– 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)*.

04/2010:0132
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,

proceed as follows. Discharge once to waste. Wait for a minimum of 5 s, shake for 5 s if necessary, and discharge again to waste. Repeat this procedure for a further 3 actuations. Weigh the container, discharge once to waste and weigh the container again. Calculate the difference between the 2 masses. Repeat the procedure for a further 9 containers. Determine the mass variation (*2.9.40*).

For semi-solid preparations supplied in metered-dose containers and in which the active substance(s) are suspended, proceed as follows. Use an apparatus capable of quantitatively retaining the dose leaving the metered-dose container. Shake 1 container for 5 s and discharge once to waste. Wait for a minimum of 5 s, shake for 5 s and discharge again to waste. Repeat this procedure for a further 3 actuations. After 2 s, fire 1 dose from the metered-dose container into the collecting vessel. Collect the contents of the collecting vessel by successive rinses. Determine the content of active substance in the combined rinses. Repeat the procedure for a further 9 containers. Determine the content uniformity (*2.9.40*).

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

STORAGE

If the preparation contains water or other volatile ingredients, store in an airtight container. If the preparation is sterile, store in a sterile, airtight, tamper-evident container.

LABELLING

The label states:

- the name of any excipient;
- where applicable, that the preparation is sterile.

Ointments

DEFINITION

An ointment consists of a single-phase basis in which solids or liquids may be dispersed.

Hydrophobic ointments

Hydrophobic ointments can absorb only small amounts of water. Typical bases used for their formulation are hard, liquid and light liquid paraffins, vegetable oils, animal fats, synthetic glycerides, waxes and liquid polyalkylsiloxanes.

Water-emulsifying ointments

Water-emulsifying ointments can absorb larger amounts of water and thereby produce water-in-oil or oil-in-water emulsions after homogenisation, depending on the nature of the emulsifiers: water-in-oil emulsifying agents such as wool alcohols, sorbitan esters, monoglycerides and fatty alcohols, or oil-in-water emulsifying agents such as sulfated fatty alcohols, polysorbates, macrogol cetostearyl ether or esters of fatty acids with macrogols may be used for this purpose. Their bases are those of the hydrophobic ointments.

Hydrophilic ointments

Hydrophilic ointments are preparations having bases that are miscible with water. The bases usually consist of mixtures of liquid and solid macrogols (polyethylene glycols). They may contain appropriate amounts of water.

Creams

DEFINITION

Creams are multiphase preparations consisting of a lipophilic phase and an aqueous phase.

Lipophilic creams

Lipophilic creams have as the continuous phase the lipophilic phase. They usually contain water-in-oil emulsifying agents such as wool alcohols, sorbitan esters and monoglycerides.

Hydrophilic creams

Hydrophilic creams have as the continuous phase the aqueous phase. They contain oil-in-water emulsifying agents such as sodium or trolamine soaps, sulfated fatty alcohols, polysorbates and polyoxyl fatty acid and fatty alcohol esters combined, if necessary, with water-in-oil emulsifying agents.

Gels

DEFINITION

Gels consist of liquids gelled by means of suitable gelling agents.

Lipophilic gels

Lipophilic gels (oleogels) are preparations whose bases usually consist of liquid paraffin with polyethylene or fatty oils gelled with colloidal silica or aluminium or zinc soaps.

Hydrophilic gels

Hydrophilic gels (hydrogels) are preparations whose bases usually consist of water, glycerol or propylene glycol gelled with suitable gelling agents such as poloxamers, starch, cellulose derivatives, carbomers and magnesium-aluminium silicates.

Pastes

DEFINITION

Pastes are semi-solid preparations for cutaneous application containing large proportions of solids finely dispersed in the basis.

Poultices

DEFINITION

Poultices consist of a hydrophilic heat-retentive basis in which solid or liquid active substances are dispersed. They are usually spread thickly on a suitable dressing and heated before application to the skin.

Medicated plasters

DEFINITION

Medicated plasters are flexible preparations containing 1 or more active substances. They are intended to be applied to the skin. They are designed to maintain the active substance(s) in close contact with the skin such that these may be absorbed slowly, or act as protective or keratolytic agents.

Medicated plasters consist of an adhesive basis, which may be coloured, containing 1 or more active substances, spread as a uniform layer on an appropriate support made of natural or synthetic material. They are not irritant or sensitising to the skin. The adhesive layer is covered by a suitable protective liner, which is removed before applying the plaster to the skin. When removed, the protective liner does not detach the preparation from the outer, supporting layer.

Medicated plasters are presented in a range of sizes directly adapted to their intended use or as larger sheets to be cut before use. Medicated plasters adhere firmly to the skin when gentle pressure is applied and can be peeled off without causing appreciable injury to the skin or detachment of the preparation from the outer, supporting layer.

TESTS

Dissolution. A suitable test may be required to demonstrate the appropriate release of the active substance(s), for example one of the tests described in *Dissolution test for transdermal patches* (*2.9.4*).

Cutaneous patches

DEFINITION

Cutaneous patches are flexible preparations containing 1 or more active substances. They are intended to be applied to the skin. They are designed to maintain the active substance(s) in close contact with the skin such that these may act locally.

Cutaneous patches consist of an adhesive basis, which may be coloured, containing 1 or more active substances, spread as a uniform layer on an appropriate support made of natural or synthetic material. The adhesive basis is not irritant or sensitising to the skin. The adhesive layer is covered by a suitable protective liner, which is removed before applying the patch to the skin. When removed, the protective liner does not detach the preparation from the outer, supporting layer.

Cutaneous patches are presented in a range of sizes adapted to their intended use. They adhere firmly to the skin when gentle pressure is applied and can be peeled off without causing appreciable injury to the skin or detachment of the preparation from the outer, supporting layer.

TESTS

Dissolution. A suitable test may be required to demonstrate the appropriate release of the active substance(s), for example one of the tests described in *Dissolution test for transdermal patches* (*2.9.4*).

01/2019:1154

STICKS

Styli

Additional requirements for sticks may be found, where appropriate, in other general monographs, for example Nasal preparations (0676).

DEFINITION

Sticks are solid preparations intended for local application. They may be single-dose or multidose preparations. They are rod-shaped or conical preparations consisting of one or more active substances, either alone or dissolved or dispersed in a suitable basis, and are usually intended to dissolve or melt at body temperature. They may be inserted into a body cavity or wound, or be applied cutaneously.

Urethral sticks and sticks for insertion into wounds are sterile.

PRODUCTION

In the manufacture, packaging, storage and distribution of sticks, 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*.

Urethral sticks and other sterile sticks 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

Uniformity of dosage units (*2.9.40*). Single-dose sticks 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, single-dose sticks with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test B. 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*). Single-dose sticks 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.

Sterility (*2.6.1*). Urethral sticks and sticks for insertion into wounds comply with the test for sterility.

LABELLING

The label states, for urethral sticks and sticks to be inserted into wounds, that they are sterile.

01/2018:0478

TABLETS

Compressi

The requirements of this monograph do not necessarily apply to preparations that are presented as tablets intended for use other than by oral administration. Requirements for such preparations may be found, where appropriate, in other general monographs; for example Rectal preparations (1145), Vaginal preparations (1164) and Oromucosal preparations (1807). This monograph does not apply to lozenges, oral pastes and oral gums. Where justified and authorised, the requirements of this monograph do not apply to tablets for veterinary use. Tablets for use in the mouth comply with the requirements of the monograph Oromucosal preparations (1807).

DEFINITION

Tablets are solid preparations each containing a single dose of one or more active substances. They are obtained by compressing uniform volumes of particles or by another suitable manufacturing technique, such as extrusion, moulding or freeze-drying (lyophilisation). Tablets are intended for oral administration. Some are swallowed whole, some after being chewed, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substance is liberated.

The particles consist of one or more active substances with or without excipients such as diluents, binders, disintegrating agents, glidants, lubricants, substances capable of modifying the behaviour of the preparation in the digestive tract, colouring matter authorised by the competent authority and flavouring substances.

Tablets are usually straight, solid cylinders, the end surfaces of which are flat or convex and the edges of which may be bevelled. They may have break-marks and may bear a symbol or other markings. Tablets may be coated.

Where applicable, containers for tablets 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 tablets for oral use may be distinguished:

- uncoated tablets;
- coated tablets;
- gastro-resistant tablets;
- modified-release tablets;
- effervescent tablets;
- soluble tablets;
- dispersible tablets;