LIQUID PREPARATIONS FOR CUTANEOUS APPLICATION

Praeparationes liquidae ad usum dermicum

Where justified and authorised, the requirements of this monograph do not apply to preparations intended for systemic and veterinary use.

DEFINITION
Liquid preparations for cutaneous application are preparations of a variety of viscosities intended for local or transdermal delivery of active ingredients. They are solutions, emulsions or suspensions that may contain 1 or more active substances in a suitable vehicle. They may contain suitable antimicrobial preservatives, antioxidants and other excipients such as stabilisers, emulsifiers and thickeners.

During development of a liquid preparation for cutaneous application containing dispersed particles, measures are taken to ensure a suitable and controlled particle size with regard to the intended use.

Emulsions may show evidence of phase separation but are readily redispersed on shaking. Suspensions may show a sediment that is readily dispersed on shaking to give a suspension that is sufficiently stable to enable a homogeneous preparation to be delivered.

Where applicable, containers for liquid 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).

When liquid preparations for cutaneous application are dispensed in pressurised containers, the containers comply with the requirements of the monograph on Pressurised pharmaceutical preparations (0523).

Preparations specifically intended for use on severely injured skin are sterile.

Several categories of liquid preparations for cutaneous application may be distinguished, for example:
- shampoos;
- cutaneous foams.

PRODUCTION
During development of a liquid preparation 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 the text on Efficacy of antimicrobial preservation (5.1.3).

During development, it must be demonstrated that the nominal content can be withdrawn from the container of liquid preparations for cutaneous application presented in single-dose containers.

In the manufacture, packaging, storage and distribution of liquid preparations for cutaneous application, suitable measures are taken to ensure their microbial quality; recommendations on this aspect are provided in the text on Microbiological quality of pharmaceutical preparations (5.1.4).

Sterile liquid 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 aspect are provided in the text on Methods of preparation of sterile products (5.1.1).

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

STORAGE
If the preparation is sterile, store in a sterile, airtight, tamper-proof container.

LABELLING
The label states:
- the name of any added antimicrobial preservative;
- where applicable, that the preparation is sterile.

Shampoos

DEFINITION
Shampoos are liquid or, occasionally, semi-solid preparations intended for application to the scalp and subsequent washing away with water. Upon rubbing with water they usually form a foam.

They are emulsions, suspensions or solutions. Shampoos normally contain surface active agents.

Cutaneous foams

DEFINITION
Cutaneous foams comply with the requirements of the monograph on Medicated foams (1105).

LIQUID PREPARATIONS FOR ORAL USE

Praeparationes liquidae peroraliae

Where justified and authorised, the requirements of this monograph do not apply to liquid preparations for oral use intended for veterinary use.

DEFINITION
Liquid preparations for oral use are usually solutions, emulsions or suspensions containing one or more active substances in a suitable vehicle; they may, however, consist of liquid active substances used as such (oral liquids).

Some preparations for oral use are prepared by dilution of concentrated liquid preparations, or from powders or granules for the preparation of oral solutions or suspensions, for oral drops or for syrups, using a suitable vehicle.

The vehicle for any preparations for oral use is chosen having regard to the nature of the active substance(s) and to provide organoleptic characteristics appropriate to the intended use of the preparation.

Liquid preparations for oral use may contain suitable antimicrobial preservatives, antioxidants and other excipients such as dispersing, suspending, thickening, emulsifying, buffering, wetting, solubilising, stabilising, flavouring and sweetening agents and colouring matter, authorised by the competent authority.
Emulsions may show evidence of phase separation but are readily redispersed on shaking. Suspensions may show a sediment, which is readily dispersed on shaking to give a suspension that remains sufficiently stable to enable the correct dose to be delivered.

Where applicable, containers for liquid preparations for oral use 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 preparations may be distinguished;
- oral solutions, emulsions and suspensions;
- powders and granules for oral solutions and suspensions;
- oral drops;
- powders for oral drops;
- syrups;
- powders and granules for syrups.

**PRODUCTION**

During development of a preparation for oral use 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 the text on **Efficacy of antimicrobial preservation** (5.1.3).

During development, it must be demonstrated that the nominal content can be withdrawn from the container, for liquid preparations for oral use presented in single-dose containers.

In the manufacturing, packaging, storage and distribution of liquid preparations for oral use, suitable measures are taken to ensure their microbial quality; recommendations on this aspect are provided in the text on **Microbiological quality of pharmaceutical preparations** (5.1.4).

In the manufacture of liquid preparations for oral use 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.** Solutions, suspensions and emulsions in single-dose containers comply with the test for uniformity of dosage units (2.9.40) or, where justified and authorised, with the test for uniformity of content 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 preparations that are suspensions comply with the following test. After shaking, empty each container as completely as possible and carry out the test on the individual contents. They comply with test B for uniformity of content of single-dose preparations.

**Uniformity of mass.** Single-dose preparations that are solutions or emulsions comply with the following test: weigh individually the contents of 20 containers, emptied as completely as possible, and determine the average mass. Not more than 2 of the individual masses deviate by more than 10 per cent from the average mass and none deviate by more than 20 per cent.

**Dose and uniformity of dose of oral drops.** Into a suitable graduated cylinder, introduce by means of the dropping device the number of drops usually prescribed for one dose, or introduce by means of the measuring device the usually prescribed quantity. The dropping speed does not exceed 2 drops per second. Weigh the liquid, repeat the addition, weigh again and carry on repeating the addition and weighing until a total of 10 masses are obtained. No single mass deviates by more than 10 per cent from the average mass. The total of 10 masses does not differ by more than 15 per cent from the nominal mass of 10 doses. If necessary, measure the total volume of 10 doses. The volume does not differ by more than 15 per cent from the nominal volume of 10 doses.

**Uniformity of mass of delivered doses from multidose containers (2.9.27).** Liquid preparations for oral use supplied in multidose containers comply with the test. Oral drops are not subject to the provisions of this test.

**LABELLING**

The label states the name of any added antimicrobial preservative.

**Oral solutions, emulsions and suspensions**

**DEFINITION**

Oral solutions, emulsions and suspensions are supplied in single-dose or multidose containers. Each dose from a multidose container is administered by means of a device suitable for measuring the prescribed volume. The device is usually a spoon or a cup for volumes of 5 ml or multiples thereof or an oral syringe for other volumes.

**Powders and granules for oral solutions and suspensions**

**DEFINITION**

Powders and granules for the preparation of oral solutions or suspensions generally conform to the definitions in the monographs on **Oral powders** (1165) or Granules (0499) as appropriate. They may contain excipients, in particular to facilitate dispersion or dissolution and to prevent caking. After dissolution or suspension, they comply with the requirements for oral solutions or oral suspensions, as appropriate.

**TESTS**

**Uniformity of dosage units.** Single-dose powders and 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 powders and 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 powders and single-dose 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.

**LABELLING**

The label states:
- the method of preparation of the solution or suspension;
- the conditions and the duration of storage after reconstitution.
Oral drops

**DEFINITION**
Oral drops are solutions, emulsions or suspensions that are administered in small volumes such as drops by the means of a suitable device.

**LABELLING**
The label states the number of drops per millilitre of preparation or per gram of preparation if the dose is measured in drops.

**TESTS**

**Uniformity of dosage units.** Single-dose powders and granules for syrups 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 powders and granules for syrups 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 powders and granules for syrups 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.

Syrups

**DEFINITION**
Syrups are aqueous preparations characterised by a sweet taste and a viscous consistency. They may contain sucrose at a concentration of at least 45 per cent m/m. The sweet taste can also be obtained by using other polyols or sweetening agents. Syrups usually contain aromatic or other flavouring agents. Each dose from a multidose container is administered by means of a device suitable for measuring the prescribed volume. The device is usually a spoon or a cup for volumes of 5 ml or multiples thereof.

**LABELLING**
The label states the name and concentration of the polyol or sweetening agent.

**Powders and granules for syrups**

**DEFINITION**
Powders and granules for syrups generally conform to the definitions in the monograph on Oral powders (1165) or Granules (0499). They may contain excipients to facilitate dissolution.

After dissolution, they comply with the requirements for syrups.

**TESTS**

**Uniformity of dosage units.** Single-dose powders and granules for syrups 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 powders and granules for syrups 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 powders and granules for syrups 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.

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**NASAL PREPARATIONS**

**Nasalia**

**DEFINITION**
Nasal preparations are liquid, semi-solid or solid preparations intended for administration to the nasal cavities to obtain a systemic or local effect. They contain one or more active substances. Nasal preparations are as far as possible non-irritating and do not adversely affect the functions of the nasal mucosa and its cilia. Aqueous nasal preparations are usually isotonic and 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, or to stabilise the preparation.

Nasal preparations are supplied in multidose or single-dose containers, provided, if necessary, with a suitable administration device, which may be designed to avoid the introduction of contaminants.

Unless otherwise justified and authorised, aqueous nasal preparations supplied in multidose containers contain a suitable antimicrobial preservative in an appropriate concentration, except where the preparation itself has adequate antimicrobial properties.

Where applicable, the containers 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 nasal preparations may be distinguished:
- nasal drops and liquid nasal sprays;
- nasal powders;
- semi-solid nasal preparations;
- nasal washes;
- nasal sticks.

**PRODUCTION**
During the development of a nasal preparation whose formulation contains an antimicrobial preservative, the efficacy of the chosen preservative shall be demonstrated to