Edition: BP 2025 (Ph. Eur. 11.6 update)

Granules

General Notices

(Ph. Eur. monograph 0499)

Unless otherwise justified and authorised, Granules comply with the appropriate requirements of the European Pharmacopoeia. These requirements are reproduced in the British Pharmacopoeia.

Ph Eur

Requirements for granules to be used for the preparation of oral solutions or suspensions are given in the monograph Liquid preparations for oral use (0672). Where justified and authorised, the requirements of this monograph do not apply to granules for veterinary use.

DEFINITION

Granules are preparations consisting of solid, dry aggregates of powder particles sufficiently robust to withstand handling. They are intended for oral administration. Some are swallowed as such, some are chewed and some are dissolved or dispersed in water or another suitable liquid before being administered.

For reasons of patient safety and to ensure the correct administration of the medicinal product, this term may also be used where very small tablets (rather than granules) are presented in a sachet, and where the entire contents of the sachet are intended for oral administration as a single dose.

Granules contain one or more active substances with or without excipients and, if necessary, colouring matter authorised by the competent authority and flavouring substances.

Granules are presented as single-dose or multidose preparations. Each dose of a multidose preparation is administered by means of a device suitable for measuring the quantity prescribed. For single-dose granules, each dose is enclosed in an individual container, for example a sachet or a vial.

Where applicable, containers for granules comply with the requirements of *Materials used for the manufacture of containers* (*3.1* and subsections) and *Containers* (*3.2* and subsections).

Several categories of granules may be distinguished:

— effervescent granules;

— coated granules;

— gastro-resistant granules;

— modified-release granules.

PRODUCTION

In the manufacture, packaging, storage and distribution of granules, suitable measures are taken to ensure their microbial quality; recommendations on this aspect are provided in general chapter *5.1.4*. *Microbiological quality of non-sterile pharmaceutical preparations and substances for pharmaceutical use*.

TESTS

Uniformity of dosage units

Single-dose granules comply with the test for uniformity of dosage units (*2.9.40*) or, where justified and authorised, with the tests for uniformity of content and/or uniformity of mass shown below. Herbal drugs and herbal drug preparations present in the dosage form are not subject to the provisions of this paragraph.

Uniformity of content (*2.9.6*)

Unless otherwise prescribed or justified and authorised, single-dose granules with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test B for uniformity of content of single-dose preparations. If the preparation has more than one active substance, the requirement applies only to those substances that correspond to the above conditions.

Uniformity of mass (*2.9.5*)

Single-dose granules except for coated granules comply with the test for uniformity of mass of single-dose preparations. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

Uniformity of mass of delivered doses from multidose containers (*2.9.27*)

Granules supplied in multidose containers comply with the test.

STORAGE

If the preparation contains volatile ingredients or the contents have to be protected, store in an airtight container.

EFFERVESCENT GRANULES

DEFINITION

Effervescent granules are uncoated granules generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide. They are intended to be dissolved or dispersed in water before administration.

TESTS

Disintegration

Place 1 dose of the effervescent granules in a beaker containing 200 mL of *water R* at 15-25 °C; numerous bubbles of gas are evolved. When the evolution of gas around the individual grains ceases, the granules have disintegrated, being either dissolved or dispersed in the water. Repeat the operation on 5 further doses. The preparation complies with the test if each of the 6 doses used disintegrates within 5 min.

STORAGE

In an airtight container.

COATED GRANULES

DEFINITION

Coated granules are usually multidose preparations and consist of granules coated with one or more layers of mixtures of various excipients.

PRODUCTION

The substances used as coatings are usually applied as a solution or suspension in conditions in which evaporation of the vehicle occurs.

TESTS

Dissolution

A suitable test may be carried out to demonstrate the appropriate release of the active substance(s), for example one of the tests described in general chapter *2.9.3. Dissolution test for solid dosage forms*.

MODIFIED-RELEASE GRANULES

DEFINITION

Modified-release granules are coated or uncoated granules that contain special excipients or that are prepared by special procedures, or both, designed to modify the rate, the place or the time at which the active substance or substances are released.

Modified-release granules include prolonged-release granules and delayed-release granules.

PRODUCTION

A suitable test is carried out to demonstrate the appropriate release of the active substance(s).

TESTS

Dissolution

Carry out a suitable test to demonstrate the appropriate release of the active substance(s), for example the test described in general chapter *2.9.3. Dissolution test for solid dosage forms*.

GASTRO-RESISTANT GRANULES

DEFINITION

Gastro-resistant granules are delayed-release granules that are intended to resist the gastric fluid and to release the active substance(s) in the intestinal fluid. These properties are achieved by covering the granules with a gastro-resistant material or by other suitable means.

PRODUCTION

A suitable test is carried out to demonstrate the appropriate release of the active substance(s).

TESTS

Dissolution

Carry out a suitable test to demonstrate the appropriate release of the active substance(s), for example the test described in general chapter *2.9.3*. *Dissolution test for solid dosage forms*.
