

# Pharmaceuticals and Medical Devices Safety Information

No. 343 May 2017

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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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**Published by**  
Ministry of Health, Labour and Welfare



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Ministry of Health, Labour and Welfare  
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# Pharmaceuticals and Medical Devices Safety Information

No. 343 May 2017

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

## [ Outline of Information ]

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1	Project of the Japan Drug Information Institute in Pregnancy		The MHLW established the Japan Drug Information Institute in Pregnancy (JDIIP) at the National Center for Child Health and Development (NCCHD) in October 2005 to provide drug consultation services and perform surveys. For a second straight year, the system has been strengthened by receiving the cooperation of newly joined hospitals (details follow). This section also shows the workflow leading up to a consultation, and concludes with a message from the director of JDIIP.	4
2	Revision of Precautions (No. 284)	P	Denosumab (and 2 others)	12
3	List of Products Subject to Early Post-marketing Phase Vigilance		List of products subject to Early Post-marketing Phase Vigilance as of March 31, 2017.	13

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
CK (CPK)	Creatine kinase (Creatine phosphokinase)
EPPV	Early Post-marketing Phase Vigilance
FY	Fiscal year
JDIIP	Japan Drug Information Institute in Pregnancy
MAH	Marketing authorization holder
MHLW	Ministry of Health, Labour and Welfare
NCCHD	National Center for Child Health and Development
PMDA	Pharmaceuticals and Medical Devices Agency
PMDSI	Pharmaceuticals and Medical Devices Safety Information
TEN	Toxic epidermal necrolysis

# Project of the Japan Drug Information Institute in Pregnancy

## 1. Project of the Japan Drug Information Institute in Pregnancy

When drugs are used during pregnancy, due attention must be paid to the effects on the fetus as well as on the mother. On the other hand, excessive worry about the risks associated with drugs can cause physicians to refrain from prescribing needed medication, or prompt a patient to quit taking a drug at her own discretion, which may worsen her condition and even harm the fetus. In some cases, women will give up on pregnancy to begin with, because they are using drugs for the treatment of a chronic disease.

The MHLW established the Japan Drug Information Institute in Pregnancy (JDIIP) at the National Center for Child Health and Development (NCCHD) in October 2005 to collect and assess the latest scientific evidence such as effect of drug on fetus, and use the information to provide consultation services to pregnant women and women who wish to become pregnant. The JDIIP also assesses pregnancy outcomes in consultation clients to establish new evidence. The project has been introduced in PMDSI No. 338 and other issues (see <Reference> for past issues).

## 2. Cooperating Medical Institutions

In addition to the JDIIP, the project has been implemented with participation of the cooperating medical institutions throughout Japan in order to strengthen the system for consultation services and prompt information collection on pregnancy and drugs, making consultation services more convenient and accessible. Women with concerns about pregnancy and drugs can receive a consultation at either the JDIIP or the cooperating medical institution of their choice. Eight new facilities (Japanese Red Cross Akita Hospital, Saiseikai Utsunomiya Hospital in Tochigi, Yamanashi Prefectural Central Hospital, Shiga University of Medical Science Hospital, Yamaguchi University Hospital, Ehime University Hospital, Kochi Medical School Hospital, and Oita University Hospital) have joined the roster of cooperating medical institutions this fiscal year (FY), deploying at least one cooperating medical institution in every prefecture or metropolitan area. The participating medical institutions are introduced on page 6 to 10.

## 3. Content of Main Activities

### (1) Consultations on pregnancy and drugs

Pregnant women and women who wish to become pregnant can receive consultation services to address their concerns about the effects of drugs on a fetus. They can either receive a consultation through their physician or have a face-to-face consultation at JDIIP or one of the cooperating medical institutions. Telephone consultations are also available on drugs that are the topic of frequent inquiries (cold medicines, anti-inflammatory analgesics, allergy medicines, and digestive medicines, etc.).

The procedure for receiving consultation services is posted on the Consultation Content and Methods page of the JDIIP website (<https://www.ncchd.go.jp/kusuri/process/index.html>; only available in Japanese language). The procedure is introduced briefly below.

#### 1) Workflow up to receiving a face-to-face consultation

- [1] Download the Medical Questionnaire and the Consultation Request Form from the website of the JDIIP.  
(<https://www.ncchd.go.jp/kusuri/process/monsin.pdf>; only available in Japanese language)

- [2] The patient herself should fill out the Medical Questionnaire, which is intended to obtain patient background information. The Consultation Request Form should be filled out by the patient's physician.
  - \* A Letter of Referral issued by the patient's physician may be substituted for the Consultation Request Form.
  - \* If the consultation will be received at the JDIIP or a cooperating medical institution, the Consultation Request Form may be omitted
- [3] Send the Medical Questionnaire, Consultation Request Form, and a self-addressed stamped envelope by post to the JDIIP.
- [4] The JDIIP will send back Notification of Consultation Method.
- [5] Following the instructions in the notice, receive a consultation by either of the methods listed below.
  - Receive an explanation at the JDIIP or at a cooperating medical institution as an outpatient.
  - The JDIIP will send a written reply to the consultation client's physician for an explanation from the physician.

If the consultation is performed at the JDIIP or a cooperating medical institution on an outpatient basis, it will be possible to have a specialist and a pharmacist present, allowing for special consideration to be given to risk communication. As a rule, women who are very anxious or are seeking consultations about drugs with a high risk of teratogenicity will receive consultations by this method. On the other hand, having a consultation with one's physician offers the advantages of a familiar setting, suitable for women who may be feeling unwell in early pregnancy and have anxieties about traveling to a distant location for a consultation.

## 2) Workflow up to receiving a telephone consultation

- [1] Download the Medical Questionnaire from the website of the JDIIP. (<https://www.ncchd.go.jp/kusuri/process/monsin.pdf>; only available in Japanese language)
- [2] The patient herself should fill out the Medical Questionnaire, which is intended to obtain patient background information.
- [3] Send the Medical Questionnaire and a self-addressed stamped envelope by post to the JDIIP.
- [4] The JDIIP will send back Notification of Consultation Method.
- [5] Following the instructions in the notice, call a dedicated phone number for a telephone consultation.

## (2) Surveys on newborns

When applying for a consultation under (1) above, consultation clients will be asked to cooperate in the survey on pregnancy outcomes. Consultation clients who have consented to participate in the survey will be mailed a survey postcard by JDIIP one month after their delivery due date and asked to return it with information filled in on the course of their pregnancy and the health status of the newborn, etc., based on the results of the one month check-up.

JDIIP makes efforts to ensure respondents' full understanding of the purpose and the significance of the survey by explaining that they can contribute to women who will conceive in the future by returning the survey postcard of the outcome of their pregnancy.

## (3) Consultations on lactation and drugs

Postpartum women can also receive consultations at JDIIP on the effect of drugs on lactation. Points to consider and other details are posted on the JDIIP website under Lactation and Drugs: <https://www.ncchd.go.jp/kusuri/lactation/jyunyu.html> (only available in Japanese language). The procedure is briefly outlined below.

- [1] Call the dedicated phone number (+81-3-3416-0510; Monday through Friday (excluding national holidays) 10:00 a.m. to 12 noon).
- [2] Answer the following questions with reference to the Mother and Child Health Handbook, drug history handbook, etc.
  - Information on the consultation client: Name, telephone number, postal code, date of birth, birth history, proportion of breast milk (ratio of breast milk to baby formula and baby food

at time of consultation)

- Information on the newborn: Date of birth, gestational age at birth (weeks and days), birth weight, age (in months) and weight at the time of consultation, underlying diseases
- Drug information: Reason why the drug is used and name of disease; name of the drug, dose, compliance

[3] Receive a consultation by telephone (approximately 10 to 15 minutes).

\* If it is difficult to respond by telephone, consultation as an outpatient will be provided.

#### 4. To Healthcare Professionals

Healthcare professionals are encouraged to introduce the consultation services of JDIIP to pregnant women, etc. who are concerned about the effects of drugs they have used during pregnancy. Patients who received consultation services from the JDIIP or cooperating medical institutions have expressed their relief regarding concerns about taking drugs.

Please also refer to the web page of the JDIIP for healthcare professionals ([https://www.ncchd.go.jp/kusuri/news\\_med/login.html](https://www.ncchd.go.jp/kusuri/news_med/login.html); only available in Japanese language), which provides information on the effects of drugs during lactation and the use of anti-influenza drugs/influenza vaccines during pregnancy.

For a JDIIP leaflet, please contact the JDIIP at its main number (+81-3-5494-7845).

##### **From JDIIP Director Atsuko Murashima**

The JDIIP was established for the threefold purpose of providing information on the use of drugs during pregnancy, accumulating pregnancy outcomes in cases where drugs were used during pregnancy, and generating evidence with the use of epidemiological research techniques.

JDIIP has assigned cooperating hospitals in prefectures and metropolitan areas to take charge of "Outpatient services for pregnancy and drugs". The cooperating hospital arrangement emerged from a meeting of knowledgeable people that was held at the time of establishment to review methods for preparing and providing information to consultation clients, where those present expressed the opinion that "Skilled experts should conduct the face-to-face counselling on drugs that involve risks". Assignment of cooperating hospitals has been completed in all 47 prefectures and metropolitan areas in FY 2017. This is entirely thanks to the understanding of the physicians and pharmacists at the institutions, and we would like to take this opportunity to express our gratitude to all of them.

One of the roles of the JDIIP is the generation of evidence from consultation cases. Thus far, information has been provided to over 10 000 consultation clients, and in turn, information on their medication and pregnancy outcomes has been assembled together in a database. This has formed the basis for evidence generation thus far, and with the substantial growth of the database, we would like to accelerate this process from now on. Since there are few consultations on drugs for the treatment of chronic diseases other than neuropsychiatric disorders, relying solely on consultation cases will make it difficult to accumulate a sufficient number of cases. For this reason, we have been conducting registration surveys of patients who are using drugs for the treatment of conditions such as Basedow's disease and rheumatoid arthritis. On the basis of this experience, we would like to generate evidence originating in Japan by constructing a mechanism that can use the network of cooperating hospitals to conduct more effective registration surveys.

In particular, since package inserts have not kept abreast of the evidence in these fields, we are seeing various distressing situations. For instance, women who are pregnant or wish to become pregnant sometimes cannot receive pharmacotherapy that they should need. On the other hand, women who are taking drugs for treatment may hesitate to become pregnant, while others may take medications without knowing they are pregnant and be distressed over whether to continue the pregnancy. The Proper Use Promotion Project for pregnant and lactating women was initiated in FY 2016 to improve such situations. A working group composed of physicians, pharmacists, and specialists in animal testing meets to consider the advisability of revising package inserts for the drugs that have been selected based on clinical importance, presence/absence of evidence, etc.

Apart from these efforts, we take pride in contributing to the development and spread of this field through cooperation with the certification system for Board Certified Pharmacy Specialist in Pharmacotherapy during Pregnancy and Lactation, launched by the Japanese Society of Hospital Pharmacists in 2008, and the Obstetric Guidelines developed by Japan Society of Obstetrics and

Gynecology and Japan Association of Obstetricians and Gynecologists. JDIIP has also made efforts to educate healthcare professionals in this field through publications and lecture meetings, etc. From now on, we would like to foster understanding among the general public as well as the healthcare community. We ask for your continued support and guidance.

List of cooperating medical institutions for FY 2017

	Name of medical institution	Contact information, reception hours, etc.
1	Japan Drug Information Institute in Pregnancy	2-10-1 Okura, Setagaya-ku, Tokyo 157-8535 in National Center for Child Health and Development TEL: (+81)-3-5494-7845 Reception hours: 10:00 – 12:00, 13:00 – 16:00 (Monday to Friday, excluding national holidays) URL: <a href="http://www.ncchd.go.jp/en/index.html">http://www.ncchd.go.jp/en/index.html</a>
Cooperating medical institutions (©: Joined since FY 2017)		
2	Hokkaido University Hospital	Kita 14, Nishi 5, Kita-ku, Sapporo-city, Hokkaido 060-8648 TEL: (+81)-11-706-7722 (Please ask for “Outpatient service for pregnancy and drugs”) FAX: (+81)-11-706-7616 Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
3	Hirosaki University Hospital	53 Honcho, Hirosaki-city, Aomori 036-8563 TEL: (+81)-172-33-5111 (Extension 6748) Reception hours: 8:30 – 17:00 (Monday to Friday, excluding national holidays)
4	Iwate Medical University Hospital	19-1 Uchimarui, Morioka-city, Iwate 020-8505 TEL: (+81)-19-624-5263 (Pregnancy and drugs counseling desk: Direct call) Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
5 ©	Japanese Red Cross Akita Hospital	222-1 Aza Nawashirosawa, Kamikitatesaruta, Akita-city, Akita 010-1495 TEL: (+81)-18-829-5000 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 14:00 – 16:00 (Monday to Friday, excluding national holidays)
6	Yamagata University Hospital	2-2-2 Iidanishi, Yamagata-city, Yamagata 990-9585 TEL: (+81)-23-628-5160 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 8:30 – 17:00 (Monday to Friday, excluding national holidays)
7	Tohoku University Hospital	1-1 Seiryomachi, Aoba-ku, Sendai-city, Miyagi 980-8574 TEL: (+81)-22-717-7000 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays) URL: <a href="http://www.hosp.tohoku.ac.jp/en/">http://www.hosp.tohoku.ac.jp/en/</a>
8	Fukushima Medical University Hospital	1 Hikarigaoka, Fukushima-city, Fukushima 960-1295 TEL: (+81)-24-547-1226 Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays) HP: <a href="http://www.fmu.ac.jp/univ/en/">http://www.fmu.ac.jp/univ/en/</a>
9	Maebashi Red Cross Hospital	3-21-36 Asahi-cho, Maebashi-city, Gunma 371-0014 TEL: (+81)-27-224-4585 (Division of Pharmacy: Extension 7709) Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays) URL: <a href="http://www.maebashi.jrc.or.jp/">http://www.maebashi.jrc.or.jp/</a> (only available in Japanese language)

10	University of Tsukuba Hospital	2-1-1 Amakubo, Tsukuba-city, Ibaraki 305-8576 TEL: (+81)-29-896-7171 FAX: (+81)-29-896-7170 Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
11	◎ Saiseikai Utsunomiya Hospital	911-1 Takebayashi-machi, Utsunomiya-city, Tochigi 321-0974 TEL: (+81)-28-626-5595 (Regional Cooperation Unit) Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays)
12	Chiba University Hospital	1-8-1 Inohana, Chuo-ku, Chiba-city, Chiba 260-8677 TEL: (+81)-43-226-2628 (Drug Information, Division of Pharmacy) Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
13	Saitama Medical University Hospital	38 Morohongo Moroyama-machi, Iruma-gun, Saitama 350-0495 TEL: (+81)-49-276-1297 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 15:00 – 17:00 (Monday to Saturday, excluding national holidays)
14	Yokohama City University Hospital	3-9 Fukuura, Kanazawa-ku, Yokohama-city, Kanagawa 236-0004 TEL: (+81)-45-787-2800 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays) URL: <a href="http://www.fukuhp.yokohama-cu.ac.jp/">http://www.fukuhp.yokohama-cu.ac.jp/</a> (only available in Japanese language)
15	◎ Yamanashi Prefectural Central Hospital	1-1-1 Fujimi, Kofu-city, Yamanashi 400-8506 TEL: (+81)-55-253-7900 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 8:30 – 17:00 (Monday to Friday, excluding national holidays)
16	Shinshu University Hospital	3-1-1 Asahi, Matsumoto-city, Nagano 390-8621 TEL: (+81)-263-37-3022 (Please ask for “Outpatient service for pregnancy and drugs”) FAX: (+81)-263-37-3072 Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
17	Niigata University Medical & Dental Hospital	1-754 Asahimachi-dori, Chuo-ku, Niigata-city, Niigata 951-8520 TEL: (+81)-25-227-2893 (Please ask for “Outpatient service for pregnancy and drugs”) FAX: (+81)-25-227-0802 Reception hours: 13:30 – 16:00 (Monday to Friday, excluding national holidays)
18	Toyama University Hospital	2630 Sugitani, Toyama-city, Toyama 930-0194 TEL: (+81)-76-434-7863 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
19	National Hospital Organization Kanazawa Medical Center	1-1 Shimoishibiki-machi, Kanazawa-city, Ishikawa 920-8650 TEL: (+81)-76-262-4161 Reception hours: 9:00 – 16:30 (Monday to Friday, excluding national holidays) URL: <a href="http://www.kanazawa-hosp.jp/pv/preg.htm">http://www.kanazawa-hosp.jp/pv/preg.htm</a> (only available in Japanese language)
20	University of Fukui	23-3, Matsuokashimoaizuki, eiheiji-cho, Yoshida-gun, Fukui 910-1193



	Hospital	TEL: (+81)-776-61-3111 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 13:00 – 15:00 (Monday to Friday, excluding national holidays)
21	Hamamatsu University Hospital	1-20-1 Handayama, Higashi-ku, Hamamatsu-city, Shizuoka 431-3192 TEL: (+81)-53-435-2637 (Regional Cooperation Unit) FAX: (+81)-53-435-2849 Reception hours: 8:30 – 18:00 (Monday to Friday, excluding national holidays and year-end/new-year)
22	Japanese Red Cross Nagoya Daiichi Hospital	3-35 Michishita-cho, Nakamura-ku, Nagoya-city, Aichi 453-8511 TEL: (+81)-52-481-5111 (Division of Pharmacy: Extension 38167) FAX: (+81)-52-482-7733 Reception hours: 13:00 – 16:00 (Monday to Friday, excluding national holidays)
23	National Hospital Organization Nagara Medical Center	1300-7 Nagara, Gifu-city, Gifu 502-8558 TEL: (+81)-58-232-7755 (Please ask for “Outpatient service for pregnancy and drugs”) FAX: (+81)-58-295-0077 Reception hours: 10:00 – 16:00 (Monday to Friday, excluding national holidays)
24	Mie University Hospital	2-174, Edobashi, Tsu-city, Mie 514-8507 TEL: (+81)-59-231-5552 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 8:30 – 17:00 (Monday to Friday, excluding national holidays)
25	Shiga University of Medical Science Hospital	Setatsukinowa-cho, Otsu-city 520-2192 TEL: (+81)-77-548-2576 (Maternal and Fetal Medicine) (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 16:00 – 17:00 (Monday to Friday, excluding national holidays)
26	University Hospital, Kyoto Prefectural University of Medicine	465 Kajii-cho, Hirokoji agaru, Kawaramachi-dori, Kamigyo-ku, Kyoto-City 602-8566 TEL: (+81)-75-251-5862 (Drug Information, Division of Pharmacy) FAX: (+81)-75-251-5859 (same as above): Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays)
27	National Hospital Organization Osaka Women's and Children's Hospital	840 Murodo-cho, Izumi-city, Osaka 594-1101 TEL: (+81)-725-56-5537 (Outpatient service for pregnancy and drugs) Reception hours: 10:00 – 12:00 , 14:00 – 17:00 (Monday to Friday, excluding national holidays) HP: <a href="http://www.mch.pref.osaka.jp/english/index.html">http://www.mch.pref.osaka.jp/english/index.html</a>
28	Kobe University Hospital	7-5-2 Kusunoki-cho, Chuo-ku, Kobe-city, Hyogo 650-0017 TEL: (+81)-78-382-5111 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 13:00 – 17:00 (Monday to Friday, excluding national holidays)
29	Nara Medical University Hospital	840 Shijo-cho, Kashihara-city, Nara 634-8522 TEL: (+81)-744-22-3051 (Division of Pharmacy: Extension 3567) Reception hours: 8:30 – 16:00 (Monday to Friday, excluding national holidays) URL: <a href="http://www.narmed-u.ac.jp/hospital/shinryokabumon/senmongairai/ninshintokusuri.html">http://www.narmed-u.ac.jp/hospital/shinryokabumon/senmongairai/ninshintokusuri.html</a> (only available in Japanese language)
30	Japanese Red Cross Wakayama	4-20 Komatsubara-dori, Wakayama-city, Wakayama 640-8558

	Medical Center	TEL : (+81)-73-421-8175 (Please ask for "Outpatient service for pregnancy and drugs") Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays) HP: <a href="http://www2.kankyo.ne.jp/others/en.html">http://www2.kankyo.ne.jp/others/en.html</a>
31	Tottori University Hospital	36-1 Nishi-cho, Yonago, Tottori 683-8504 TEL: (+81)-859-38-6642 (Please ask for "Outpatient service for pregnancy and drugs") Reception hours: 16:00 – 17:00 (Monday to Friday, excluding national holidays) HP: <a href="http://www2.hosp.med.tottori-u.ac.jp/en/">http://www2.hosp.med.tottori-u.ac.jp/en/</a>
32	National Hospital Organization Okayama Medical Center	1711-1 Tamasu, Kita-ku, Okayama-city 701-1192 TEL: (+81)-86-294-9556 (Please ask for "Outpatient service for pregnancy and drugs") FAX: (+81)-86-294-9557 Reception hours: 8:30 – 18:00 (Monday to Friday, excluding national holidays) URL: <a href="http://okayamamc.jp/04_bumon/04-04_bumon/04-04_03-02yakuzai.html">http://okayamamc.jp/04_bumon/04-04_bumon/04-04_03-02yakuzai.html</a> (only available in Japanese language)
33	Shimane University Hospital	89-1 Enya-cho, Izumo-city, Shimane 693-8501 TEL: (+81)-853-20-2061 (Please ask for "Outpatient service for pregnancy and drugs") Reception hours: 8:30 – 17:15 (Monday to Friday, excluding national holidays)
34	Hiroshima University Hospital	1-2-3 Kasumi, Minami-ku, Hiroshima-city, Hiroshima 734-8551 TEL: (+81)-82-257-5064 Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
35 ◎	Yamaguchi University Hospital	1-1-1 Minamikogushi, Ube-city, Yamaguchi 755-8505 TEL : (+81)-836-22-2668 (Please ask for "Outpatient service for pregnancy and drugs") Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays)
36	National Hospital Organization Shikoku Medical Center for Children and Adults	2-1-1 Senyu-cho, Zentsuji-city, Kagawa 765-8507 TEL: (+81)-877-62-1000 (Please ask for "Outpatient service for pregnancy and drugs") FAX: (+81)-877-62-6311 Reception hours: 8:30 – 17:00 (Monday to Friday, excluding national holidays)
37	Tokushima University Hospital	2-50-1 Kuramoto-cho, Tokushima-city, Tokushima 770-8503 TEL: (+81)-70-6586-0831 Reception hours: 9:00 – 16:00 (Monday to Friday, excluding national holidays)
38 ◎	Ehime University Hospital	Shitsukawa, Toon-city, 791-0295 TEL: (+81)-89-960-5572 (Please ask for "Outpatient service for pregnancy and drugs") Reception hours: 13:00 – 16:00 (Monday to Friday, excluding national holidays) <a href="https://www.hsp.ehime-u.ac.jp/english/">https://www.hsp.ehime-u.ac.jp/english/</a>
39 ◎	Kochi Medical School Hospital	185-1 Kohasu, Oko-cho, Nankoku-shi, Kochi 783-8505 TEL: (+81)-88-880-2445 (Please ask for "Outpatient service for pregnancy and drugs") Reception hours: 14:00 – 17:00 (Monday to Friday, excluding national holidays)
40	Kyushu University Hospital	3-1-1 Maidashi, Higashi-ku, Fukuoka-city, Fukuoka 812-8582 TEL: (+81)-92-642-5900 (Please ask for "Outpatient service for pregnancy and drugs")

		and drugs”) Reception hours: 14:00 – 17:00 (Monday to Friday, excluding national holidays)
41	Saga University Hospital	5-1-1 Nabeshima, Saga-city, Saga 849-8501 TEL: (+81)-952-34-3482 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 9:00 – 17:00 (Monday to Friday, excluding national holidays)
42 ◎	Oita University Hospital	1-1 Idaigaoka, Hazama-machi, Yuhu-city, Oita 879-5593 TEL: (+81)-97-586-6920 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 11 : 00 – 12 : 30, 14 : 30 – 16 : 00 (Monday, Wednesday and Friday, excluding national holidays)
43	Japanese Red Cross Kumamoto Hospital	2-1-1 Nagamine Minami, Higashi-ku, Kumamoto-city, Kumamoto 861-8520 TEL: (+81)-96-384-2111 (Gynecology outpatient: 6240) (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 14:00 – 16:00 (Monday to Friday, excluding national holidays)
44	Nagasaki University Hospital	1-7-1 Sakamoto, Nagasaki-city, Nagasaki 852-8501 TEL: (+81)-95-819-7249 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 10:00 – 16:00 (Monday to Friday, excluding national holidays)
45	University of Miyazaki Hospital	5200 Kihara, Kiyotake-cho, Miyazaki-city, Miyazaki 889-1692 TEL: (+81)-985-85-1512 (Please ask for “Outpatient service for pregnancy and drugs”) Reception hours: 8:30 – 17:15 (Monday to Friday, excluding national holidays) URL: <a href="http://www.med.miyazaki-u.ac.jp/home/hospital/for-foreigners/">http://www.med.miyazaki-u.ac.jp/home/hospital/for-foreigners/</a>
46	Kagoshima City Hospital	37-1 Uearata-cho, Kagoshima-city, Kagoshima 892-8760 TEL: (+81)-99-230-7000 (Pharmacy department: Extension 2271) (Please ask for “Outpatient service for pregnancy and drugs”) FAX: (+81)-99-230-7075 Reception hours: 8:30 – 17:15 (Monday to Friday, excluding national holidays)
47	Okinawa Chubu Hospital	281 Miyazato, Uruma-city, Okinawa 904-2293 TEL: (+81)-98-973-4111 (Please ask for “Outpatient service for pregnancy/breastfeeding and drugs”) Reception hours: 13:00 – 16:00 (Tuesday, Thursday, and Friday, excluding national holidays)

### <References>

- JDIIP website: <http://www.ncchd.go.jp/en/index.html>
- PMDSI No. 268: <https://www.pmda.go.jp/files/000153737.pdf>
- PMDSI No. 279: <https://www.pmda.go.jp/files/000153493.pdf>
- PMDSI No. 290: <https://www.pmda.go.jp/files/000153540.pdf>
- PMDSI No. 305: <https://www.pmda.go.jp/files/000153659.pdf>
- PMDSI No. 316: <https://www.pmda.go.jp/files/000153674.pdf>
- PMDSI No. 328: <https://www.pmda.go.jp/files/000208994.pdf>
- PMDSI No. 338: <https://www.pmda.go.jp/files/000214953.pdf>

## 2

# Revision of Precautions (No. 284)

This section presents details of revisions to the Precautions section of package inserts and brand names of drugs in accordance with the Notifications dated April 20, 2017

### 1 Miscellaneous metabolism agents-Miscellaneous

## Denosumab (genetical recombination) (drug product with the indication for osteoporosis)

<b>Brand name</b>	Pralia Subcutaneous Injection Syringe 60 mg (Daiichi-Sankyo Company, Limited)
<b>Important Precautions</b>	<u>In patients with osteoporosis, multiple vertebral fractures, which may be associated with a temporary increase in bone resorption, may occur after discontinuation of denosumab treatment. If the treatment is discontinued, transitioning to an alternative antiresorptive agent should be considered.</u>
<b>Adverse reactions (clinically significant adverse reactions)</b>	<u>Multiple vertebral fractures after discontinuation of denosumab treatment: In patients with osteoporosis, multiple vertebral fractures may occur after discontinuation of denosumab treatment.</u>

### 2 Antineoplastics-Miscellaneous

## Pembrolizumab (genetical recombination)

<b>Brand name</b>	Keytruda Injection 20 mg and 100 mg (MSD K.K.)
<b>Adverse reactions (clinically significant adverse reactions)</b>	<u>Myocarditis: Myocarditis may occur. Chest pain, increased CK (CPK), electrocardiographic abnormality, etc. should be carefully monitored. If any abnormalities are observed, administration of this drug should be discontinued and appropriate measures should be taken.</u>

### 3 Antibiotics-Acting mainly on mold

## Caspofungin Acetate

<b>Brand name</b>	Cancidas for Intravenous Drip Infusion 50 mg and 70 mg (MSD K.K.)
<b>Adverse reactions (clinically significant adverse reactions)</b>	<u>Toxic epidermal necrolysis (TEN) and oculomucocutaneous syndrome (Stevens-Johnson syndrome): TEN and 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 taken.</u>

## 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 Marketing authorization holder (MAH) is responsible for collecting Adverse drug reaction (ADR) 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 March 31, 2017)

⊙: Products for which EPPV was initiated after March 1, 2017

Nonproprietary name		Name of the MAH	Date of EPPV initiate
Brand name			
⊙	Golimumab (Genetical Recombination) <sup>*1</sup> Simponi Subcutaneous Injection 50 mg, 100 mg Syringe	Janssen Pharmaceutical K.K.	March 30, 2017
⊙	Zinc Acetate Dihydrate <sup>*2</sup> Nobelzin Capsules 25 mg, 50 mg, Nobelzin Tablets 25 mg, 50 mg	Nobelpharma Co., Ltd.	March 24, 2017
⊙	Omalizumab (Genetical Recombination) <sup>*3</sup> Xolair for S.C. Injection 75 mg, 150 mg	Novartis Pharma K.K.	March 24, 2017
⊙	Linaclotide Linzess Tablets 0.25 mg	Astellas Pharma Inc.	March 22, 2017
⊙	Artemether/Lumefantrine Riamet Combination Tablets	Novartis Pharma K.K.	March 7, 2017
⊙	Triamcinolone Acetonide MaQaid Intravitreal Injection 40 mg	Wakamoto Co., Ltd.	March 2, 2017
⊙	Choriogonadotropin Alfa (Genetical Recombination) Ovidrel Syringe 250 µg	Merck Serono Co., Ltd.	March 1, 2017
⊙	Apremilast Otezla Tablets 10 mg, 20 mg, 30 mg	Celgene K.K.	March 1, 2017
	Dimethyl Fumarate Tecfidera Capsules 120 mg, 240 mg	Biogen Japan Ltd.	February 22, 2017
	Plerixafor Mozobil Subcutaneous Injection 24 mg	Sanofi K.K.	February 22, 2017
	Tenofovir Alafenamide Fumarate Vemlidy Tablets 25 mg	Gilead sciences K.K.	February 15, 2017
	Daclatasvir Hydrochloride / Asunaprevir / Beclabuvir Hydrochloride Ximency Combination Tablets	Bristol-Myers Squibb K.K.	February 15, 2017
	Etelcalcetide Hydrochloride Parsabiv Intravenous Injection for Dialysis 2.5 mg, 5 mg, 10 mg	ONO Pharmaceutical Co., Ltd.	February 15, 2017
	Pembrolizumab (Genetical Recombination) Keytruda Injection 20 mg, 100 mg <sup>*4</sup>	MSD K.K.	February 15, 2017

Nonproprietary name	Name of the MAH	Date of EPPV initiate
Brand name		
Pembrolizumab (Genetical Recombination) Keytruda Injection 20 mg, 100 mg <sup>5</sup>	MSD K.K.	February 15, 2017
Ticagrelor Brilinta Tablets 60 mg, 90 mg	AstraZeneca K.K.	February 8, 2017
Emtricitabine/TenofovirAlafenamide Fumarate Descovy Combination Tablets LT and HT	Japan Tobacco Inc.	January 27, 2017
DarunavirEthanolate/Cobicistat Prezcobix Combination Tablets	Janssen Pharmaceutical K.K.	January 4, 2017
Carglumic Acid Carbaglu Dispersible Tablets 200 mg	Pola Pharma Inc.	December 22, 2016
Canakinumab (Genetical Recombination) Ilaris for Subcutaneous Injection 150 mg <sup>6</sup>	Novartis Pharma K.K.	December 19, 2016
Eplerenone Selara Tablets 25, 50 mg <sup>7</sup>	Pfizer Japan Inc.	December 19, 2016
LomitapideMesilate Juxtapid Capsules 5, 10, 20 mg	Aegerion Pharmaceuticals Inc.	December 15, 2016
Dienogest DINagest Tablets 1 mg, DINagest OD Tablets 1 mg <sup>8</sup>	Mochida Pharmaceutical Co., Ltd.	December 2, 2016
PasireotidePamoate Signifor LAR Kit for I. M. Injection 20, 40, 60 mg	Novartis Pharma K.K.	December 2, 2016
Trafermin (genetical recombination) Regroth Dental Kit 600µg, 1200µg	Kaken Pharmaceutical Co., Ltd.	December 1, 2016
Albutrepenonacog Alfa (Genetical Recombination) Idelvion I.V. Injection 250, 500, 1000, 2000	CSL Behring K.K.	November 29, 2016
Rifaximin Rifxima Tablets 200 mg	Aska Pharmaceutical. Co., Ltd.	November 29, 2016
Budesonide Zentacort Capsules 3 mg	Zeria Pharmaceutical Co., Ltd.	November 29, 2016
Alogliptin Benzoate/Metformin Hydrochloride Inisync Combination Tablets	Takeda Pharmaceutical Company Limited	November 29, 2016
Zoledronic Acid Hydrate Reclast for I.V. Injection 5 mg	Asahi Kasei Pharma Corporation	November 25, 2016
Ponatinib Hydrochloride Iclusig Tablets 15 mg	Otsuka Pharmaceutical Co., Ltd.	November 21, 2016
Selexipag Uptravi Tablets 0.2 mg, 0.4 mg	Nippon Shinyaku Co., Ltd.	November 21, 2016
Ixekizumab (Genetical Recombination) Taltz 80 mg Syringe for SC Injection, Taltz 80 mg Auto-Injector for SC Injection	Eli Lilly Japan K.K.	November 21, 2016
Grazoprevir Hydrate Grazyna Tablets 50 mg	MSD K.K.	November 18, 2016
Elbasvir Erelsa Tablets 50mg	MSD K.K.	November 18, 2016
Elotuzumab (Genetical Recombination) Empliciti I.V. Injection 300 mg, 400 mg	Bristol-Myers Squibb K.K.	November 18, 2016

Nonproprietary name		Name of the MAH	Date of EPPV initiate
Brand name			
	Bilastine Bilanoa Tablets 20 mg	Taiho Pharmaceutical Co., Ltd.	November 18, 2016
	Telmisartan/Amlodipine Besilate/ Hydrochlorothiazide Micatio Combination Tablets	Nippon Boehringer Ingelheim Co., Ltd.	November 18, 2016
	Idarucizumab (Genetical Recombination) Prizbind Intravenous Solution 2.5 g	Nippon Boehringer Ingelheim Co., Ltd.	November 18, 2016
	Desloratadine Desalex Tablets 5 mg	MSD K.K.	November 18, 2016
	Adapalene/Benzoyl Peroxide Epiduo Gel	Galderma S.A.	November 4, 2016

- \*1 Improvement and maintenance for moderate to severe ulcerative colitis (for use only in patients who have not sufficiently responded to conventional treatments)
- \*2 Hypozincemia
- \*3 Idiopathic chronic urticaria (limited to patients who are not adequately responsive to conventional treatments)
- \*4 PD-L1-positive, unresectable, advanced or relapsed non-small cell lung cancer
- \*5 Radically unresectable malignant melanoma
- \*6 Familial mediterranean fever, Tumour necrosis factor receptor-associated periodic syndrome, Mevalonate kinase deficiency/Hyper IgD syndrome
- \*7 Chronic cardiac failure
- \*8 Improvement of pain in adenomyosis uteri