Pharmaceuticals and Medical Devices Safety Information

No. 297 December 2012

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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) website (http://www.pmda.go.jp/english/index.html) and on the MHLW website (http://www.mhlw.go.jp/, only available in Japanese language).

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Pharmaceuticals and Medical Devices Safety Information
No. 297 December 2012

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

[Outline of Information]

D: Distribution of Dear Healthcare Professional Letters *P*: Revision of Precautions *C*: Case Reports

PMDA medi-navi (Pharmaceuticals and Medical Devices Information E-mail Alert Service)

PMDA is providing the "PMDA medi-navi" a Pharmaceuticals and Medical Devices Information E-mail Alert Service (only available in Japanese language), when important safety information regarding pharmaceuticals and medical devices including Dear Healthcare Professional Letters or Revision of Precautions is issued. This e-mail service will enable you to obtain safety information faster and more efficiently, free of charge. Please feel free to use this service for your faster information collection.
See our website for details of the service. → http://www.info.pmda.go.jp/info/idx-push.html

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

ADRs	Adverse drug reactions
DM	Direct mail
DSU	Drug Safety Update
EPPV	Early Post-marketing Phase Vigilance
FY	Fiscal year
GI	Gastrointestinal
MAH	Marketing authorization holder
MR	Medical representative
MS	Marketing specialist

1

Surveillance on Dissemination and Utilization of Safety Information in Medical Institutions

1. Introduction

In order to ensure appropriate use of drugs and medical devices, MHLW and PMDA are jointly conducting safety measures such as revisions of the Precautions section of package inserts, based on evidence including reports of adverse drug reaction. The safety information on these measures is provided to medical institutions via various routes such as from the MHLW, PMDA, and pharmaceutical companies. It is essential that the most up-to-date information available be disseminated to, and utilized by, healthcare professionals at clinical settings in an appropriate manner.

PMDA, based on the Second Mid-term Plan,* has been conducting surveillance starting from fiscal year (FY) 2010 to grasp the status of the receipt, dissemination, and utilization of safety information at medical institutions and pharmacies, to determine the most appropriate style and method for providing information for easy access at clinical settings, and to propose ideal ways for receiving, distributing, and utilizing safety information. This section presents the results of the surveillance conducted in FY 2011.

* The Second Mid-term Plan **(excerpt)**:

PMDA will conduct, in a stepwise manner starting from FY 2010, surveillance to check how companies conduct safety measures, including whether information is properly disseminated to medical institutions, and to check how the information provided by companies is disseminated and utilized within each medical institution.

2. Results of surveillance in FY 2011

(1) Surveillance method

The surveillance period was from January 20 to February 10, 2012. The questionnaire sheets were sent by mail to 8647 hospitals across Japan.

The surveillance was conducted using 3 types of questionnaire sheets: Sheet A for the drug safety management supervisors and Sheet B and Sheet C for physicians (B for the surveillance related to an anticoagulant, C for the surveillance related to antidiabetics). Seven copies comprising 1 Sheet A and 3 each of Sheet B and Sheet C were sent to the drug safety management supervisors, requesting that Sheet B and Sheet C for physicians be delivered to physicians with different specialties and years of clinical experience **(Figures 1 and 2)**.

Figure 1 Overview of Surveillance

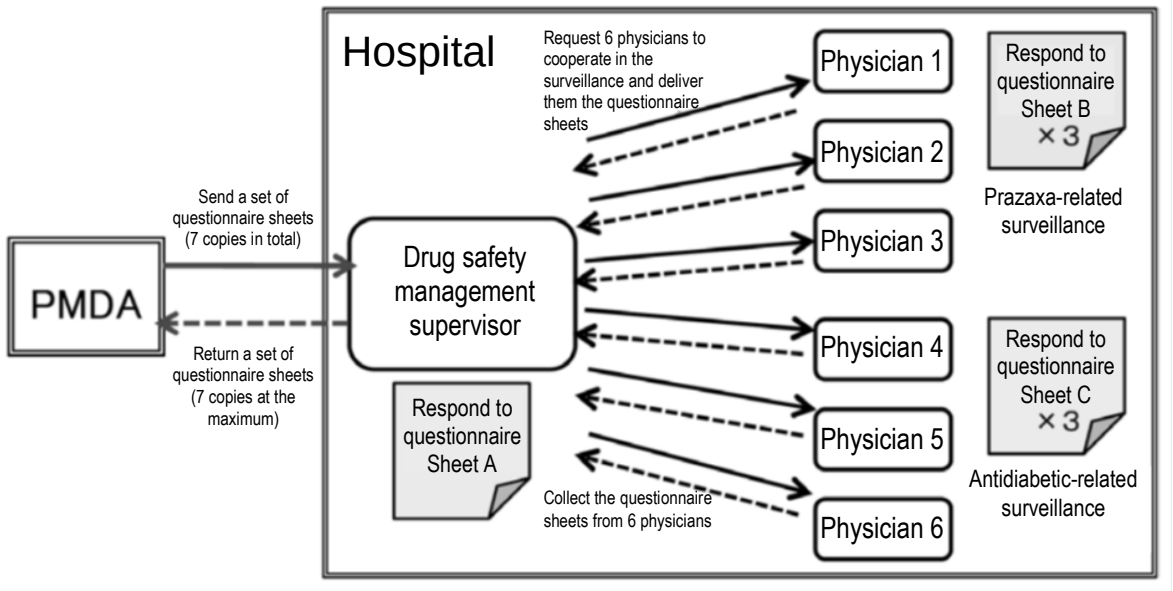


Figure 2 Respondent to each questionnaire sheet

Questionnaire sheet		Respondent
A: For drug safety management supervisor		Drug safety management supervisor
B: For physicians: Prazaxa-related surveillance	Physician 1	Physician with clinical experience of approximately 10 years or longer who belongs to a clinical department where Prazaxa is prescribed often
	Physician 2	Young physician with clinical experience of approximately less than 5 years who belongs to a clinical department where Prazaxa is prescribed often
	Physician 3	Physician who does not belong to the above clinical department (regardless of clinical experience)
C: For physicians: Antidiabetics-related surveillance	Physician 4	Physician with clinical experience of approximately 10 years or longer who belongs to a clinical department where antidiabetics are prescribed often
	Physician 5	Young physician with clinical experience of approximately less than 5 years who belongs to a clinical department where antidiabetics are prescribed often
	Physician 6	Physician who does not belong to the above clinical department (regardless of clinical experience)

In addition to questions on routine handling of safety information, the questionnaire covered cases with 3 drugs for which alerts were issued and revisions of the package insert were required in FY 2011 – an anticoagulant dabigatran (Prazaxa), an antidiabetic drug liraglutide (ViCTOZA), and another antidiabetic drug pioglitazone (ACTOS) –, and asked about the specific source of the safety information, method for dissemination, status of utilization, as well as possible changes in the awareness and actions of physicians after obtaining the safety information. In addition, the questionnaires asked about the use status, and source and management of safety information of drugs prescribed exclusively for extramural dispensing and drugs brought to the hospital by patients (bring-in drugs).

(2) Surveillance results and issues to be addressed

A total of 2242 respondents (2242 medical institutions) responded to the questionnaire to Sheet A, 2334 respondents (1276 medical institutions) responded to Sheet B, and 2675 respondents (1439 medical institutions) responded to sheet C. The percentage of collection was 25.9% for Sheet A, 14.8% for Sheet B, and 16.6% for Sheet C (the collection rates for Sheets B and C were calculated based on the number of medical institutions). In the surveillance in FY 2010 conducted by sending similar questionnaire sheets to drug safety management supervisors, the percentage of collection was 41.2%, and there were no major differences in the trend of responses to similar questions between these two surveillance results, suggesting that the analysis result was not very much biased.

Results of the surveillance were reviewed by the "Review Committee on the Status of the Dissemination and Utilization of Safety Information on Drugs, etc., in Medical Institutions" consisting of experts on medical safety and pharmaceutical practices established in PMDA, and summarized based on the opinions of the committee members. This section describes, among the surveillance results, "the development of a drug safety management system according to the scale and the conditions of each medical institution," "proper information dissemination that facilitates changes in the awareness and actions when prescribing drugs," "enhancement of safety information management of drugs prescribed exclusively for extramural dispensing," and "enhancement of safety information management of bring-in drugs."

a. Development of a drug safety management system according to the scale and the conditions of each medical institution

1) Ensuring the safety information source at small-scale medical institutions

The sources for obtaining drug safety information that are routinely and actively used by small-scale medical institutions (less than 100 beds) were, in the order of decreasing use frequency, "pharmaceutical company medical representatives (MRs)," "direct mails (DMs) from pharmaceutical companies," "Drug Safety Updates (DSUs)," and "Pharmaceuticals and Medical Devices Safety Information." Results showed that, in small-scale medical institutions, MRs were used as information sources less frequently than in large-scale institutions, whereas DMs tended to be used more frequently. Results also showed that the web-based information source including the "PMDA website" and "PMDA medi-navi" was used by only 20% of small-scale medical institutions, a smaller percentage compared with large-scale institutions (**Figure 3**). As regards drugs for which safety information was issued, such as Prazaxa, there were drug safety management supervisors in several medical institutions who replied that they "did not obtain" the safety information, despite the fact that the drug was prescribed in the medical institution (**Figure 4**).

In Small-scale medical institutions, physicians can have a closer contact with personnel who are in charge of drug information in hospitals compared with large-scale medical institutions, which is an advantage for proper dissemination of information. The major challenge for a small-scale medical institution, however, is to ensure information sources so that safety information is obtained promptly and properly.

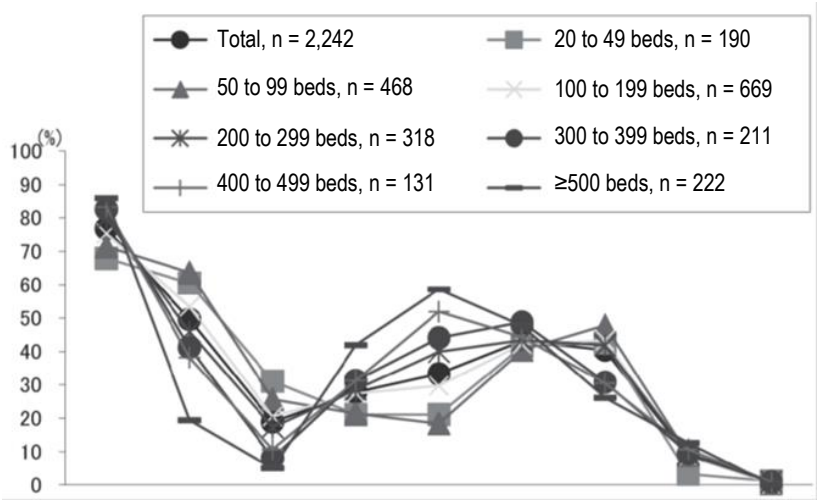
2) Establishment of a scheme for proper dissemination of safety information within a large-scale medical institution

The surveillance results showed that the sources for obtaining drug safety information that are routinely and actively used by large-scale medical institutions (400 beds or more) were, in the order of decreasing use frequency, "MRs," "PMDA medi-navi," "Pharmaceuticals and Medical Devices Safety Information," and the "PMDA website," indicating that prompt access to web-based information has been progressing (**Figure 3**). However, the results also revealed that although the drug safety management supervisors could obtain the information including Prazaxa-related safety information, there was a certain percentage of physicians, regardless of the scale of the institution, who actually prescribed the drug but "did not know" the details of alerts issued for the drug (**Figure 5**).

Thus, in large-scale medical institutions, although the sources for obtaining safety information are secured relatively, it is often difficult to decide to whom the information should be disseminated and to confirm to whom the information has been disseminated. In addition to ensuring the

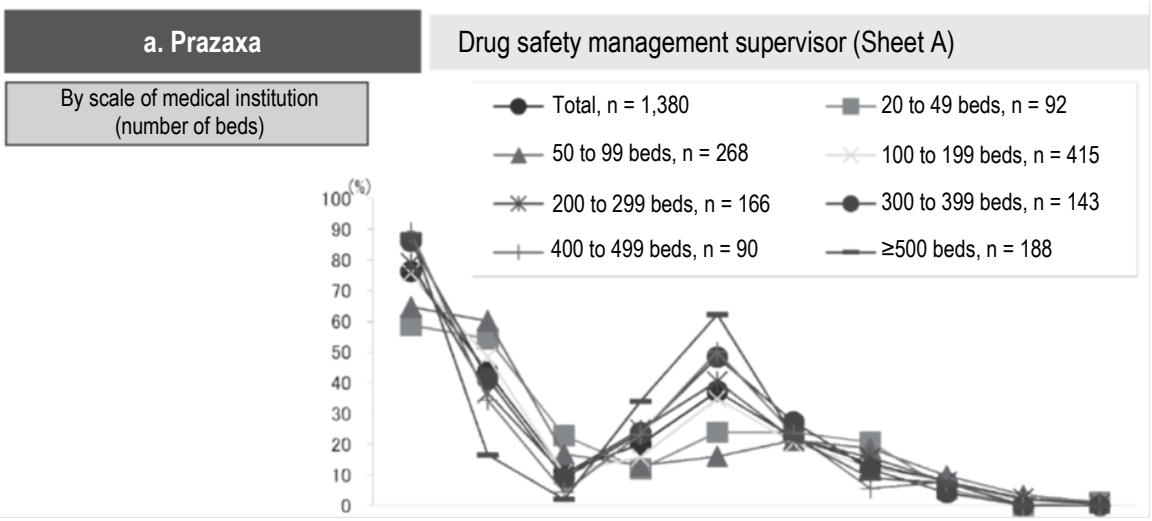
information sources, the major challenge for large-scale medical institutions is to establish a scheme for properly disseminating the information to all physicians who prescribe the drugs which are targets of information dissemination.

Figure 3 Routinely and actively used safety information sources



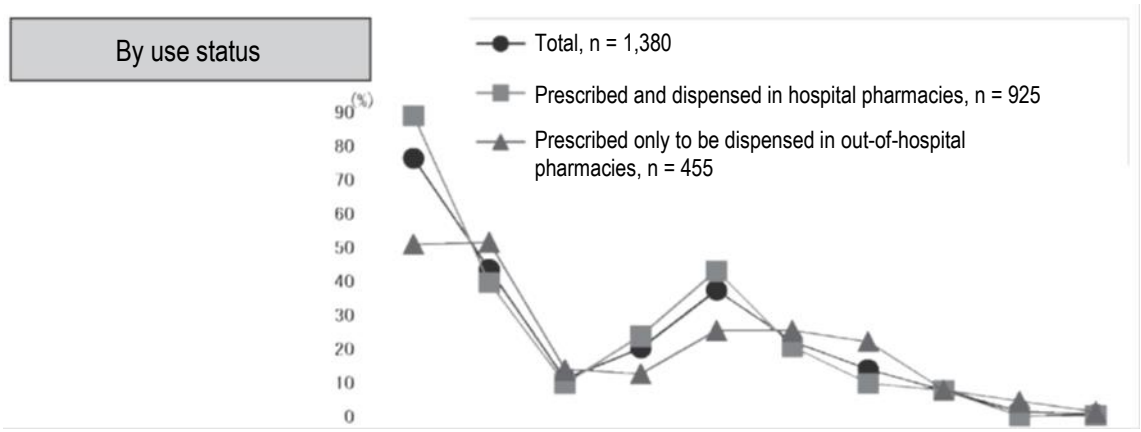
Scale of medical institution (number of beds)		n	1 Pharmaceutical company MR	2 Pharmaceutical company DM	3 Drug wholesaler marketing specialist (MS)	4 The PMDA website	5 PMDA medi-navi	6 Pharmaceuticals and Medical Devices Safety Information (published by MHLW)	7 DSU (published by the Federation of Pharmaceutical Manufacturers' Associations of Japan)	8 Other	No response
	Total	(2,242)	76.8	49.6	18.9	27.8	33.3	43.2	40.4	8.8	0.6
1	20 to 49 beds	(190)	67.9	60.5	31.1	21.1	21.1	41.6	42.6	3.2	1.1
2	50 to 99 beds	(468)	71.4	63.7	25.6	21.4	18.4	40.4	47.9	9.0	0.4
3	100 to 199 beds	(669)	75.3	53.4	20.5	27.4	29.7	42.2	43.3	8.7	0.3
4	200 to 299 beds	(318)	79.9	45.9	17.3	28.6	39.9	43.4	41.8	9.1	0.9
5	300 to 399 beds	(211)	82.5	41.2	8.1	31.3	44.1	48.8	30.8	9.5	0.9
6	400 to 499 beds	(131)	83.2	38.2	10.7	31.3	51.9	44.3	30.5	10.7	0.8
7	≥500 beds	(222)	86.0	19.4	5.0	41.9	58.6	47.7	26.1	12.6	0.0

Figure 4 Sources of safety information for Prazaxa



	Scale of medical institution (number of beds)	n	1 Pharmaceutical company MR	2 Pharmaceutical company DM	3 Drug wholesaler marketing specialist (MS)	4 The PMDA website	5 PMDA medi-navi	6 Pharmaceuticals and Medical Devices Safety Information (published by MHLW)	7 DSU (published by the Federation of Pharmaceutical Manufacturers' Associations of Japan)	8 Other	9 Not received	No response
	Total	(1,380)	76.2	43.4	11.0	20.1	37.2	22.1	13.8	7.6	1.4	0.5
1	20 to 49 beds	(92)	58.7	54.3	22.8	12.0	23.9	23.9	20.7	5.4	0.0	1.1
2	50 to 99 beds	(268)	64.6	60.1	16.8	13.1	16.0	21.3	18.7	9.7	3.4	1.1
3	100 to 199 beds	(415)	75.7	48.4	10.8	15.9	34.9	20.5	12.5	7.7	1.4	0.5
4	200 to 299 beds	(166)	78.9	36.7	10.2	24.7	40.4	21.7	15.7	7.8	2.4	0.6
5	300 to 399 beds	(143)	86.0	41.3	9.1	23.8	48.3	27.3	11.9	4.2	0.0	0.0
6	400 to 499 beds	(90)	88.9	34.4	4.4	23.3	50.0	23.3	5.6	7.8	0.0	0.0
7	≥500 beds	(188)	87.8	16.5	2.1	34.0	62.2	22.3	9.0	7.4	0.0	0.0

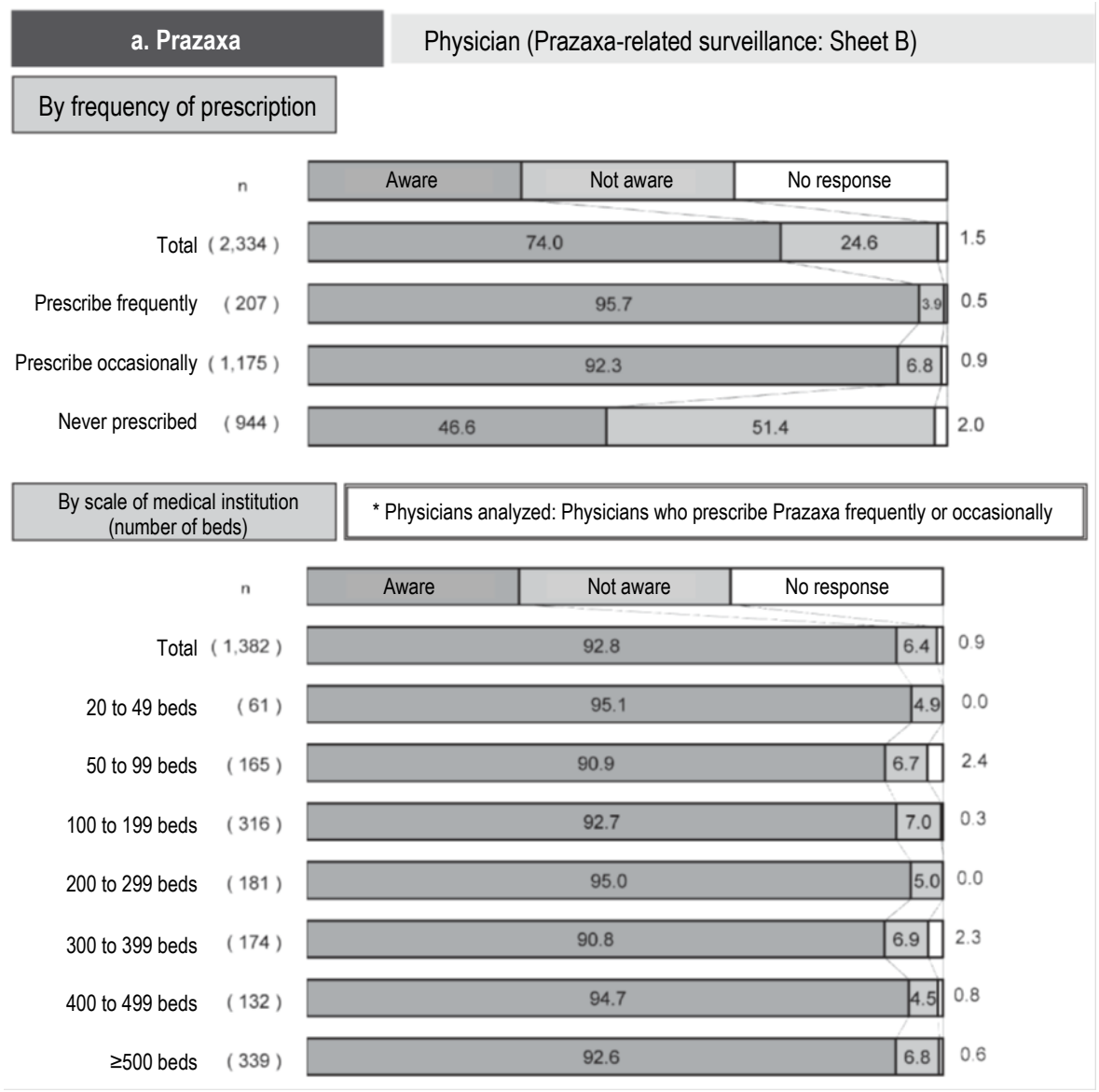
By use status



Use status of dabigatran etexilate methanesulfonate		n	1 Pharmaceutical company MR	2 Pharmaceutical company DM	3 Drug wholesaler marketing specialist (MS)	4 The PMDA website	5 PMDA medi-navi	6 Pharmaceuticals and Medical Devices Safety Information (published by MHLW)	7 DSU (published by the Federation of Pharmaceutical Manufacturers' Associations of Japan)	8 Other	9 Not received	No response
	Total	(1,380)	76.2	43.4	11.0	20.1	37.2	22.1	13.8	7.6	1.4	0.5
1	Prescribed and dispensed in-house	(925)	88.8	39.5	9.6	23.8	43.0	20.5	9.7	7.6	0.0	0.1
2	Prescribed in-house for out-of-house dispensing	(455)	50.8	51.4	13.8	12.5	25.3	25.3	22.0	7.7	4.4	1.3

* Similar results were obtained with ViCTOZA and ACTOS (data not shown).

Figure 5 Physicians' awareness of alerts in the Blue Letter for Prazaxa



* Similar results were obtained with ViCTOZA and ACTOS (data not shown).

b. Proper information dissemination that facilitates changes in the awareness and actions when prescribing drugs

Some physicians answered that they "did not know" the safety information on Prazaxa, etc., despite the fact that they actually prescribed the drug. The percentage of those who "did not know" was higher among physicians who "occasionally prescribe" the drug than among those who "frequently prescribe" the drug (**Figure 5**).

There was a tendency for the drug safety management supervisor to use greater varieties of measures for disseminating information in medical institutions where physicians who "know" worked than in the institutions where physicians who "did not know" worked. In the former medical institutions, the safety measures against alerts tended to be actively taken, such as by explaining the information through interviews with prescribing physicians and by checking whether tests are appropriately performed in individual patients.

On the other hand, among prescribing physicians who replied that they "know" about the contents of alerts, it was shown that proper dissemination and recognition of the alerts made a change in their awareness and actions according to the contents of alerts, such as more careful monitoring for

signs of adverse reactions when prescribing the drug and more careful checking for patient conditions through tests, etc.

These results suggested that proper recognition of the details of alerts helps the prescribing physicians to comply with the alerts. The following measures are considered to be effective as methods for disseminating the information to prescribing physicians:

- To educate prescribing physicians by continuous dissemination of the information (reminding) so that the information is remembered not only by frequently prescribing physicians but also by occasionally prescribing physicians.
- To disseminate the information using multiple methods: The information should be provided not only by paper or e-mail but also by more active measures against alerts by means of face-to-face communication, such as interviews with the prescribing physicians and by involvement in the decision of patient treatment.

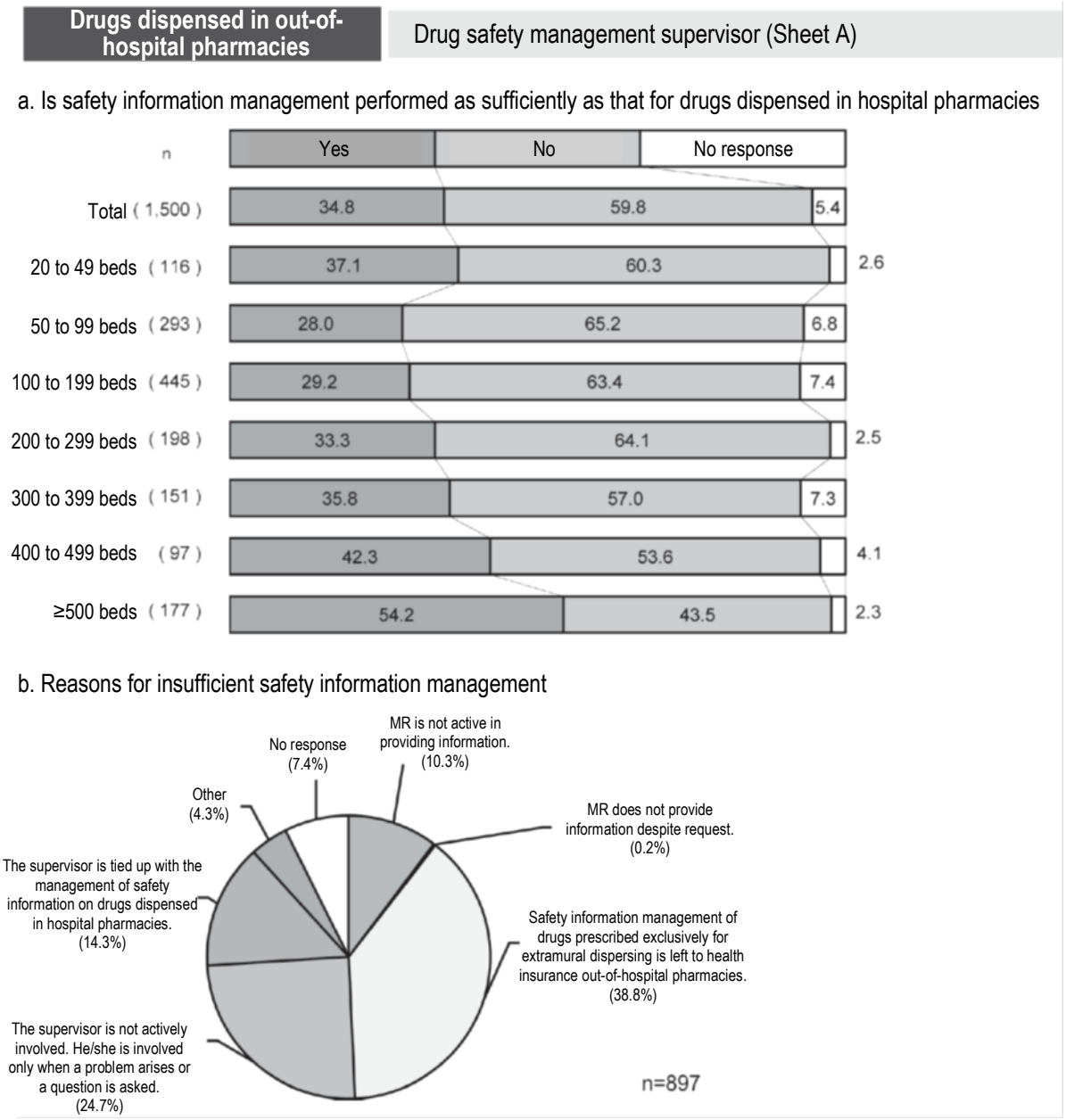
c. Enhancement of safety information management of drugs prescribed exclusively for extramural dispensing

The sources of information on drugs dispensed in out-of-hospital pharmacies showed a similar tendency as those of drug safety information routinely and actively used, but the percentage of use tended to be lower as a whole. As regards drugs for which the safety information was issued, such as Prazaxa, the percentage of obtaining the information from MRs was approximately 30% to 40% lower in institutions where the drug can be "prescribed exclusively for dispensing in out-of-hospital pharmacies" compared with the institutions where the drug is "prescribed and dispensed in hospital pharmacies" (**Figure 4**). Among the former institutions, some respondents answered that they "did not obtain" the information including Rapid Safety Communications (Blue Letters) of Prazaxa.

Moreover, there were many institutions that answered that "safety information management is not performed sufficiently" despite the fact that they have used increasingly drugs prescribed exclusively for extramural dispensing because of "increase in new drugs," "increase in patients referred from other medical institutions," and "suppression of the number of drugs in hospital pharmacies." The main reason for insufficient safety information management was that they leave the management to out-of-hospital pharmacies (**Figure 6**).

It is indispensable for prescribing physicians to be aware of the most up-to-date safety information in an appropriate manner. In addition to that, it is encouraged to develop a system that allows out-of-hospital pharmacies in charge of dispensing drugs to check the prescription.

Figure 6 Management status of safety information on drugs prescribed exclusively for extramural dispensing



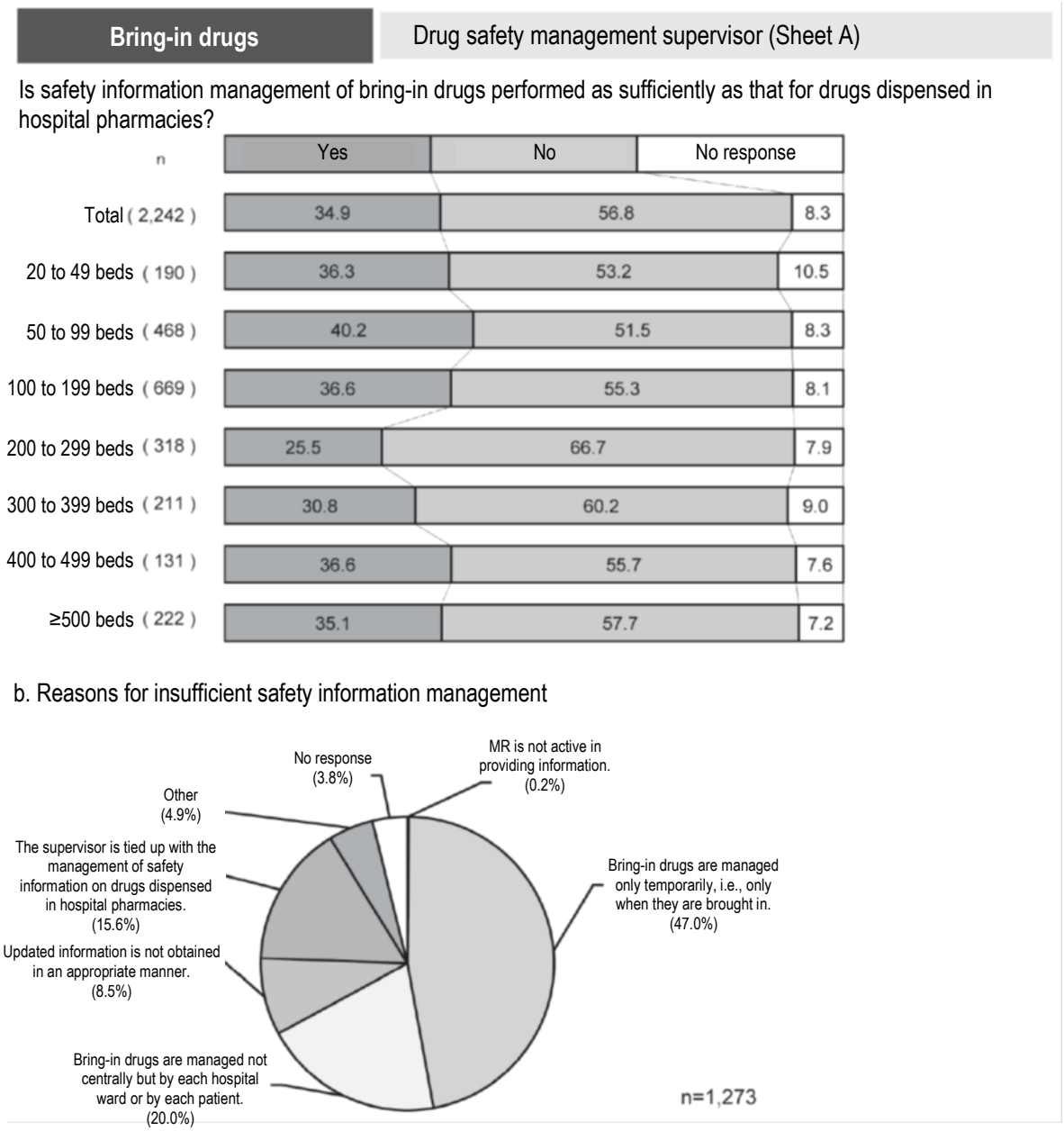
d. Enhancement of safety information management of bring-in drugs

Approximately 80% of medical institutions answered that they used bring-in drugs. Most of these institutions used bring-in drugs even if they did not belong to in-hospital dispensed drugs. A small percentage of institutions used bring-in drugs only if they belonged to in-hospital dispensed drugs.

Approximately 50% of medical institutions, regardless of the scale of the institutions, replied that safety information management of bring-in drugs is not performed sufficiently. The major reasons include "bring-in drugs are managed only temporarily, i.e., only when they are brought in," "bring-in drugs are managed not centrally but by each hospital ward or by each patient" (**Figure 7**).

Since there is a possibility that various types of drugs are used as bring-in drugs, it is necessary to enhance the safety management system to allow awareness of the most up-to-date drug information.

Figure 7 Management status of safety information of bring-in drugs



3. Conclusions

PMDA medi-navi and the PMDA website allow healthcare professionals to ensure prompt access to safety information on drugs. They can also be used for information management of drugs prescribed exclusively for extramural dispensing and bring-in drugs which are not dispensed in the hospital. Use of these information sources provided by PMDA is strongly recommended.

The above information is only a part of the results of the surveillance conducted in FY 2011. The PMDA website presents the outline and the detailed report of the surveillance results.

PMDA is very grateful for medical institutions that collaborated in this surveillance, and asks for further collaboration in a similar surveillance, which is scheduled in FY 2012 (P 15).

[PMDA website]
http://www.info.pmda.go.jp/

[Outline of the results of the FY2011 surveillance and detailed report on the surveillance results]
http://www.info.pmda.go.jp/kyoten_iyaku/dentatsu_katsuyou.html (only available in Japanese language)

Request for Collaboration in "Surveillance on the Status of the Receipt, Dissemination, and Utilization of Safety Information in Medical Institutions and Pharmacies" in FY 2012

The Pharmaceuticals and Medical Devices Agency (PMDA) has been conducting surveillance to grasp the methods for the receipt, dissemination, and utilization of safety information in medical institutions and pharmacies, thereby to help promote the safe use of drugs, etc. at clinical settings. PMDA now plans to conduct a surveillance for FY 2012, and your collaboration will be greatly appreciated.

Objectives:

It is required that the most up-to-date information (most up-to date findings on adverse reactions, etc.) on drugs and medical devices and on noteworthy safety measures supplied by the Ministry of Health, Labour, and Welfare, PMDA, pharmaceutical companies, etc., be obtained, disseminated, and utilized in an appropriate manner in medical institutions and pharmacies.

This surveillance is conducted to grasp the status of the receipt, dissemination, and utilization of safety information in medical institutions and pharmacies, thereby to determine the most appropriate style and method for providing information for more easy access at clinical settings. PMDA plans, based on the results of the surveillance, to propose the ideal methods for the receipt, dissemination, and utilization of information, thereby to help promote the safe use of drugs, etc.

Scope:

All hospitals in Japan (approximately 8,600 institutions) and half of health insurance pharmacies (approximately 27,000 institutions)

Planned surveillance period:

Approximately 3 weeks starting from January 7 (Mon), 2013

Surveillance method:

Questionnaire sheets, etc., will be sent by the surveillance contractor to the drug safety management supervisor in each target institution.

Responses to the surveillance questionnaire should be done by inputting them in the questionnaire sheet on the website, as a general rule. The website for the surveillance questionnaire can be found at the PMDA website (http://www.info.pmda.go.jp/index.html), etc. In case it is impossible to respond to the questionnaire via the Internet, fill in the questionnaire sheets provided and send them back using the attached return-mail envelope.

The information contained in the answer will not be used for purposes other than the analysis of the surveillance results and safety measure activities conducted by PMDA.

2

Precautions for Using Gastrointestinal Stents

1. Introduction

Gastrointestinal (GI) stents including esophageal stents, gastroduodenal stents, and colonic stents are medical devices that are placed to relieve GI obstructions/strictures caused by progression of cancer, etc. and to maintain patency of the GI tracts. In Japan, the esophageal stent was approved in 1995, the gastroduodenal stent in 2009, and the colonic stent in 2011. Currently, 8 different types of GI stents listed in the following table are available in the market.

Reported cases of GI perforation caused by GI stents are described below. Healthcare professionals are requested to take extreme caution when using GI stents.

List of GI stents

Generic Name	Marketing authorization holder	Brand Name
Esophageal stent	Boston Scientific Japan K.K.	• Ultraflex Uncovered Esophageal Stent System • Ultraflex Covered Esophageal Stent System
	Century Medical, Inc.	Niti-S Esophageal stents
	MC Medical, Inc.	HANAROSTENT Esophagus Covered Stent
	Piolax Medical Devices, Inc.	FlexELLA-J
Gastroduodenal stent	Boston Scientific Japan K.K.	WallFlex Duodenal Stent System
	Century Medical, Inc.	Niti-S Pyloric/Duodenal stents
Colonic stent	Boston Scientific Japan K.K.	WallFlex Colonic Stent System

2. Adverse event reports related to GI perforation*

In Japan, 53 cases of confirmed or suspected GI perforation after GI stent placement have been reported (5 cases with esophageal stents, 19 cases with gastroduodenal stents, and 29 cases with colonic stents). Of 53 cases, 16 cases resulted in fatal outcome due to peritonitis, etc. (1 case with esophageal stent, 8 cases with gastroduodenal stent, and 7 cases with colonic stent).

In some cases, it was reported that the gastrointestinal tissue had become fragile due to radiation therapy and chemotherapy performed prior to stent placement, and that the stent dilation was likely to have caused the GI perforation in that condition.

* Adverse events reported to PMDA as of November 30, 2012, which include cases where the relationship between the medical device and the health damage is unknown.

3. Safety measures

It is known that GI perforation occurs as a result of tumor infiltration or serious inflammation of tissue caused by cancer therapy such as radiation therapy and chemotherapy. Stent placement in patients with such conditions may increase the risk of GI perforation. It is necessary to evaluate the appropriateness of placing the GI stent by carefully monitoring the patient conditions.

In order to mitigate the risk, MHLW required, on November 7, 2012, the marketing authorization holders (MAHs) of GI stents to revise the package insert and provide information to healthcare professionals[1)]. It is required that the package inserts should include, in the "Warnings" section, a description requiring careful evaluation of the appropriateness of using the stent in the following patients:

- Patients who have received radiation therapy or chemotherapy prior to stent placement
- Patients with significant tumor infiltration

Healthcare professionals are requested to carefully evaluate the appropriateness of using the GI stent in the above patients giving consideration to the risk of GI perforation caused by stent insertion and to an alternative treatment method such as bypass surgery.

The details of the revision of the package inserts are as follows.

○ "Warnings" section of the package insert:

Cases of perforation at the site of stent placement have been reported. The appropriateness of placing the stent should be evaluated carefully, especially in the following patients:

1) Patients who have received radiation therapy or chemotherapy prior to stent placement
2) Patients with significant tumor infiltration

<Reference> **(including provisionally translated titles)**

1) Joint PFSB/SD Notification No.1107-1 and PFSB/ELD/OMDE No.1107-1, by the Director of Safety Division, Pharmaceutical and Food Safety Bureau and by the Director of Office of Medical Device Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW, dated November 7, 2012 "Revision of Precautions for Gastrointestinal Stents" http://wwwhourei.mhlw.go.jp/hourei/doc/tsuchi/T121115I0010.pdf (only available in Japanese language)

3

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 new drugs. It is imposed that its Marketing Authorization Holder is responsible for collecting the adverse drug reactions (ADRs) from all of the medical institutions where the drugs are used and for 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 adverse drug reactions. EPPV is specified as a condition of approval.

(As of December 1, 2012)

Nonproprietary name Brand name	Name of the marketing authorization holder	Date of EPPV initiate
Anagliptin SUINY Tab. 100 mg	Sanwa Kagaku Kenkyusho Co., Ltd.	November 30, 2012
Aflibercept (Genetical Recombination) EYLEA solution for IVT inj. 40 mg/mL	Bayer Yakuhin, Ltd.	November 27, 2012
Stiripentol DIACOMIT DRYSYRUP 250 mg, 500 mg, DIACOMIT CAPSULES 250 mg	Meiji Seika Pharma Co., Ltd	November 27, 2012
Glycopyrronium Bromide seebri inhalation capsules 50 μg	Novartis Pharma K.K.	November 22, 2012
Tigecycline Tygacil Injection 50 mg	Pfizer Japan Inc.	November 22, 2012
Lubiprostone Amitiza Capsules 24 μg	Sucampo Pharma Ltd.	November 22, 2012
Botulinum Toxin Type A BOTOX for injection 50 Unit, 100Unit*1	GlaxoSmithKline K.K.	November 21, 2012
Everolimus AFINITOR tablets 5 mg, 2.5 mg*2	Novartis Pharma K.K.	November 21, 2012
Triamcinolone Acetonide MaQaid intravitreal injection 40 mg*3	Wakamoto Co., Ltd.	November 21, 2012
Adsorbed Diphtheria-purified Pertussis-tetanus-inactivated polio (Sabin strain) Combined Vaccine TETRABIK Subcutaneous Injection Syringe	The Research Foundation for Microbial Diseases of Osaka University	October 31, 2012
Adsorbed Diphtheria-purified Pertussis-tetanus-inactivated polio (Sabin strain) Combined Vaccine Quattrovac Subcutaneous Injection Syringe	The Chemo-Sero-Therapeutic Research Institute	October 31, 2012
Degarelix Acetate Gonax 80 mg for Subcutaneous Injection, Gonax 120 mg for Subcutaneous Injection	Astellas Pharma. Inc.	October 23, 2012
Clopidogrel Sulfate PLAVIX 25 mg Tablets, 75 mg Tablets*4	Sanofi-aventis K.K.	September 28, 2012

Tazobactam Sodium/Piperacillin Sodium ZOSYN for Intravenous Injection 2.25, 4.5*[5]	Taiho Pharmaceutical Co., Ltd.	September 28, 2012
Pazopanib Hydrochloride Votrient Tablets 200 mg	GlaxoSmithKline K.K.	September 28, 2012
Iguratimod KOLBET Tablets 25 mg	Toyama Chemical Co., Ltd.	September 12, 2012
Iguratimod Careram Tablets 25 mg	Eisai Co., Ltd.	September 12, 2012
Teneligliptin Hydrobromide Hydrate TENELIA Tablets 20 mg	Mitsubishi Tanabe Pharma Corporation	September 10, 2012
Formoterol Fumarate Hydrate Oxis 9 μg Turbuhaler 28 doses, 60 doses*[6]	AstraZeneca K.K.	September 3, 2012
Inactivated Poliomyelitis Vaccine (Salk Vaccine) IMOVAX POLIO subcutaneous	Sanofi Pasteur K.K.	August 31, 2012
Axitinib Inlyta Tablets 1 mg, 5 mg	Pfizer Japan Inc.	August 30, 2012
Ropinirole Hydrochloride ReQuip CR Tablets 2 mg, 8 mg	GlaxoSmithKline K.K.	August 28, 2012
Atomoxetine Hydrochloride Strattera Capsule 5 mg, 10 mg, 25 mg, 40 mg*[7]	Eli Lilly Japan K.K.	August 24, 2012
Sulbactam Sodium/Ampicillin Sodium UNASYN-S for Intravenous Use 0.75 g, 1.5 g, UNASYN-S KIT for Intravenous Use 1.5 g, 3 g*[8, 9]	Pfizer Japan Inc.	August 10, 2012
Budesonide/Formoterol Fumarate Hydrate Symbicort Turbuhaler 30 doses, 60 doses*[10]	AstraZeneca K.K.	August 10, 2012
Perflubutane SONAZOID FOR INJECTION 16 μL*[11]	Daiichi Sankyo Company, Limited	August 10, 2012
Sunitinib SUTENT Capsule 12.5 mg*[12]	Pfizer Japan Inc.	August 10, 2012
Apomorphine Hydrochloride Hydrate Apokyn subcutaneous injection 30 mg	Kyowa Hakko Kirin Co., Ltd.	July 27, 2012
Rotavirus Vaccine, Live, Oral, Pentavalent RotaTeq Oral Solution	MSD K.K.	July 20, 2012
Gabapentin Enacarbil Regnite Tablets 300 mg	Astellas Pharma. Inc.	July 10, 2012
Bixalomer Kiklin Capsules 250 mg	Astellas Pharma. Inc.	June 26, 2012
Azithromycin Hydrate ZITHROMAC Intravenous use 500 mg, ZITHROMAC Tablets 250 mg*[13]	Pfizer Japan Inc.	June 22, 2012
Aprepitant EMEND Capsules 125 mg, 80 mg, EMEND Capsules Set*[14]	Ono Pharmaceutical Co., Ltd.	June 22, 2012
Esomeprazole Magnesium Hydrate Nexium Capsules 10 mg, 20 mg*[15]	AstraZeneca K.K.	June 22, 2012
Pregabalin LYRICA Capsules 25 mg, 75 mg, 150 mg*[16]	Pfizer Japan Inc.	June 22, 2012
Lidocaine Penles Tape 18 mg*[17]	Nitto Denko Corporation	June 22, 2012

Dornase Alfa (Genetical Recombination) PULMOZYME Inhalation Solution 2.5 mg	Chugai Pharmaceutical Co., Ltd.	June 8, 2012
Rilpivirine Hydrochloride EDURANT Tablets 25 mg	Janssen Pharmaceutical K.K.	June 8, 2012

*1 An additional indication for “treatment of patients with severe primary axillary hyperhidrosis”

*2 An additional indication for “treatment of patients with renal angiomyolipoma associated with tuberous sclerosis, subependymal giant cell astrocytoma associated with tuberous sclerosis”

*3 An additional indication for “treatment of patients with diabetic macular oedema”

*4 An additional indication for “prevention of thrombus and embolus formation in patients with peripheral arterial disease”

*5 An additional indication for “treatment of patients with peritonitis, intra-abdominal abscess, cholecystitis, or cholangitis”

*6 An additional indication for “remission of various symptoms associated with airway obstructive disorder in patients with chronic obstructive pulmonary disease (including chronic bronchitis and emphysema)”

*7 An additional indication for “treatment of patients with attention deficit/hyperactivity disorder (AD/HD) in adulthood”

*8 An additional indication for “Streptococcus pneumonia, Moraxella (Branhamella) catarrhalis”

*9 An additional administration for “severe infections”

*10 An additional indication for “remission of various symptoms in patients with chronic obstructive pulmonary disease (including chronic bronchitis and emphysema) (for patients who require concomitant use of inhaled corticosteroids and long acting inhaled beta-2 agonist)”

*11 An additional indication for “contrast enhanced imaging for breast mass lesion in mammary ultrasonography”

*12 An additional indication for “treatment of patients with pancreatic neuroendocrine tumour”

*13 An additional indication for “treatment of patients with pelvic inflammatory disease”

*14 An additional administration for “pediatrics (aged 12 and older)”

*15 An additional indication for “treatment of patients with suppression of recurrent gastric ulcer or duodenal ulcer associated with administration of low-doses aspirin”

*16 An additional indication for “treatment of pain in patients with fibromyalgia”

*17 An additional indication for “relief of pain at removal of molluscum contagiosum”