity Subcutaneous Injection 0.75 mg Ateos, 1.5 mg Ateos (Eli Lilly Japan K.K.)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Hepatic impairment

2 Other antitumor agents

[1] Atezolizumab (genetical recombination)
[2] Avelumab (genetical recombination)
[3] Cemiplimab (genetical recombination)

Brand name	[1] Tecentriq for Intravenous Infusion 840 mg, 1200 mg (Chugai Pharmaceutical Co., Ltd.) [2] Bavencio intravnous infusion 200 mg (Merck Biopharma Co., Ltd) [3] Libtayo I.V. Infusion 350 mg (Regeneron Japan KK)
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Immune thrombocytopenia

3 Other antitumor agents

[1] Dabrafenib mesilate
[2] Trametinib dimethyl sulfoxide

Brand name	[1] Tafinlar Capsules 50 mg, 75 mg, Tafinlar Dispersible tablets for Pediatric 10 mg (Novartis Pharma K.K.) [2] Mekinist Tablets 0.5 mg, 2 mg, Mekinist Dry syrup for Pediatric 4.7 mg (Novartis Pharma K.K.)
8. IMPORTANT PRECAUTIONS (newly added)	Neutropenia or leukopenia may occur. Patients should be carefully monitored through periodic blood tests, etc. during treatment with this drug.
11. ADVERSE REACTIONS **11.1 Clinically Significant Adverse Reactions (newly added)**	Neutropenia, leukopenia

4 [1] Axicabtagene ciloleucel
[2] Idecabtagene vicleucel
[3] Tisagenlecleucel
[4] Lisocabtagene maraleucel

Brand name	[1] Yescarta Intravenous Drip Infusion (Gilead Sciences K.K.) [2] Abecma Intravenous Infusion (Bristol-Myers Squibb K.K.) [3] Kymriah Suspension for Intravenous Infusion(Novartis Pharma K.K.) [4] Breyanzi Suspension for Intravenous Infusion (Bristol-Myers Squibb K.K.)
8. IMPORTANT PRECAUTIONS (newly added)	Occurrences of lymphoid neoplasm of CAR-positive T-cell origin have been reported in patients treated with regenerative medical products containing CAR-expressing T-cells. Although the causal relationship with the products is not clear, caution should be exercised regarding the onset of lymphoid neoplasms of T-cell origin.
15. OTHER PRECAUTIONS **15.1 Information Based on Clinical Use**	(deleted)

5 Ciltacabtagene autoleucel

Brand name	Carvykti Suspension for Intravenous Infusion (Janssen Pharmaceutical K.K.)
8. IMPORTANT PRECAUTIONS	Occurrences of lymphoid neoplasm of CAR-positive T-cell origin have been reported in patients treated with regenerative medical products containing CAR-expressing T-cells. Although the causal relationship with the products is not clear, caution should be exercised regarding the onset of lymphoid neoplasms of T-cell origin.

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 February 28, 2025)
◎: Products for which EPPV was initiated after January 1, 2025

	Nonproprietary name / Brand name	Name of the MAH	Date of EPPV initiation
	Insulin Icodec (genetical recombination) Awiqli injection FlexTouch 300 units, 700 units	Novo Nordisk Pharma Ltd.	January 30, 2025
	Articaine hydrochloride/adrenaline bitartrate Septocaine Combination Injection Cartridge	GC SHOWAYAKUHIN CORPORATION	January 21, 2025
	Amifampridine phosphate Firdapse Tablets 10 mg	DyDo Pharma, Inc.	January 15, 2025
	Benralizumab (genetical recombination)[*1] Fasenra Subcutaneous Injection 30 mg Syringe	AstraZeneca K.K.	December 27, 2024
	Efgartigimod alfa (genetical recombination)/vorhyaluronidase alfa (genetical recombination)[*2] Vyvdura Combination Subcutaneous Injection	argenx Japan K.K.	December 27, 2024
	Daridorexant hydrochloride Quviviq Tablets 25 mg, 50 mg	Nxera Pharma Japan Co., Ltd.	December 19, 2024
	Aceneuramic acid Acenobel Extended Release Tablets 500 mg	Nobelpharma Co., Ltd.	December 19, 2024
	Estetrol hydrate/drospirenone alyssa combination tablets	Fuji Pharma Co., Ltd.	December 3, 2024
	Donanemab (genetical recombination) kisunla Intravenous Infusion 350 mg	Eli Lilly Japan K.K.	November 26, 2024
	Fruquintinib	Takeda Pharmaceutical Company Limited	November 22, 2024

	Nonproprietary name Brand name	Name of the MAH	Date of EPPV initiation
	Fruzaqla capsules 1 mg, 5 mg		
	Sacituzumab govitecan (genetical recombination)	Gilead Sciences K.K.	November 20, 2024
	Trodelvy for Injection 200 mg		
	Amivantamab (genetical recombination)	Janssen Pharmaceutical K.K.	November 20, 2024
	Rybrevant Intravenous Infusion 350 mg		
	Repotrectinib	Bristol-Myers Squibb K.K.	November 20, 2024
	Augtyro capsules 40 mg		
	Mecobalamin[*3]	Eisai Co., Ltd.	November 20, 2024
	Rozebalamin for Injection 25 mg		
	Teprotumumab (genetical recombination)	Amgen K.K.	November 20, 2024
	Tepezza for Intravenous Infusion 500 mg		
	Voclosporin	Otsuka Pharmaceutical Co., Ltd.	November 20, 2024
	Lupkynis Capsules 7.9 mg		
	Tasurgratinib succinate	Eisai Co., Ltd.	November 20, 2024
	Tasfygo Tablets 35 mg		
	Avibactam sodium/ceftazidime hydrate	Pfizer Japan Inc.	November 12, 2024
	Zavicefta Combination for Intravenous Infusion		
	Tapinarof	Japan Tobacco Inc.	October 29, 2024
	Vtama cream 1%		
	Gumarontinib hydrate	Haihe Biopharma K.K.	October 11, 2024
	Haiyitan tablets 50 mg		
	Live attenuated influenza vaccine	Daiichi Sankyo Co., Ltd.	October 3, 2024
	Flumist Intranasal Spray		
	Coronavirus (SARS-CoV-2) RNA vaccine[*4]	Meiji Seika Pharma Co., Ltd.	September 30, 2024
	Kostaive intramuscular injection		
	Brexpiprazole[*5]	Otsuka Pharmaceutical Co., Ltd.	September 24, 2024
	Rexulti tablets 1 mg, 2 mg, Rexulti OD tablets 0.5 mg, 1 mg, 2 mg		
	Treprostinil[*6]	Mochida Pharmaceutical Co., Ltd.	September 24, 2024
	Treprost Inhalation Solution 1.74 mg		
	Inactivated tissue culture tick-borne encephalitis vaccine	Pfizer Japan Inc.	September 13, 2024
	Ticovac suspension liquid for intramuscular injection 0.5 mL, Ticovac Junior suspension liquid for intramuscular injection 0.25 mL		
	Freeze-dried human protein C concentrate	Takeda Pharmaceutical Company Limited	September 6, 2024

Nonproprietary name / Brand name		Name of the MAH	Date of EPPV initiation
	Ceprotin for Intravenous Injection 1000 IU		

*1 Eosinophilic granulomatosis with polyangiitis in patients who have not sufficiently responded to conventional treatments

*2 Chronic inflammatory demyelinating polyradiculoneuritis

*3 Slowing the progression of functional impairment in amyotrophic lateral sclerosis (ALS)

*4 Prevention of disease caused by SARS-CoV-2 infection (COVID-19)

*5 Excessive motor activity or physically/verbally aggressive behavior due to rapid changes in mood, irritability, and/or outbursts associated with dementia due to Alzheimer's disease

*6 Pulmonary hypertension associated with interstitial lung disease