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To: Commissioners of Prefectural Health Departments (Bureaus)

Director, Pharmaceutical Safety Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Provision of Information on Precautions, etc. for Drugs, etc.

The Act Partially Amending on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 63 of 2019; hereinafter referred to as the “Amendment Act”) was promulgated on December 4, 2019. In addition, Ministerial Ordinance on the Development of Related Ministerial Ordinances in Accordance with Partial Enforcement of the Act Partially Amending the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (MHLW Ordinance No. 15 of 2021; hereinafter referred to as the “Ministerial Ordinance for Amendment of the Act”) was promulgated on January 29, 2021.

It has been mandatory so far to indicate necessary information on precautions, etc. for use and handling of drugs, medical devices, and cellular and tissue-based products (hereinafter referred to as “drugs, etc.”) on a document or container/wrapping attached to each product (hereinafter referred to as “package insert, etc.”). After amendment of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Law No. 145 of 1960; hereinafter referred to as the “Act”) as per the Amendment Act, however, it has become mandatory to disclose information on precautions, etc. for drugs (excluding drugs requiring guidance, OTC drugs, etc.),

medical devices (excluding medical devices, etc. mainly intended to be used for the life of general consumers), and cellular and tissue-based products by means of information communication technology, pursuant to the provisions of Article 52, Paragraph 1; Article 63-2, Paragraph 1; Article 65-3; and Article 68-2. In addition, the obligation to include information on precautions, etc. in package inserts, etc. has been abolished in principle, and it has become mandatory to print a code, etc. necessary to obtain such information on the container or wrapping (hereinafter referred to as "container, etc.") of each product.

Detailed rules have been stipulated in the Regulation for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices after the amendment as per the Ministerial Ordinance for Amendment of the Act (Ministry of Health and Welfare Ordinance No. 1 of 1961; hereinafter referred to as the "Enforcement Regulation of the Act"), which will come into effect on August 1, 2021.

The amendments concerning information on precautions, etc. for drugs, etc. are as detailed below. Please understand the amendments and inform the relevant organizations under your jurisdiction.

I. "Information on Precautions, etc."

The Act before the amendment obligated the inclusion of necessary information on precautions, etc. for use and handling of drugs, etc. in their package inserts, etc., and such information was defined as "matters to be indicated on package inserts" (Article 52, Paragraph 1, etc. of the Act before the amendment).

After the amendment, pursuant to the provisions of Article 68-2 of the Act, it has become mandatory to disclose necessary information on precautions, etc. for use and handling of drugs (excluding guidance-mandatory drugs , OTC drugs, etc.), medical devices (excluding medical devices, etc. provided primarily for the ordinary use of general consumers), and cellular and tissue-based products (hereinafter referred to as "drugs, etc. requiring information disclosure") by means of information communication technology, and such information has been newly defined as "information on precautions, etc." (Article 68-2, Paragraph 1 and Paragraph 2 of the Act).

Necessary information on precautions, etc. for use and handling of drugs and medical devices, not covered by Article 68-2 of the Act, is defined as “information on precautions, etc. defined in Article 52, Paragraph 2” in Article 218-2, etc. of the Enforcement Regulation of the Act and is continuously required to be included in package inserts, etc. (Article 52, Paragraph 2, etc. of the Act)

The terms after the amendment are defined as follows.

- In the present notification, “information on precautions, etc.” defined in Article 68-2, Paragraph 2 of the Act and “information on precautions, etc. defined in Article 52, Paragraph 2” in Article 218-2, etc. of the Enforcement Regulation of the Act are collectively called “information on precautions, etc.”
- When a document containing information on precautions, etc. is attached to a drug, etc., the document is called a “package insert,” as it was before the amendment.
- A document containing information on precautions, etc. to be released on the website of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as the “PMDA”) is called an “electronic package insert.”

II. Printing of Codes, etc. on Containers, etc. (Article 52, Paragraph 1, etc. of the Act)

1. Printing of Codes, etc. on Containers, etc. (Article 52, Paragraph 1, etc. of the Act)

In principle, drugs, etc. requiring information disclosure must have a code on their containers, etc. necessary to obtain information on precautions, etc. by means of information communication technology, pursuant to the provisions of Article 52, Paragraph 1; Article 63-2, Paragraph 1; and Article 65-3 of the Act.

(1) Target drugs, etc. (drugs, etc. requiring information disclosure)

Printing of a code, etc. is necessary for the drugs, etc. requiring information disclosure listed below:

a. Drugs other than guidance-mandatory drugs, OTC drugs (including in vitro diagnostics), and pharmacy-compounded drugs
b. Medical devices other than those provided primarily for the ordinary use of general consumers (Table 4-2 Attached to the Enforcement Regulation of the Act, and the Medical Devices Designated by Minister of Health, Labour and Welfare Pursuant to Provisions in Table 4-2 Attached to the Enforcement Regulation of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices [Public Notice No. 44 of the

Ministry of Health, Labour and Welfare, 2021; hereinafter referred to as “Public Notice of the Designation of Medical Devices Provided Primarily for the Ordinary Use of General Consumers”])

c. Cellular and tissue-based products

(2) Method of utilizing information communication technology

The method of browsing the PMDA’s website via a code printed on each container, etc. is to be used. (Article 210-2 of the Enforcement Regulation of the Act)

Prior to posting information on the website, refer to a notification about the method of registration that will be issued separately by the PMDA.

(3) Codes

Codes to obtain information on precautions, etc. shall be barcodes or two-dimensional codes necessary to browse the PMDA’s website where the information on precautions, etc. is posted. (Article 210-2 of the Enforcement Regulation of the Act)

Barcodes or two-dimensional code types shall be GS1 DataBar Limited, GS1 DataBar Stacked, or their composite symbol (CC-A), or GS1-128 Symbol for prescription drugs, and GS1-128 Symbol or GS1 Datamatrix for medical devices and in vitro diagnostics. For medical devices and in vitro diagnostics that already use GS1 DataBar Limited, GS1 DataBar Stacked, or their composite symbol (CC-A) barcodes at the time of issuance of the present notification, however, use of these GS1 DataBar Limited, GS1 DataBar Stacked, or their composite symbol (CC-A) barcodes is permitted for the time being.

For cellular and tissue-based products, appropriate barcodes or two-dimensional codes among those above shall be used according to the characteristics, etc. of individual products.

Product codes shall be compliant with internationally harmonized standards, and it is required to use GS1 product codes that are popular and available in Japan (Global Trade Item Number [GTIN]; more specifically, GTIN-13 [generally called JAN code in Japan], GTIN-14, or GTIN-12]).

For a product that has multiple barcodes or two-dimensional codes, such as products imported from overseas, the barcode or two-dimensional code to obtain

information on precautions, etc. shall be indicated clearly to prevent healthcare professionals from being confused.

For any questions about barcodes or two-dimensional codes, refer to the website, etc. of GS1 Japan (General Incorporated Foundation Distribution Systems Research Institute) shown below.

https://www.dsri.jp/standard/barcode/ (Only in Japanese)
https://www.gs1jp.org/

(4) Registration of necessary information to enable the browsing of electronic package inserts via a code

Marketing authorization holders (herein referred to as “MAH”s) of drugs, etc. requiring information disclosure must register the information that links each product code to each package insert number (unique number assigned to each electronic package insert when posted on the PMDA’s website) in the safety information posting system located on the PMDA’s website for MAHs, in order to enable users to obtain information on precautions, etc. by means of information communication technology. For the method of registration, refer to the PMDA’s website for MAHs.

(5) Containers, etc. requiring the printing of codes

Minimum unit of containers, etc. requiring the printing of codes to obtain information on precautions, etc. shall be the sales packaging unit (minimum packaging unit usually sold from wholesalers, etc. to medical institutions, etc. [minimum sales unit]).

2. Exceptions to the Printing of Codes on Containers, etc. (Proviso to Article 52, Paragraph 1 of the Act)

(1) Drugs (including in vitro diagnostics)

a. Drugs packed in containers, etc. with a small surface area

If a code is indicated on a document attached to the drug, it is not necessary to print a code on its container, etc. (Article 211, Paragraph 3 of the Enforcement Regulation of the Act)

b. Medical gases, etc.

For a medical gas, etc. for which it is not appropriate to print a code on its container, etc. because of its usage, if a code is indicated on a document attached to the gas, it is not necessary to print a code on its container, etc. (Article 212-2 of the Enforcement Regulation of the Act)

c. Drugs for manufacturing only

For a drug used only for manufacture, if information such on precautions, etc. (excluding dosage and administration and other necessary precautions for use and handling) is included in its package insert, etc., it is not necessary to print a code on its container, etc. (Article 214, Paragraph 3 of the Enforcement Regulation of the Act)

d. Drugs only for dispensing of medicines

When an exception to the labeling of drugs intended for dispensing is permitted and if information on precautions, etc. or a code is included in the package insert, etc. of a drug held by a pharmacy proprietor to whom drugs intended for dispensing are sold, it is not necessary to print a code on the container, etc. of the drug intended for dispensing. (Article 216, Paragraph 2 of the Enforcement Regulation of the Act)

e. Drugs for export

For a drug for export, it is not necessary to print a code on its container, etc. (Article 74, Paragraph 2 of the Order for the Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Cabinet Order No. 11 of 1961; hereinafter referred to as “Enforcement Order of the Act”) after the amendment as per the Ministerial Ordinance on the Development of Related Ministerial Ordinances in Accordance with Partial Enforcement of Partial Amendment of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Government Ordinance No. 1 of 2021).

f. Specially approved drugs

For a specially approved drug, it is not necessary to print a code on its container, etc. if a code is indicated on a document attached to the drug or if information on

precautions, etc. is included in its package insert, etc. (Article 75, Paragraph 5 of the Enforcement Order of the Act)

(2) Medical devices

a. Medical devices packed in containers, etc. with a small surface area

If a code is indicated on a document attached to the medical device, it is not necessary to print a code on its container, etc. (Article 224, Paragraph 4, Item 1 of the Enforcement Regulation of the Act)

b. Medical devices that cannot be packed in containers, etc. due to their structure and properties

If a code is indicated on a document attached to the medical device, it is not necessary to print a code on its container, etc. (Article 224, Paragraph 4, Item 2 of the Enforcement Regulation of the Act)

c. Medical device programs

For a recording medium storing a medical device program, a code must be printed on the container, etc. of the recording medium, and an electromagnetic record in which information on precautions, etc. is recorded by a method that allows a user of the medical device program to read it easily must be provided. (Article 224, Paragraph 6 of the Enforcement Regulation of the Act)

For a medical device program provided via a telecommunication line, information on precautions shall be provided by either of the following methods (i) or (ii): (Article 224, Paragraph 8 of the Enforcement Regulation of the Act)

(i) The distributor of a medical device program provides information on precautions, etc. before providing the medical device program.

(ii) The MAH of a medical device program provides an electromagnetic record in which information on precautions, etc. is recorded by a method that allows a user of the medical device program to see it easily, together with the medical device program.

d. Medical devices for manufacturing only

For a medical device used only for manufacture, if information on precautions, etc. (excluding usage and other necessary precautions for use and handling) is included in its package insert, etc., it is not necessary to print a code on its

container, etc. (Article 214, Paragraph 3 applied mutatis mutandis to Article 228 of the Enforcement Regulation of the Act)

e. Medical devices for export

For a medical device for export, it is not necessary to print a code on its container, etc. (Article 74-2, Paragraph 2 of the Enforcement Order of the Act)

f. Specially approved medical devices for emergency

For a specially approved medical device, it is not necessary to print a code on its container, etc. if a code is indicated on a document attached to the medical device or if information on precautions, etc. is included in its package insert, etc. (Article 75, Paragraph 5 of the Enforcement Order of the Act)

(3) Cellular and tissue-based products

a. Cellular and tissue-based products packed in containers, etc. with a small surface area

If a code is indicated on a document attached to the cellular and tissue-based product, it is not necessary to print a code on its container, etc. (Article 228-5, Paragraph 3 of the Enforcement Regulation of the Act)

b. Cellular and tissue-based products for manufacturing only

For a cellular and tissue-based product used only for manufacture, if information on precautions, etc. (excluding dosage and administration, instructions for use, and other necessary precautions for use and handling) is included in its package insert, etc., it is not necessary to print a code on its container, etc. (Article 214, Paragraph 3 applied mutatis mutandis to Article 228-9 of the Enforcement Regulation of the Act)

c. Cellular and tissue-based products for export

For a cellular and tissue-based product for export, it is not necessary to print a code on its container, etc. (Article 74-3, Paragraph 2 of the Enforcement Order of the Act)

d. Specially approved cellular and tissue-based products

For a specially approved cellular and tissue-based product, it is not necessary to print a code on its container, etc. if a code is indicated on a document attached to the medical device or if information on precautions, etc. is included in its package insert, etc. (Article 75, Paragraph 5 of the Enforcement Order of the Act)

3. Drugs and Medical Devices Requiring the Inclusion of Information on precautions, etc. in Package Inserts, etc. (Article 52, Paragraph 2, etc. of the Act)

(1) Target drugs, etc.

Drugs or medical devices requiring the inclusion of information on precautions, etc. in their package insert shall be the following:

a. Guidance-mandatory drugs, OTC drugs (including in vitro diagnostics), and pharmacy-compounded drugs (Article 210-3 of the Enforcement Regulation of the Act)

b. Medical devices provided primarily for the ordinary use of general consumers (Table 4-2 Attached to the Enforcement Regulation of the Act and Public Notice of the Designation of Medical Devices Provided Primarily for the Ordinary Use of General Consumers)

(2) In cases where any change has been made to information on precautions, etc.

If an MAH has made a change to information on precautions, etc. for a drug, etc. among those listed in (1) above, the package insert, etc. of the drug, etc. that has already been manufactured and marketed before the change shall not need to include the changed information on precautions, etc.

In addition, if an MAH has made a change to information on precautions, etc. for a drug, etc. among those above, and if all of the conditions shown below are met, the package insert, etc. of the drug, etc. shall not need to include the changed information on precautions, etc. Even in such cases, however, an MAH shall manufacture and market as soon as possible a drug, etc. with the package insert, etc. containing the changed information on precautions, etc.

a. The drug, etc. will be manufactured and marketed within 6 months (or 1 year if the drug, etc. is designated by the Minister of Health, Labour and Welfare as requiring tests pursuant to the provisions of Article 43, Paragraphs 1 and 2 of the Act, or if a change has been made to the information on precautions, etc. for many drugs, etc., and if the product with the package insert, etc. containing the

changed information on precautions, etc. cannot be promptly manufactured and marketed) from the day of the change.

b. The changed information on precautions, etc. for the drug, etc. is posted on the PMDA's website.

c. The MAH of the drug, etc. will promptly inform the healthcare professionals who handle the drug, etc. about the change made to information on precautions, etc.

(3) In cases where it is desirable to include information on precautions, etc. in package inserts, etc.

Even for a medical device, other than medical devices provided primarily for the ordinary use of general consumers, if it is assumed that consumers will purchase such a medical device directly instead of through a medical institution, information on precautions, etc. shall be included in the package insert, etc. of the medical device, in principle, in addition to the printing of a code.

In such cases, if the MAH has made a change to the information on precautions, etc. for the medical device, the MAH shall take the same action as described in (2) above.

III. Disclosure, etc. of Information on Precautions, etc. for Drugs, etc. Requiring Information Disclosure (Article 68-2 of the Act)

1. Method of Disclosing Information on Precautions, etc.

Information on precautions, etc. shall be disclosed by the method of using the PMDA's website. (Article 228-10-2 and Article 235-2 of the Enforcement Regulation of the ACT)

For the method and format of disclosing information on precautions, etc., and the handling of such information at the time of succession, refer to the PMDA's website for MAHs, etc.

2. Handling of Biological Products

Information to call attention to the characteristics of biological products shall be disclosed as information on precautions, etc. (Article 68-20-2 of the Act and Article 235-3 of the Enforcement Regulation of the Act)

3. Exceptions to the Disclosure of Information on Precautions, etc.

(1) For products to be distributed exclusively as drugs for manufacturing only, medical devices for manufacturing only, or cellular and tissue-based products for manufacturing only, it is not necessary to disclose information on precautions, etc. if information on precautions, etc. (excluding dosage and administration, instructions for use, and other necessary precautions for use and handling) is included in their package inserts, etc. (Article 228-10-3 of the Enforcement Regulation of the Act)

(2) For products to be distributed exclusively as drugs for export, medical devices for export, or cellular and tissue-based products for export, it is not necessary to disclose information on precautions, etc. (Article 74, Paragraph 2; Article 74-2, Paragraph 2; and Article 74-3, Paragraph 2 of the Enforcement Order of the Act)

(3) For specially approved drugs, medical devices, or cellular and tissue-based products, it is not necessary to disclose information on precautions, etc. if information on precautions, etc. is included in their package inserts, etc. (Article 75, Paragraph 14 of the Enforcement Order of the Act)

4. Points to Consider

(1) Change in information on precautions, etc.

Even if a change has been made to information on precautions, etc., if there are products in the market for which it is necessary to refer to the information on precautions, etc. before the change, the information on precautions, etc. before the change shall be disclosed continuously.

(2) Drugs, etc. requiring notification of information on precautions, etc.

Pursuant to the provisions of Article 68-2-3 of the Act, notification of information on precautions, etc. to the Minister of Health, Labour and Welfare is necessary for drugs, medical devices, or cellular and tissue-based products designated by the Minister of Health, Labour and Welfare, and it is not necessary for other drugs or medical devices.

(3) Termination of the disclosure of information on precautions, etc.

MAHs of drugs, etc. shall not terminate the disclosure of information on precautions, etc. for a drug, etc. immediately after termination of the marketing of the drug, etc., but shall terminate the disclosure of information on precautions, etc. in consideration of the expiration date, shelf life, distribution status, and usage of the drugs, etc. at hospitals, etc.

IV. Establishment of a System to Provide Information on Precautions, etc. for Drugs, etc. Requiring Information Disclosure (Article 68-2-2 of the Act)

Taking into account that information on precautions, etc. for drugs, etc. is important information that should be transmitted to physicians, dentists, pharmacists, veterinarians, and other healthcare professionals, MAHs of drugs, etc. shall disclose information on precautions, etc. by posting it on the PMDA's website, and establish a system to provide necessary information so that healthcare professionals can obtain information on precautions, etc. appropriately at the time they need it.

Especially for healthcare professionals who currently have an inadequate environment to utilize information communication technology, MAHs of drugs, etc. need to provide information on precautions, etc. appropriately by supplying a document containing the information on precautions, etc.

1. System to Provide Information on Precautions, etc. (Article 228-10-6 of the Enforcement Regulation of the Act)

A system necessary for MAHs of drugs, etc. to provide by shall be the following:

(1) System necessary to provide the information on precautions, etc. specified in Article 68-2, Paragraph 2 of the Act for proprietors of pharmacies, proprietors of hospitals, clinics, or domestic animal clinics, physicians, dentists, pharmacists, veterinarians, or other healthcare professionals who will first purchase, rent, or obtain a drug, medical device, or cellular and tissue-based product, or receive a medical device program via a telecommunication line (hereinafter referred to as "first purchaser, etc.")

(2) Systems necessary to promptly provide information about a change made to the information on precautions, etc. for a drug, medical device, or cellular and tissue-based product for proprietors of pharmacies, proprietors of hospitals, clinics, or domestic animal clinics, physicians, dentists, pharmacists, veterinarians, or other

healthcare professionals who handle the drug, medical device, or cellular and tissue-based product

2. Method of Providing Information on Precautions, etc.

(1) For a first purchaser, etc. information on precautions, etc. shall be provided by supplying a document containing the information on precautions, etc. However, if there is a common understanding with a healthcare professional, it is acceptable to provide information on precautions, etc. by sending electronic data or using other methods that make it easier for the healthcare professional to check the information on precautions, etc.

(2) Information about a change made to information on precautions, etc. for a drug, etc. shall be provided for a healthcare professional by supplying a document containing the information on precautions, etc., sending electronic data, or using other methods that make it easier for the healthcare professional to check the information on precautions, etc. so that the healthcare professional handling the drug, etc. can receive the information.

3. Criteria for a System to Provide Information on Precautions, etc.

A system necessary for MAHs to provide information on precautions, etc. of drugs, etc. shall meet the following criteria:

(1) An MAH of drugs, etc. must have sufficient personnel who are capable of properly and smoothly conducting the operations related to the provision of information on precautions, etc.

(2) To properly and smoothly conduct the operations related to the provision of information on precautions, etc., an MAH of drugs, etc. must prepare a written operating procedure for providing information on precautions, etc. that describes the following procedures:

a. Procedure for providing information on precautions, etc.

b. Procedure for mutual cooperation when information on precautions, etc. is provided in cooperation with a licensed distributor or a wholesale distributor

c. Other procedures necessary to properly and smoothly conduct the operations related to the provision of information on precautions, etc.

(3) When an MAH of drugs, etc. has prepared a written operating procedure for providing information on precautions, etc. or revised it, the MAH must record the date in the operating procedure and retain it.

(4) An MAH of drugs, etc. must have personnel in charge of the operations related to the provision of information on precautions, etc. perform such operations in accordance with the written operating procedure for the provision of information on precautions, etc.

4. Other Cases Requiring the Provision of Information on Precautions, etc.

MAHs of drugs, etc. shall not only provide information through an established system, as described in 1 above, but also provide information on precautions, etc. appropriately by a method requested by a healthcare professional when the healthcare professional requests provision of information.

V. Transitional Measures, etc.

For drugs, etc. requiring information disclosure manufactured and marketed by the day when 2 years have passed since the enforcement date (August 1, 2021), a code or information on precautions, etc. shall be included in their package insert, etc.

It should be noted that there are no transitional measures for the disclosure of information on precautions, etc. by using the PMDA's website (Article 68-2 of the Act). It is desirable for MAHs of drugs, etc. requiring information disclosure to register, by the enforcement date (August 1, 2021), information that links each product code to each package insert number (unique number assigned to each electronic package insert when posted on the PMDA's website) in the safety information posting system on the PMDA's website for MAHs so that information on precautions, etc. can be obtained by means of information communication technology via the code printed on the container, etc. of each drug, etc. requiring information disclosure.

VI. Replacement of Phrases in the Already Issued Notifications

In the notifications issued by the Ministry of Health, Labour and Welfare before the enforcement of the Amendment Act and the Ministerial Ordinance for Amendment of the Act, the terms and phrases used before the amendment as per the Amendment Act etc. shall be replaced by the terms and phrases after the amendment.

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This English version 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.