PMDA/ORM Notification No. 1007001
October 7, 2016
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To (note)

Pharmaceuticals and Medical Devices Agency
Director of Office of Review Management

Submission of conversion factors to calculate the maximum daily amount of use of a pharmaceutical excipient

The Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA") has been running the database of pharmaceutical excipients to properly control the maximum daily amount of use of pharmaceutical excipients and to appropriately respond to consultations on the search for precedents of use of excipients. To improve accuracy of the database, this document is issued. Upon the issuance, the applicant will be asked to submit conversion factors to calculate the maximum daily amount of use of a pharmaceutical excipient when they file an application for marketing approval of an ethical drug (including an application for marketing approval of a drug manufactured in foreign countries, hereinafter referred to as "approval application") or an application for approval of partial changes in approved items for drug marketing (including an application for approval of partial changes in approved items for marketing of drugs manufactured in foreign countries, hereinafter referred to as "partial change approval application"). Please inform your member companies of this matter.

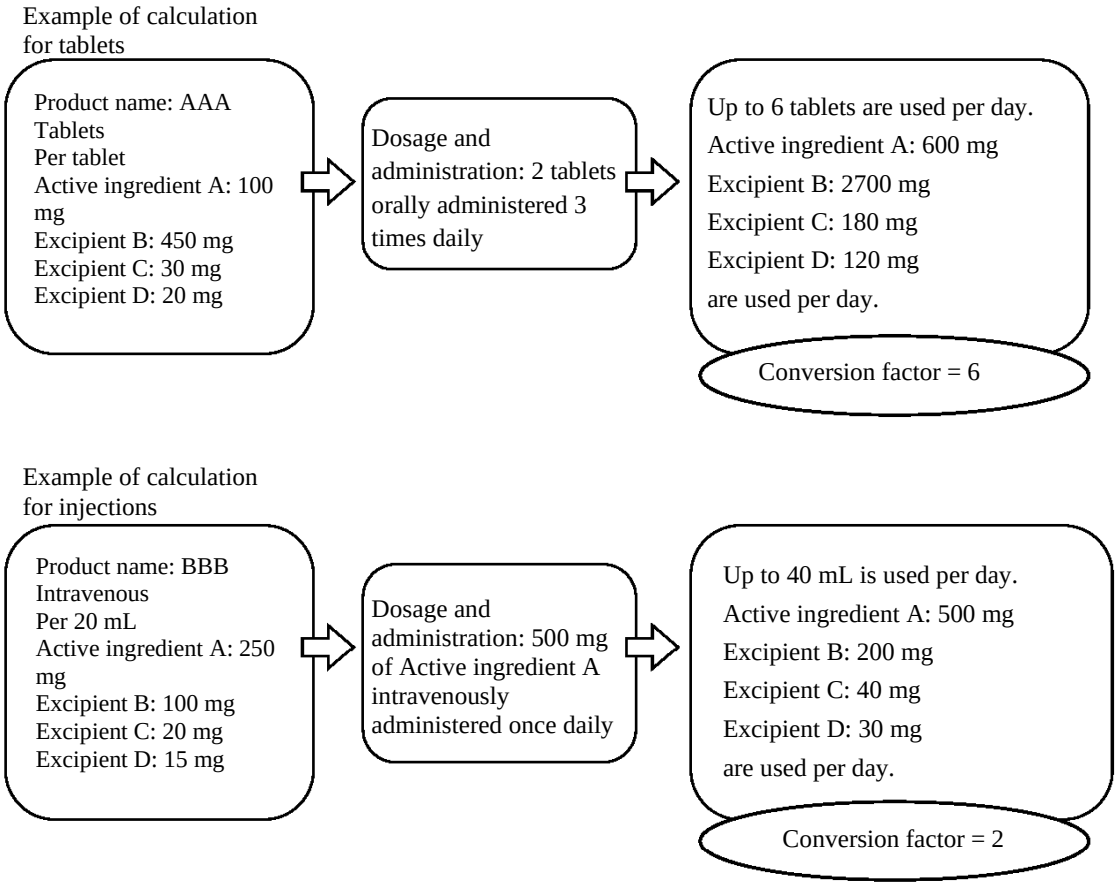
Of note, this document will require the applicant to submit conversion factors for drugs for which an application is filed on or after April 1, 2017 but does not refuse the submission before that.

Notice

1. Applications subject to submission of conversion factors
   (1) Type of drugs subject to the submission
   New drugs and generic drugs (submission is not required for OTC drugs)
   (2) Applications subject to the submission
   New approval applications and partial change approval applications in the case of potentially leading to changes in the components or amount of use of an excipient (changes to ingredients and composition, route of administration, or dosage and administration in the approval certificate)

2. Calculation method of conversion factors

The maximum daily amount of use of a pharmaceutical excipient should be calculated by multiplying the amount of the excipient per unit amount in the approval application form by the conversion factor determined with the dosage and administration of the drug taken into account. For example, the tablet shown below is provided with the unit amount of 1 tablet and the daily dose of 6 tablets; thus, the conversion factor is determined to be 6. For another example, the injection shown below is provided with the unit amount of 20 mL and the daily dose of 40 mL; thus, the conversion factor is determined to be 2.



For drug products for external use (including otolaryngological and ophthalmic drug products for external use), the conversion factor should be 1 because the maximum amount of use is calculated based on the concentration (mg/g, mg/mL, etc.). In the column of reason for calculation of conversion factor, a note stating “because the concentration is used in the calculation) should be entered. In addition, for the drug products administered transdermally for desirable systemic effects, those applied sublingually, those applied to the rectum, vagina, and urethra, and those for external dental use and use in the oral cavity, data on both the maximum daily use and concentrations may be available, but only the conversion factor based on the maximum daily amount of use should be

documented and submitted. Of note, cases potentially useful in calculating the maximum daily amount of use to determine the conversion factor are presented as “Points to consider when calculating the maximum daily amount of use of a pharmaceutical excipient” on the PMDA website[1] and may be used as needed.

3. How to create data to be submitted

Firstly, the XML file of the application form should be loaded into the “Creation of conversion factor input file.vbs” available on the PMDA website, and then the created CSV file should be filled with necessary information such as conversion factors to obtain the data to be submitted. For the detailed creation method, refer to “How to create a CSV for excipient conversion factors" provided on the same website.

As described in “How to create a CSV for excipient conversion factors,” a CSV file filled with the minimum necessary information (hereinafter referred to as a “simplified CSV file”) may be submitted for partial change applications to reduce workload.

4. Timing of data submission

The data should be submitted anytime between the filing of an approval application for the relevant drug and the receipt of itsapproval. The submission at the earliest possible time after filing of the approval application is desirable. If the maximum daily amount of use of a pharmaceutical excipient is changed in response to resubmission for purposes such as a request for replacement, the post-change value should be submitted again by the time of approval.

5. How to submit the data

The created CSV file should be sent as an e-mail attachment to the following e-mail address.

- If the relevant drug is a new drug : ndexcip@pmda.go.jp
- If the relevant drug is a generic drug : gdexcip@pmda.go.jp

The subject title of the e-mail should consist of [Reviewing office], the system receipt number (13 digits) of the relevant drug, the drug name, a phrase of “Excipient conversion factor,” and the applicant’s company name. For the reviewing office and company names, their abbreviations may be used. For generic drugs, the type of application (new, partial change, or brand name change) should be added. (for example, [Office of Generic Drugs (new)] 5122908000001 Testol Injection, Excipient conversion factor (XXX Pharmaceutical))

If you have any questions about how to create the file, please contact the reviewer of the relevant drug or send it to the above e-mail address. Because the question will be answered by telephone or e-mail, the e-mail, if used for the contact, must include the name of the person in charge, a telephone number, and a reply-enabled e-mail address.

Online reception via the gateway system is also available, but if you want to submit the simplified CSV file through the application using the gateway system, please submit it by attaching to the above e-mail. In addition, “How to create a CSV for excipient conversion factors” includes an “e-mail template to send CSV files,” which may be used as needed.

[1] https://www.pmda.go.jp/review-services/drug-reviews/pharmaceutical-excipients/0001.html

(note)
President of the Federation of Pharmaceutical Manufacturers' Associations of Japan

President of Japan Pharmaceutical Manufacturers Association

Chair of Science and Regulatory Committee, Pharmaceutical Research and Manufacturers of America

Chairperson of Technical Committee, European Federation of Pharmaceutical Industries and Associations

President of the Japan Generic Medicines Association

Chairman of the International Pharmaceutical Excipients Council Japan