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Administrative Notice
May 31, 2022

To: Prefectural Health Department (Bureau)

Pharmaceutical Safety Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare

Questions and Answers (Qs and As) on Early Post-marketing Phase Vigilance for Prescription Drugs

The implementation method, etc. of early post-marketing phase vigilance for prescription drugs has been instructed in the “Implementation Method, etc. of Early Post-marketing Phase Vigilance for Prescription Drugs” (PFSB/SD Notification No. 0324001 by the Director of Safety Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare (hereinafter referred to as “MHLW”) dated March 24, 2006; hereinafter referred to as “previous notification”) and in the “Q&A on Early Post-marketing Phase Vigilance for Prescription Drugs” (Administrative Notice of the Pharmaceutical Safety Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW dated August 8, 2019; hereinafter referred to as “previous administrative notice”).

Now that the previous notification has been abolished and the Notification entitled “Implementation Method, etc. of Early Post-marketing Phase Vigilance for Prescription Drugs” (PSEHB/PSD Notification No.0531-1 by the Director of Pharmaceutical Safety Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW dated May, 31, 2022; hereinafter referred to as “new notification”) has been issued, the contents of the previous administrative notice have been reviewed and the “Q&A on Early Post-marketing Phase Vigilance for Prescription Drugs” has been newly compiled as shown in the Appendix. Please inform the relevant organizations and medical institutions under your jurisdiction of this matter.

The previous administrative notice will be abolished upon issuance of this administrative notice. For the appended form mentioned in Q28, however, it is

acceptable to use the appended form in the previous administrative notice only if it is submitted to the Pharmaceuticals and Medical Devices Agency (herein after referred to as PMDA) by May 31, 2023.

In addition, for the submission of documents by e-mail mentioned in Q29 and Q30, it is acceptable to submit documents by mail until July 31, 2022.

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Appendix

Q&A on Early Post-marketing Phase Vigilance for Prescription Drugs

Abbreviations

Act:	Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960)
Regulation:	Regulation for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Ministry of Health and Welfare (herein after referred to as “MHW”) Ministerial Ordinance No. 1 of 1961)
GVP Ordinance:	Ministerial Ordinance on Good Vigilance Practice for Drugs, Quasi-drugs, Cosmetics, Medical Devices, and Regenerative Medicine Products (MHLW Ministerial Ordinance No. 135 of 2004)
MR:	Medical Representative
PMDA:	Pharmaceuticals and Medical Devices Agency (refers to the Office(s) of new drug for matters before approval and the Office(s) of pharmacovigilance for matters after approval and related to early post-marketing phase vigilance)

Objective of Early Post-marketing Phase Vigilance and Target Products:

Q1

What kind of survey is early post-marketing phase vigilance? What kind of drugs are subject to the survey?

A1

The “early post-marketing phase vigilance” is a survey conducted during the first 6 months after the initial marketing of a drug by a marketing authorization holder, which is primarily designed to promote understanding of proper use of the drug by providing information certainly and calling for attention to medical institutions, and to minimize health damage such as adverse reactions by promptly collecting cases suspected of involving an adverse reaction(s) of the drug (cases, etc. listed in Article 228-20, Paragraph 1, Item 1-(a), 1-(c)-(i) to -(v),

and 1-(g) as well as Paragraph 1, Item 2-(a) of the Regulation) and taking necessary safety measures.

Drugs subject to the survey are new drugs specified in Article 14-4, Paragraph 1, Item 1 of the Act. However, there are some cases where new drugs are not subject to the survey for any reasonable reason.

Reference: Regulation for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (MHW Ministerial Ordinance No. 1 of1961) (excerpt)

Reporting of Adverse Reactions, etc.:

Article 228-20 When marketing authorization holders or persons with special approval for foreign-manufactured pharmaceuticals, etc. learn of any of the events in the following items concerning the drugs which they market or have obtained approval for, they shall report this fact to the Minister within the period specified for the event concerned.

(1) The following matters: 15 days

(a) Death occurrence suspected to be caused by the adverse reactions to the pharmaceuticals

(b) (Omitted)

(c) Among the following occurrences of cases, etc., cases suspected to be caused by some adverse reactions of the pharmaceuticals or foreign pharmaceuticals that cannot be predicted from the Precautions, etc. of the drug concerned, or when it can be predicted from the Precautions, etc. of the drug concerned but its occurrence trend cannot be predicted or whose change of the occurrence trend may show a risk of the occurrence or spread of a hazard in health and hygiene (excluding matters set forth in (d) and (e))

(i) Disability

(ii) A case which may lead to death or disability

(iii) A case which requires hospitalization in a hospital or clinic or extension of a hospitalization period for treatment (excluding a matter set forth in (ii))

(iv) A case of death or a serious disease according to cases set forth in (i) to (iii)

(v) A congenital disease or abnormality in later generations

(d) From among the occurrences of cases set forth in (c) (i) to (v) pertaining to the drugs which have obtained approval prescribed in Article 14, Paragraph 1 of the Act with active ingredients different from those of approved drugs pursuant to the provisions of Article 7, Paragraph 1, Item (1) (a) (i) of the Cabinet Order for Fees related to the Act on Securing Quality, Efficacy and Safety of Product Including Pharmaceuticals and Medical Devices, and for which two years have not yet elapsed from the day of the approval, a case suspected to be caused by side effects to the pharmaceuticals

(e) From among the occurrences of cases set forth in (c) (i) to (v) those suspected to be caused by the adverse reactions of the pharmaceuticals, and obtained in EPPV (excluding matters set forth in (d))
(f) The occurrences of cases due to infectious diseases suspected to be caused by the use of the pharmaceuticals and which cannot be expected from precautions for the use of the pharmaceuticals
(g) The occurrences of death or cases set forth in (c) (i) to (v) due to infectious diseases suspected to be caused by the use of the pharmaceuticals or foreign pharmaceuticals (excluding those set forth in (f))
(h) (Omitted)

(2) The following matters: 30 days
(a) Occurrence of cases set forth in (c) (i) to (v) of the preceding item which are suspected to be caused by the adverse reactions of the pharmaceuticals (excluding matters set forth in (c), (d), and (e) of the preceding item)

(3) (Omitted)

2 to 5 (Omitted)

Q2
What does “there are some cases where new drugs are not subject to the survey for any reasonable reason” mentioned in A1 mean specifically?

A2
Specific cases include a case where an approval application for partial changes to approved matters is submitted for a drug (hereinafter referred to as “partial change application”) to add a new indication(s) and a case where an approval application is submitted for a combination drug consisting of approved single ingredient drugs that have been concomitantly used frequently in clinical practice. However, both of the following two requirements must be met:

(1) Safety information has been sufficiently accumulated for the concerned drug or approved drugs.
(2) No changes are expected in clinical use, such as when there is no change in the existing indication(s), dosage and administration, or hospital departments where the drug is used and when no new special precautions are required concerning the safety of the drug.

Q3
What should a marketing authorization holder do when a reasonable reason for not conducting early post-marketing phase vigilance is considered to exist for a new drug, for which early post-marketing phase vigilance is required?

A3

The marketing authorization holder should document the reason for not conducting early post-marketing phase vigilance and submit it to the PMDA as an attachment to Module 1.11 of the Common Technical Document (CTD), separately from the draft risk management plan, at the time of an application for approval.

Q4

What is the relationship between early post-marketing phase vigilance and the adverse reaction/infection reporting system pursuant to the provision of Article 68-10, Paragraph 1 of the Act?

A4

In early post-marketing phase vigilance, a marketing authorization holder, etc. of a drug should periodically request physicians, etc. who use the drug:

(1) To understand that the drug is a new drug and to make efforts to use it properly,
(2) To utilize provided safety management information to ensure proper use,
(3) To promptly report any serious adverse reactions or infections.

By repeatedly requesting and raising their attention to the above, if any serious adverse reactions or infections occur, the survey enables prompt reporting of information on the serious adverse reactions or infections without being unrecognized or unreported. Therefore, if a marketing authorization holder, etc. is notified of a “serious adverse reaction or infection” by a medical institution through early post-marketing phase vigilance, the marketing authorization holder, etc. should report it to the PMDA pursuant to the provision of Article 68-10, Paragraph 1 of the Act.

It should be noted that a serious case, etc. suspected of being caused by an adverse drug reaction, for which information is obtained through early post-marketing phase vigilance, must be reported to the PMDA within 15 days, regardless of predictability from the Precautions, pursuant to the provision of Article 228-20, Paragraph 1, Item 1 (e) of the Regulation.

Reference: Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960) (excerpt)

Reporting of Adverse Reactions, etc.:

Article 68-10 When holders of marketing authorization for pharmaceuticals, quasi-pharmaceutical products, cosmetics, medical products or regenerative medicine

products, or persons with special approval for foreign-manufactured pharmaceuticals, etc. learn of the occurrence of any disease, disability or death suspected to be caused by the adverse reactions, etc. of the pharmaceuticals, quasi-pharmaceutical products, cosmetics, medical devices or regenerative medicine products that they manufactured and sold or received approval specified in Article 19-2, 23-2-17 or Article 23-37 for, the occurrence of any infectious disease suspected to be caused by the use of such items, and other matters on the efficacy and safety of pharmaceuticals, quasi-pharmaceutical products, cosmetics, medical devices or regenerative medicine products specified by MHLW Ministerial Ordinance No. 135 of 2004 such holders of marketing authorization for pharmaceuticals, quasi-pharmaceutical products, cosmetics, medical products or regenerative medicine products, or persons with special foreign approval must report the same to the Minister of Health, Labour and Welfare, pursuant to the provisions of MHLW Ministerial Ordinance No. 135 of 2004.

2 and 3 (Omitted)

Implementation plan for Early Post-marketing Phase Vigilance:

Q5
Is it necessary to submit an early post-marketing phase vigilance implementation plan before the start of early post-marketing phase vigilance?

A5
It is not always necessary to submit an early post-marketing phase vigilance implementation plan in advance. However, marketing authorization holders should consult the PMDA for any issues when preparing an implementation plan, as necessary.

Q6
What exactly is meant by the date of “launch” specified in Article 10 of the GVP Ordinance?

A6
In principle, it should be the release date specified by the marketing authorization holder.

Q7
What exactly is meant by the date of “launch” in the case of addition of an indication(s) or dosage and administration?

A7

In principle, it should be the date of approval of partial changes to approved matters for an indication(s) or dosage and administration (hereinafter referred to as “partial change approval”). In this case, concerning an explanation of early post-marketing phase vigilance and a request for cooperation to a medical institution, which are required to take place before delivery of the drug to a medical institution, marketing authorization holders are allowed to make the explanation and request within approximately 2 weeks after the partial change approval.

However, when the new drug is delivered to a medical institution for the first time, marketing authorization holders should provide an explanation of early post-marketing phase vigilance and make a request for cooperation before delivery.

Q8

How should the end date of early post-marketing phase vigilance be specified?

A8

In principle, the “end date of early post-marketing phase vigilance period” is the date when 6 months have passed since the start of the survey, but it may be specified to be the end of the month of the scheduled end date. In this case, marketing authorization holders should submit an early post-marketing phase vigilance report within 2 months from the end date of the survey.

Q9

In the case where a marketing authorization holder delivers the drug product to a medical institution where the drug product was delivered before (limiting to a medical institution which, after the delivery of the drug product, has returned all of the unused products to a marketing authorization holder), how should a marketing authorization holder conduct early post-marketing phase vigilance?

A9

Marketing authorization holders should start early post-marketing phase vigilance on the date of re-delivery. If a marketing authorization holder provided an explanation of early post-marketing phase vigilance and made a request for cooperation at the time of the first supply, the marketing authorization holder may not repeat the explanation and request.

However, even if a marketing authorization holder has made periodic requests for cooperation and called for attention after the first delivery, the marketing authorization holder should start periodic requests for cooperation, etc. on the date of re-delivery.

Q10

The new notification presents the standard method of early post-marketing phase vigilance, stating “Although the implementation method of early post-marketing phase vigilance should be determined for each drug (partly omitted), the standard method, etc. of early post-marketing phase vigilance is indicated below.” However, if intending to conduct it using a method that takes into account product characteristics, safety profile, etc. (e.g., changing the frequency of face-to-face interviews, online interviews, etc.), how should a marketing authorization holder conduct early post-marketing phase vigilance?

A10

If intending to conduct early post-marketing phase vigilance using a method that takes into account product characteristics, safety profile, etc. (e.g., changing the frequency of face-to-face interviews, online interviews, etc. according to drugs, indications, target populations, and issues to be addressed), the marketing authorization holder should consult the PMDA when having prepared a draft early post-marketing phase vigilance implementation plan.

Q11

Is it necessary to conclude a contract with a medical institution before the start of early post-marketing phase vigilance?

A11

No, it is not necessary.

Unlike drug use-results surveys, etc., early post-marketing phase vigilance is not a survey on individual patients, but a part of the conventional provision, collection, and reporting of safety management information pursuant to the provisions of Article 68-2, Paragraph 1 and Article 68-10, Paragraph 1 of the Act.

Medical Institutions Subject to Early Post-marketing Phase Vigilance:

Q12

Are pharmacies subject to early post-marketing phase vigilance?

A12

In general, hospitals and clinics are subject to early post-marketing phase vigilance, and pharmacies are not considered to be subject to it. However, necessary information should be provided to pharmacies as well.

Q13

For a prescription drug, to which an indication(s) to be treated with at a different hospital department from those treating with the original indication, is added (additional indication, etc.) through a partial change application, is it acceptable to conduct early post-marketing phase vigilance only at medical institutions that have the department where the drug may be prescribed for the additional indication?

A13

It is acceptable to do so in principle, but the PMDA should be consulted with.

Explanation about Early Post-marketing Phase Vigilance and Request for Cooperation:

Q14

In principle, the method of explaining early post-marketing phase vigilance and making a request for cooperation by MRs, etc. is a face-to-face visit to medical institutions by MRs, etc. Are there any other methods to provide an explanation and to make a request for cooperation?

A14

For example, MRs, etc. may explain early post-marketing phase vigilance and make a request for cooperation by real-time communication through online interviews, telephone calls, etc.

Q15

If it is impossible for MRs, etc. to explain early post-marketing phase vigilance and to make a request for cooperation through face-to-face or online interviews, etc. before delivery of a drug, what kind of documents to explain the survey and to make a request for cooperation should be prepared? Also, specifically, how should the explanation and request for cooperation be made?

A15

For example, the document refers to a written request prepared by a marketing authorization holder that describes the purpose of early post-marketing phase vigilance and the request for cooperation. However, the written information cannot be replaced by the “Prescription Drug Product Information Brochure” or “Explanation on the ‘Precautions’ of a New Drug.”

As for the contacting method, it is acceptable to provide the document by mail, fax, e-mail, or via a wholesaler, etc. In this case, an explanation of the survey and a request for cooperation should be made, in principle, through a face-to-face or online interview by MRs, etc. within 2 weeks after the start of delivery.

Q16

When MRs, etc. hold a product explanatory meeting for multiple medical institutions to explain early post-marketing phase vigilance and to make a request for cooperation, is it acceptable to substitute this explanation and request for cooperation for an explanation and a request for cooperation before delivery to individual medical institutions participating in the explanatory meeting?

A16

It is acceptable provided that individual medical institutions participating in the explanatory meeting can be confirmed. In such an explanatory meeting, however, a marketing authorization holder should explain that the explanatory meeting is intended to explain early post-marketing phase vigilance and to make a request for cooperation.

Q17

Is it inappropriate to supply a drug to a medical institution that will not cooperate in early post-marketing phase vigilance despite an explanation and a request for cooperation before delivery of the drug?

A17

Early post-marketing phase vigilance does not restrict the supply of the drug to a medical institution. However, the marketing authorization holder should continue to explain the purpose of this system and to make a request for cooperation even after the start of delivery.

Q18
What time point does the delivery of a drug refer to for a medical institution issuing external prescriptions?

A18
In a medical institution issuing external prescriptions, early post-marketing phase vigilance should, in principle, be initiated on the start date of prescriptions (or the date when the market authorization holder recognized that the drug product was prescribed) or the date of adoption of the drug by the medical institution, whichever is earlier. If the prescription of the drug is recognized for the first time by spontaneous adverse reaction reports, information from dispensing pharmacies, etc., MRs, etc. should explain early post-marketing phase vigilance and make a request for cooperation within approximately 2 weeks from that time point.

Q19
If it is found that a drug has been delivered to a medical institution that has not been provided with an explanation and a request for cooperation, which should be provided prior to delivery, how should an explanation and a request for cooperation be provided?

A19
Prior to delivery of the drug products, efforts should be made to ascertain the medical institutions to which the drug products are being supplied. However, if such a case is detected after the start of delivery, MRs, etc. should explain early post-marketing phase vigilance and make a request for cooperation within approximately 2 weeks since it turned out that the drug had been delivered.

Q20
Is it necessary to keep the records of an explanation and a request for cooperation before (or after) delivery of a drug, periodic requests for cooperation, and calling for attention after delivery?

A20
In order to properly conduct early post-marketing phase vigilance, it is necessary to retain the written documents for explanations and requests for cooperation before and after the delivery of the drug, as well as to establish the procedures for ascertaining the implementation status of face-to-face or online interviews by MRs, etc., and to record such an implementation status, etc.

The records on the conduct of early post-marketing phase vigilance should be prepared for each medical institution and be managed appropriately as stipulated in Part 2-2, (9), (d) of the PFSB Notification No. 0812-4 by the Director, Pharmaceutical and Food Safety Bureau, MHLW dated August 12, 2014, entitled "Enforcement of Ministerial Ordinance on Good Vigilance Practice for Drugs, Quasi-drugs, Cosmetics, Medical Devices and Regenerative Medicine Products, etc."

Reference: PFSB Notification No. 0812-4 by the Director, Pharmaceutical and Food Safety Bureau, MHLW dated August 12, 2014 (Excerpt)

Part 2-2, (9), d Early Post-marketing Phase Vigilance (in relation to Article 10 and Article 10-2)

(a) to (c) (Omitted)

(d) First-class marketing authorization holders shall collect and evaluate safety control information related to early post-marketing phase vigilance and take necessary measures based on the results of the evaluation, pursuant to the provisions of Article 7, 8, and 9, respectively, of the GVP Ordinance. Records on the conduct of early post-marketing phase vigilance should be prepared for each medical institution and be managed appropriately.

Q21

How should periodic requests for cooperation and calling for attention after delivery be provided specifically?

A21

It is desirable to provide periodic requests for cooperation and to call for attention through face-to-face or online interviews, etc. by MRs, etc. to ensure prompt information provision and collection in view of the purpose of early post-marketing phase vigilance. However, it is also acceptable to conduct such activities by mail, fax, e-mail, etc., as well as via a wholesaler, etc. provided that the purpose of early post-marketing phase vigilance is achieved. It should be noted that if any serious adverse reactions or infections occur, MRs, etc. need to collect information, etc. in accordance with the post-marketing safety control operating procedures of each marketing authorization holder.

Q22

What are alternative methods to face-to-face or online interviews by MRs, etc. to conduct early post-marketing phase vigilance? What are the precautions for using alternative methods?

A22

Alternative methods include letters, faxes, e-mails, and direct mails (hereinafter referred to as “DMs”). When communication is made by any of these alternative methods, instead of carrying out one-way communication alone, it should be explained that the alternative method enables provision and collection of information with certainty and promptness to medical institutions to achieve the purpose of early post-marketing phase vigilance.

Q23

For a drug product with a single name marketed by multiple distributors, should the multiple distributors make a request for cooperation, etc. in early post-marketing phase vigilance?

A23

It is the responsibility of the marketing authorization holder of the drug product and not the responsibility of individual distributors. It is acceptable to outsource the operations within a specified scope.

Q24

When information provision activities such as periodic calling for attention to medical institutions are outsourced to a wholesaler, is it necessary to conclude a contract with the wholesaler?

A24

When outsourcing the activities specified in Article 97 of the Regulation (Scope of post-marketing safety management activities that may be outsourced), it is necessary to conclude a contract with the contractor pursuant to the provisions of Article 98-2 (Methods for outsourcing post-marketing safety management activities for prescription drugs) or Article 98-3 (Methods for outsourcing post-marketing safety management activities for non-prescription drugs) of the Regulation.

Evaluation of Early Post-marketing Phase Vigilance Results, etc.:

Q25

Is it necessary to provide safety management information obtained through early post-marketing phase vigilance to medical institutions?

A25

Safety management information obtained through early post-marketing phase vigilance should be provided to medical institutions, etc. at an appropriate frequency, for example, by summarizing safety information monthly and providing the information along with measures to ensure safety in the case that many serious adverse reactions are reported.

Q26

When safety assurance measures, such as revision of the Precautions, are taken based on early post-marketing phase vigilance, is the Office of Pharmacovigilance I or II of the PMDA to be contacted for consultation?

A26

Yes.

Early Post-marketing Phase Vigilance Report:

Q27

What are the “safety assurance measures” to be described in the early post-marketing phase vigilance report?

A27

For example, they refer to revision in the electronic package insert and information provision activities to ensure safety, etc. that are taken when a marketing authorization holder obtains information on the “occurrence of serious adverse reactions or infections” from medical institutions.

Q28

What kind of documents should be attached to the early post-marketing phase vigilance implementation plan and the early post-marketing phase vigilance report?

A28

To confirm the implementation status of early post-marketing phase vigilance and the validity of safety measures, the following data should be attached:

(1) Documents provided to medical institutions, etc. during and/or after the end of early post-marketing phase vigilance

(2) Documents related to the implementation status of early post-marketing phase vigilance at medical institutions, etc. prepared by using the appended form. The documents should include at least the following:
- The number of institutions where a request for cooperation, etc. before delivery of a drug is made through a face-to-face or online interview, etc. or an explanatory meeting by MRs, etc., and the ratio of the number of such institutions to the number of total target institutions. Institutions where no face-to-face or online interview, or contact by e-mail, DMs, etc. is made should be counted as “institutions not contacted.”
- Results of tabulation of the number of institutions to which periodical requests for cooperation, etc. after delivery of the drug are made, and the ratio of the number of such institutions to the number of total target institutions, shown by the methods of making requests for cooperation, etc. or the number of requests made
- If there is any institution not contacted through face-to-face or online interviews by MRs, etc. before or after the delivery of a drug, the reason for not contacting the institution and the handling of the institution (including an explanation about whether the purpose of early post-marketing phase vigilance has been achieved or not). If it is considered necessary to improve the implementation method, the improvement measures should also be described.

Q29
Should the early post-marketing phase vigilance report and the periodic safety report be submitted separately?

A29
They should be submitted separately. A company intending to submit an early post-marketing phase vigilance report should consult the PMDA sufficiently before the reporting deadline of early post-marketing phase vigilance.

Before consultation, a consultation application form and the data (early post-marketing phase vigilance implementation plan, early post-marketing phase vigilance report, and documents to be attached) should be submitted as electronic files attached to an e-mail to the “Face-to-Face Consultation Application (anzen2-menkai@pmda.go.jp)," the address dedicated to consultation with PMDA Office of Safety I and Office of Safety II. The maximum capacity to send data per e-mail is approximately 10 MB. Therefore, if it is impossible to send data with a single e-mail, the data should be divided into

multiple files, and the order and the total number of files to be sent should be indicated, for example, “1/3,” “2/3,” and “3/3.” If it is impossible to submit the data by e-mail, the PMDA should be consulted about the submission method.

Q30
Are there any rules for how to submit electronic files (e.g., e-mail title, file name)?

A30
The title of the e-mail should include the document name (described as “early post-marketing phase vigilance report-related submission”), the marketing authorization holder name, and the brand name.

At present, there are no particular rules for file names, but the early post-marketing phase vigilance implementation plan and the early post-marketing phase vigilance report should be prepared as separate electronic files. Other data to be attached should be prepared in an appropriate electronic format, with file names that can identify the contents of the respective data.

Publicity of Drug Products Subject to Early Post-marketing Phase Vigilance:

Q31
For a drug on which approval conditions are imposed to conduct early post-marketing phase vigilance specified in Article 10 of the GVP Ordinance, is it necessary to describe the approval conditions in the electronic package insert of the drug?

A31
It is not necessary to describe them.

Q32
How should the fact that a new drug is subject to early post-marketing phase vigilance be clearly stated?

A32
The fact should be clearly stated in the “Prescription Drug Product Information Brochure,” the “Explanation on the ‘Precautions’ for a New Drug,” the Interview Form, etc. for 6 months after the start of marketing. It is also acceptable to use a

mark, sticker, etc. unified in the pharmaceutical industry provided that it is clearly stated that the drug is subject to early post-marketing phase vigilance.

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Appended Form

	No. of total target institutions	Before delivery [1)]	Week 2 [2)]	Week 4	Week 6	Week 8	Month 3	Month 4	Month 5	Month 6
No. of total target institutions	●	●	●	●	●	●	●	●	●	●
No. of institutions contacted [3,4)]	–	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)
Methods of contact: Face-to-face or online interview, etc. [3)]	–	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)
E-mail, DM, etc. [3,5)]	–	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)
No. of institutions not contacted [3,6)]	–	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)

1) Tabulation of activities before delivery

The number of institutions contacted for activities before delivery should include the following institutions:

- Institutions where a face-to-face or online interview, etc. or an explanatory meeting, etc. is implemented before delivery (counted as “Face-to-face or online interview, etc.”)
- Institutions where an e-mail or DM, etc. is sent before delivery, and then, a face-to-face or online interview, etc., or an explanatory meeting, etc. by MRs, etc. is implemented within 2 weeks (approximately) after the start of delivery (counted as “Face-to-face or online interview, etc.”)
- Institutions where an e-mail, DM, etc. is sent before delivery, but a face-to-face or online interview, etc. or an explanatory meeting, etc. by MRs, etc. cannot be implemented for an unavoidable reason within 2 weeks (approximately) after the start of delivery (counted as “E-mail, DM, etc.”)

The following institutions should be excluded from the number of total target institutions and the number of institutions contacted, with a note to

explain whether each institution falls under “a” or “b” below along with the number of such institutions. For “a,” whether a face-to-face or online interview, etc. or explanatory meeting is implemented within 2 weeks (approximately) after detection should be explained. For any institution excluded for a reason other than the following, the reason should be explained using a note.

a. Institutions where an explanation and request for cooperation should have been made before delivery but have not been made, and a drug has been delivered

b. Institutions where a drug has been delivered since before the date of partial change approval, which is the start date of early post-marketing phase vigilance (because these institutions need no explanation before delivery)

Institutions not contacted include those where no explanation or request for cooperation can be made through a face-to-face or online interview, or any means such as e-mail or DM.

2) The frequency of contact (from Week 2 to Month 6) in the attached form should be modified as appropriate based on the early post-marketing phase vigilance implementation plan.
3) The number (percentage) of institutions should be described. The percentage of institutions should be calculated as a percentage regarding the number of total target institutions.
4) If it is considered necessary to improve the implementation method of early post-marketing phase vigilance, the improvement measures should be explained using a note.
5) The details of alternative means (e-mail, DM, etc.), the reason for using it, and the status of implementation (including whether the purpose of early post-marketing phase vigilance is achieved) should be explained using a note.
6) The reason for not contacting the institution and the handling of the institution should be explained using a note.

It is acceptable to use attachments, etc. to explain 1), and 4) to 6) above.