01/2019:0523

PRESSURISED PHARMACEUTICAL PREPARATIONS

Praeparationes pharmaceuticae in vasis cum pressu

Additional requirements for preparations presented in pressurised containers may be found, where appropriate, in other general monographs, for example Preparations for inhalation (0671), Liquid preparations for cutaneous application (0927), Powders for cutaneous application (1166), Nasal preparations (0676) and Ear preparations (0652).

DEFINITION

Pressurised pharmaceutical preparations are usually multidose preparations presented in special containers under pressure of a gas and often fitted with a metering valve, and contain one or more active substances. The preparations are released from the container, upon actuation of an appropriate valve, in the form of an aerosol (dispersion of solid or liquid particles in a gas, the size of the particles being adapted to the intended use) or of a liquid or semisolid jet such as a foam. The pressure for the release is generated by suitable propellants.

The preparations are intended for local application to the skin or to mucous membranes of various body orifices, or for inhalation. Pressurised pharmaceutical preparations are provided with a delivery device appropriate for the intended application. Pressurised pharmaceutical preparations intended to be used on severely injured skin or large open wounds are sterile and comply with the test for sterility. Suitable excipients may also be used, for example solvents, solubilisers, emulsifying agents, suspending agents and lubricants for the valve to prevent clogging.

Pressurised pharmaceutical preparations may have the following components.

Propellants. The propellants are either gases liquefied under pressure or compressed gases or low-boiling liquids. Liquefied gases are, for example, fluorinated hydrocarbons and low-molecular-mass hydrocarbons (such as propane and butane). Compressed gases are, for example, carbon dioxide, nitrogen and nitrous oxide.

Mixtures of these propellants may be used to obtain optimal solution properties and desirable pressure, delivery and spray characteristics.

Containers. The containers are tight and resistant to the internal pressure and may be made of metal, glass, plastic or combinations of these materials. They are compatible with their contents. Glass containers are protected with a plastic coating.

Spraying device. The valve keeps the container tightly closed when not in use and regulates the delivery of the contents during use. The spray characteristics are influenced by the type of spraying device, in particular by the dimensions, number and location of orifices. Some valves provide a continuous release, others (metering valves) deliver a defined quantity of product upon each valve actuation.

The various valve materials in contact with the contents are compatible with them.

PRODUCTION

Special requirements may be necessary regarding the selection of propellants, the particle size and the dose delivered by the metering valve, depending on the intended application. Sterile pressurised preparations are prepared using materials and methods designed to ensure sterility and to avoid the introduction of contaminants and the growth of micro-organisms; recommendations on this aspect are provided in general chapter *5.1.1. Methods of preparation of sterile products*.

TESTS

Sterility (*2.6.1*). Where the label indicates that the preparation is sterile, it complies with the test for sterility.

LABELLING

The label states:
- where applicable, that the preparation is sterile;
- the method of use;
- any precautions to be taken;
- for a container with a metering valve, the quantity of active substance delivered per actuation.

01/2008:1145
corrected 10.0

RECTAL PREPARATIONS

Rectalia

DEFINITION

Rectal preparations are intended for rectal use in order to obtain a systemic or local effect, or they may be intended for diagnostic purposes.

Where applicable, containers for rectal preparations comply with the requirements for materials used for the manufacture of containers (*3.1* and subsections) and containers (*3.2* and subsections).

Several categories of rectal preparations may be distinguished:
- suppositories;
- rectal capsules;
- rectal solutions, emulsions and suspensions;
- powders and tablets for rectal solutions and suspensions;
- semi-solid rectal preparations;
- rectal foams;
- rectal tampons.

PRODUCTION

During the development of a rectal preparation whose formulation contains an antimicrobial preservative, the need for and the efficacy of the chosen preservative shall be demonstrated to the satisfaction of the competent authority. A suitable test method together with criteria for judging the preservative properties of the formulation are provided in chapter *5.1.3. Efficacy of antimicrobial preservation*.

During development, it must be demonstrated that the nominal contents can be withdrawn from the container of liquid and semi-solid rectal preparations presented in single-dose containers.

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

In the manufacture of semi-solid and liquid rectal preparations containing dispersed particles, measures are taken to ensure a suitable and controlled particle size with regard to the intended use.

TESTS

Uniformity of dosage units (*2.9.40*). Liquid and semi-solid single-dose rectal preparations comply with the test. Solid single-dose rectal preparations comply with the test 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, solid single-dose rectal preparations with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test A (tablets) or test B (suppositories, rectal capsules). If the preparation contains more than one active substance, this requirement applies only to those substances that correspond to the above conditions.

Uniformity of mass (*2.9.5*). Solid single-dose rectal preparations comply with the test. If the test for uniformity of content is prescribed for all active substances, the test for uniformity of mass is not required.

Dissolution. A suitable test may be required to demonstrate the appropriate release of the active substance(s) from solid single-dose rectal preparations, for example *2.9.42. Dissolution test for lipophilic solid dosage forms*.

Where a dissolution test is prescribed, a disintegration test may not be required.

LABELLING

The label states the name of any added antimicrobial preservative.

Suppositories

DEFINITION

Suppositories are solid, single-dose preparations. The shape, volume and consistency of suppositories are suitable for rectal administration.

They contain 1 or more active substances dispersed or dissolved in a suitable basis that may be soluble or dispersible in water or may melt at body temperature. Excipients such as diluents, adsorbents, surface-active agents, lubricants, antimicrobial preservatives and colouring matter, authorised by the competent authority, may be added if necessary.

PRODUCTION

Suppositories are prepared by compression or moulding. If necessary, the active substance(s) are previously ground and sieved through a suitable sieve. When prepared by moulding, the medicated mass, sufficiently liquefied by heating, is poured into suitable moulds. The suppository solidifies on cooling. Various excipients are available for this process, such as hard fat, macrogols, cocoa butter, and various gelatinous mixtures consisting of, for example, gelatin, water and glycerol. The determination of the softening time of lipophilic suppositories (*2.9.22*) is carried out.

A suitable test is carried out to demonstrate the appropriate release of the active substance(s) from suppositories intended for modified release or for prolonged local action.

In the manufacture of suppositories containing dispersed active substances, measures are taken to ensure a suitable and controlled particle size.

TESTS

Disintegration (*2.9.2*). Unless intended for modified release or for prolonged local action, they comply with the test. For suppositories with a fatty base, examine after 30 min, and for suppositories with a water-soluble base, examine after 60 min, unless otherwise justified and authorised.

Rectal capsules

DEFINITION

Rectal capsules (shell suppositories) are solid, single-dose preparations generally similar to soft capsules as defined in the monograph *Capsules (0016)* except that they may have lubricating coatings. They are of elongated shape, are smooth and have a uniform external appearance.

PRODUCTION

A suitable test is carried out to demonstrate the appropriate release of the active substance(s) from rectal capsules intended for modified release or for prolonged local action.

TESTS

Disintegration (*2.9.2*). Unless intended for modified release or for prolonged local action, they comply with the test. Examine the state of the capsules after 30 min, unless otherwise justified and authorised.

Rectal solutions, emulsions and suspensions

DEFINITION

Rectal solutions, emulsions and suspensions are liquid preparations intended for rectal use in order to obtain a systemic or local effect, or they may be intended for diagnostic purposes.

Rectal solutions, emulsions and suspensions are supplied in single-dose containers and contain 1 or more active substances dissolved or dispersed in water, glycerol or macrogols or other suitable solvents. Emulsions may show evidence of phase separation but are readily redispersed on shaking. Suspensions may show a sediment that is readily dispersible on shaking to give a suspension that remains sufficiently stable to enable the correct dose to be delivered.

Rectal solutions, emulsions and suspensions may contain excipients, for example to adjust the viscosity of the preparation, to adjust or stabilise the pH, to increase the solubility of the active substance(s) or to stabilise the preparation. These substances do not adversely affect the intended medical action or, at the concentrations used, cause undue local irritation.

Rectal solutions, emulsions and suspensions are supplied in containers containing a volume in the range of 2.5 mL to 2000 mL. The container is adapted to deliver the preparation to the rectum or is accompanied by a suitable applicator.

Powders and tablets for rectal solutions and suspensions

DEFINITION

Powders and tablets intended for the preparation of rectal solutions or suspensions are single-dose preparations that are dissolved or dispersed in water or other suitable solvents at the time of administration. They may contain excipients to facilitate dissolution or dispersion or to prevent aggregation of the particles.

After dissolution or suspension, they comply with the requirements for rectal solutions or rectal suspensions, as appropriate.

TESTS

Disintegration (*2.9.1*). Tablets for rectal solutions or suspensions disintegrate within 3 min, using *water R* at 15-25 °C as the liquid medium.

LABELLING

The label states:

– the method of preparation of the rectal solution or suspension;

– the conditions and duration of storage of the solution or suspension after constitution.

Semi-solid rectal preparations

DEFINITION

Semi-solid rectal preparations are ointments, creams or gels.

They are often supplied as single-dose preparations in containers provided with a suitable applicator.

Semi-solid rectal preparations comply with the requirements of the monograph *Semi-solid preparations for cutaneous application (0132)*.

Rectal foams

DEFINITION

Rectal foams comply with the requirements of the monograph *Medicated foams (1105)*.

Rectal tampons

DEFINITION

Rectal tampons are solid, single-dose preparations intended to be inserted into the lower part of the rectum for a limited time.

They comply with the requirements of the monograph *Medicated tampons (1155)*.

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corrected 10.0

SEMI-SOLID PREPARATIONS FOR CUTANEOUS APPLICATION

Praeparationes molles ad usum dermicum

The requirements of this monograph apply to all semi-solid preparations for cutaneous application. Where appropriate, additional requirements specific to semi-solid preparations intended to be applied to particular surfaces or mucous membranes may be found in other general monographs, for example Ear preparations (0652), Nasal preparations (0676), Rectal preparations (1145), Eye preparations (1163) and Vaginal preparations (1164).

DEFINITION

Semi-solid preparations for cutaneous application are intended for local or transdermal delivery of active substances, or for their emollient or protective action. They are of homogeneous appearance.

Semi-solid preparations for cutaneous application consist of a simple or compound basis in which, usually, 1 or more active substances are dissolved or dispersed. According to its composition, the basis may influence the activity of the preparation.

The basis may consist of natural or synthetic substances and may be single phase or multiphase. According to the nature of the basis, the preparation may have hydrophilic or hydrophobic properties; it may contain suitable excipients such as antimicrobial preservatives, antioxidants, stabilisers, emulsifiers, thickeners and penetration enhancers.

Semi-solid preparations for cutaneous application intended for use on severely injured skin are sterile.

Where applicable, containers for semi-solid preparations for cutaneous application 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 semi-solid preparations for cutaneous application may be distinguished:

– ointments;
– creams;
– gels;
– pastes;
– poultices;
– medicated plasters;
– cutaneous patches.

According to their structure, ointments, creams and gels generally show viscoelastic behaviour and are non-Newtonian in character, e.g. plastic, pseudoplastic or thixotropic type flow at high shear rates. Pastes frequently exhibit dilatancy.

PRODUCTION

During development of semi-solid preparations for cutaneous application whose formulation contains an antimicrobial preservative, the need for and the efficacy of the chosen preservative shall be demonstrated to the satisfaction of the competent authority. A suitable test method together with criteria for judging the preservative properties of the formulation are provided in *Efficacy of antimicrobial preservation* (*5.1.3*). In the manufacture, packaging, storage and distribution of semi-solid preparations for cutaneous application, suitable measures are taken to ensure their microbiological quality; recommendations on this are provided in *5.1.4. Microbiological quality of non-sterile pharmaceutical preparations and substances for pharmaceutical use*. Sterile semi-solid preparations for cutaneous application are prepared using materials and methods designed to ensure sterility and to avoid the introduction of contaminants and the growth of micro-organisms; recommendations on this are provided in *Methods of preparation of sterile products* (*5.1.1*).

During development, it must be demonstrated that the nominal content can be withdrawn from the container of semi-solid preparations for cutaneous application presented in single-dose containers.

In the manufacture of semi-solid preparations for cutaneous application, suitable measures are taken to ensure that the defined rheological properties are fulfilled. Where appropriate, the following non-mandatory tests may be carried out: measurement of consistency by penetrometry (*2.9.9*), viscosity (apparent viscosity) (*2.2.10*) and a suitable test to demonstrate the appropriate release of the active substance(s).

In the manufacture of semi-solid preparations for cutaneous application containing 1 or more active substances that are not dissolved in the basis (e.g. emulsions or suspensions), measures are taken to ensure appropriate homogeneity of the preparation to be delivered.

In the manufacture of semi-solid preparations for cutaneous application containing dispersed particles, measures are taken to ensure a suitable and controlled particle size with regard to the intended use.

TESTS

Uniformity of dosage units. Semi-solid preparations that are supplied either in single-dose containers that represent 1 dose of medicinal product or in metered-dose containers, and that are intended for transdermal delivery of the active substance(s) in view of a systemic effect, comply with the test for uniformity of dosage units (*2.9.40*). Semi-solid preparations in which the active substance(s) are dissolved comply with the test for mass variation; semi-solid preparations in which the active substance(s) are suspended comply with the test for content uniformity. Follow the procedure described for liquid dosage forms. Herbal drugs and herbal drug preparations present in the dosage form are not subject to the provisions of this paragraph.

For semi-solid preparations presented in metered-dose containers and in which the active substance(s) are dissolved,