Provisional Translation (as of March 2025) *

PSB/PED Notification No. 0319-1
PSB/MDED Notification No. 0319-1
March 19, 2024

To: Directors of Prefectural Health Department (Bureau)

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

Revision of "Points to consider for application for approval of drugs to be administered based on specific biomarkers that were developed by investigator-initiated clinical trials in patients with rare cancer"

Regarding drugs for which application should be submitted at the same time as the application for the corresponding companion diagnostics (hereinafter referred to as CDx) in principle based on "Notification on Approval Application of In Vitro Companion Diagnostics and Corresponding Therapeutic Products" (PFSB/ELD Notification No. 0701-10 by the Director of the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated July 1, 2013), handling concerning the application for approval of drugs that were developed by investigator-initiated clinical trials in patients with rare cancer for which approval application is planned but an approval application for corresponding CDx cannot be made at the same time has been described in "Points to consider for application for approval of drugs to be administered based on specific biomarkers that were developed by investigator-initiated clinical trials in patients with rare cancer" (PSEHB/PED Notification No. 0224-5 and PSEHB/MDED Notification No. 0224-1 by the Director of the Pharmaceutical Evaluation Division and the Director of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated February 24, 2023; hereinafter referred to as Joint

* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

Notification).

We have recently organized policy on the approval application when in vitro diagnostics or medical devices that have been approved for other indications (hereinafter referred to as "in vitro diagnostics, etc.") are used as a clinical trial assay to identify subjects in the investigator-initiated clinical trial in patients with rare cancer and have revised the notice in the Joint Notification as follows. Please inform the relevant medical institutions and relevant marketing authorization holders under your jurisdiction of this matter and give the instructions.

Notice

1. Scope

This notification applies to a drug that falls under both (1) and (2) below and falls under either (3) or (4). Regarding whether the approval application can be made based on this notification, consultation with Pharmaceutical Evaluation Division should be requested in advance by filling out the attached application form.

(1) A drug for which the marketing authorization holder plans to make a partial change approval application based on the results obtained by an investigator-initiated clinical trial in patients with rare cancer

(2) A drug for which the marketing authorization holder of in vitro diagnostics, etc. cannot submit the approval application for the corresponding CDx at the same time

(3) A drug for which the applicant can explain that the efficacy and safety of the drug is expected to be equivalent to those in the subjects of the clinical studies when the relevant drug is used based on the results of cancer genome profiling test using a gene mutation analysis program, etc. that obtained a regulatory approval.

(4) A drug for which in vitro diagnostics, etc. approved for other indications are used as a clinical trial assay to identify subjects in the investigator-initiated clinical trial described in above (1) and it can be explained that the efficacy and safety equivalent to those in subjects of the clinical studies will be expected when the relevant drug is used based on the results obtained from the relevant in vitro diagnostics or other alternative in vitro diagnostics.

2. Policy on the approval application

For a drug that falls under 1. above, a partial change approval application of the drug may be made prior to CDx approval application.

Even if this notification can apply to a drug, however, it should be noted that whether or not the in vitro diagnostics, etc. which are not approved as a corresponding CDx of the relevant drug can be used in identification of eligible patients shall be eventually determined in the review of the drug and clearly described in the review report of the drug. For drugs for which a partial change approval application is made based on this notification, CDx should be developed in principle. Therefore, even after the drugs are launched, discussion with marketing authorization holders of in vitro diagnostics, etc. should be continued for the development of CDx.

Attachment

Application for consultation on drugs developed by an investigator-initiated clinical trial for rare cancer for which approval application for CDx cannot be made at the same time as the approval application for the relevant drug

To person in charge of evaluation, Pharmaceutical Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare

Company name	Name of the person who requests for the consultation (name of attendee and the department)
Contact telephone number/FAX number/E-mail Tel ( ) — Fax ( ) — E-mail	Preferred consultation date The first choice: Month Day, Year; AM/PM The second choice: Month Day, Year; AM/PM The third choice: Month Day, Year; AM/PM
Target drug	
Proposed indications	
Brand name and approval number of a gene panel test that is expected to be used when the relevant drug is administered or in vitro diagnostics, etc. used at the time of enrollment in the investigator-initiated clinical trial or name and approval number of the alternative product	
Rationale of the idea that the gene panel test that is expected to be used or in vitro diagnostics, etc. approved for other indication, or the alternative product are considered to have performance equivalent to the clinical trial assay in the pivotal clinical study	
Status of consultation with Office of New Drug, Pharmaceuticals and Medical Devices Agency regarding CDx development policy	