MEDICINES EVALUATION BOARD

Policy for assigning RVG numbers

MEB 39

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Introduction

This document describes the Medicines Evaluation Board policy for assigning RVG numbers. This policy is based on the definitions presented in the Guideline "*categorisation of extension applications versus variation applications*" of July 2019.

Policy for assigning RVG number

(1) Each composition receives its own RVG number.
Each medicine with a different composition receives its own RVG number. The only exception applies to combination packages (i.e. two or more different products in one package). A combination package is registered under one RVG number. If a change in composition occurs, the MEB will evaluate on a case-by-case basis whether a new RVG number needs to be assigned. That depends – among other factors – on whether the difference in composition could have an effect on the safety and efficacy of the medicine.

(2) Each pharmaceutical form receives its own RVG number.
A pharmaceutical form is defined as follows[1]:

> *The pharmaceutical form is the combination of the form in which a pharmaceutical product is presented by the manufacturer (form of presentation) and the form in which it is administered including the physical form (form of administration). If the physical form in which the product is supplied by the manufacturer is different from that in which it is to be administered to/used by the patient, that is, if transformation of the product is required before it can be administered/used, both these elements of information need to be conveyed within the term. If the product has certain special characteristics that are relevant to its use, these need to be included in the term.*
> *In some cases the pharmaceutical form needs to be further qualified: "effervescent powder", "modified-release tablet" or "prolonged-release tablet", "gastro-resistant capsule" should be used and are considered as different pharmaceutical forms. As stated in the "Standard Terms" document, in certain cases a complete characterization of the pharmaceutical form requires additional information about the container. This applies in any case to pre-filled syringes, pressurised preparations and single-dose preparations which are considered as specific pharmaceutical forms. The same applies also where the administration of the same physical form differs due to a different design of the container/administration device. A pressurised container and a spray pump are considered as specific pharmaceutical forms ("cutaneous spray, solution, pressurized container" and "cutaneous spray, solution, spray pump" are two pharmaceutical forms).*

The MEB uses the list of Standard Terms composed by the EDQM, with the exception of the list of Combined Terms.
Some examples:

- "Powder for solution for infusion" and "Powder and solvent for solution for infusion" are two different pharmaceutical forms and therefore each receive their own RVG number.

- "Nasal drops, solution", "Nasal drops, suspension" and "Nasal drops, emulsion" are three different pharmaceutical forms and therefore each receive their own RVG number.

(3) Each strength receives its own RVG number.
Strength is defined as follows[1]:

> *The quantitative composition in terms of active substance represents the strength. The concept of strength and the concept of concentration are inherently linked. The strength represents the amount of active substance in the pharmaceutical form, which can be defined per unit dose or as a concentration. The concentration can be stated per unit of mass (250mg/g) or per unit of volume (2mg/ml) or in percentage (5%). For the purpose of this Guideline:*
> - *for single-dose preparations, total use, the strength is defined as the amount of active substance per unit dose;*
> - *for single-dose preparations, partial use, the strength is defined as the concentration expressed as the amount of active substance per ml, per puff, per drop, per kg, per m2, in percentage as appropriate;*
> - *for multi-dose preparations, the strength is defined as the concentration expressed as the amount of active substance per ml, per puff, per drop, per kg, per m2 as appropriate;*
> - *for powder for reconstitution (powder for oral solution or suspension, powder for solution for injection, etc.) the strength is defined as the concentration after dissolution or suspension (reconstitution) to the volume and liquid recommended;*
> - *for concentrates for solutions (for injection or for infusion) the strength is defined as the concentration of the concentrate before dilution;*
> - *for transdermal patches the strength is defined as the amount of active substance released from the patch in 24h.*

If a medicine is suitable for partial or complete administration, then the rule for partial administration is applied.

The following definitions of single-dose preparations and multi-dose preparations are used[1]:

> *Single-dose preparations are supplied in an individual container (sachet, vial, prefilled syringe, ampoule, small bottle). A single-dose container holds a quantity of the preparation intended for total or partial use as a single administration. This definition encompasses:*
> - *medicinal products designed in such a way that the amount of active substance in the individual container is given **in total** ("total use") as a single administration;*
> - *medicinal products which hold a certain quantity intended for use by a single administration. The dose to be administered is usually calculated on an individual patient basis (in mg/kg bodyweight, in mg/m2) and any unused portion of the preparation is to be discarded ("partial use"). The presentation could be provided with a suitable measuring device.*
>
> *Multi-dose preparations are supplied in a multi-dose container (bottle, tube, large vial, cartridge for pen) which hold two or more doses and which are usually*

administered by a suitable measuring device (spoon, graduated empty syringe, dosing cup).

Some examples:

- A solution for injection consists of various vial sizes: 10 mL, 20 mL and 50 mL. They are all intended for partial use. The strength is therefore defined as x mg/mL and all three vial sizes are registered under the same RVG number (they are all the same strength).
- A solution for injection consists of two vial sizes: 5 mL and 10 mL. They are both intended for single use. The strength is defined as the quantity of substance per vial, x mg and y mg. The different vial sizes are registered under different RVG numbers (they are different strengths).
- If a product has both a single dose (partial use) and a multi-dose version with the same strength indication, then both are registered under different RVG numbers.

(4) Different package sizes and package forms (e.g. blister and container) are registered under one RVG number, unless there are reasons based on other criteria listed in this document to assign a different RVG number.

(5) Different administration routes are registered under one RVG number, unless a different pharmaceutical form or strength is required for the various administration routes.

(6) Enclosed medical device

Products with or without included medical device (e.g. measuring cup, holding chamber) are registered under one RVG number, unless they differ in strength or pharmaceutical form.

Some examples:

- A solution for infusion and a solution for infusion in an administration system are registered under two RVG numbers as these are two pharmaceutical forms ("solution for infusion" and "solution for infusion in an administration system").
- An inhalation powder with or without holding chamber is registered under one RVG number as this is the same pharmaceutical form ("inhalation powder").
- A solution for injection in vials and pre-filled syringes is registered under separate RVG numbers as the pharmaceutical form is not the same, see also the second point on page 2.

Reference:

[1] GUIDELINE ON THE CATEGORISATION OF EXTENSION APPLICATIONS (EA) versus VARIATIONS APPLICATIONS (V) July 2019