Rectal preparations

2015-01

Definition

Rectal preparations are liquid, semi-solid or solid preparations containing one or more active ingredients. They are intended for rectal application in order to obtain a systemic or local effect.

Rectal preparations may require the use of excipients of various types. Any excipient must be proven through product development studies not to adversely affect the stability of the final product, nor the availability of the active ingredient(s) at the site of action; incompatibility between any of the components of the dosage form should be avoided.

The different categories of rectal preparations include:

– suppositories;

– rectal capsules;

– rectal solutions, emulsions and suspensions;

– powders and tablets for rectal solutions and suspensions;

– semi-solid rectal preparations.

Manufacture

The following information is intended to provide broad guidelines concerning main steps to be followed during production.

Manufacturing and filling processes for rectal preparations should meet the requirements of good manufacturing practices (GMP).

During development the effectiveness of any antimicrobial preservative present in the preparation shall be demonstrated to the satisfaction of the relevant regulatory authority.

During development it must be demonstrated that the nominal contents can be withdrawn from the container of liquid and semi-solid rectal preparations presented in single-dose containers.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 the chapter *Microbial examination of non-sterile products: acceptance criteria for pharmaceutical preparations,* published in the Supplementary information section.

In the manufacture of rectal preparations containing dispersed particles measures are taken to ensure a suitable and controlled particle size.

Throughout manufacturing certain procedures should be validated and monitored by carrying out appropriate in-process controls. These should be designed to guarantee the effectiveness of each stage of production.

Labelling

Every rectal preparation must comply with the labelling requirements established under GMP.

The label should include:

1) name of the pharmaceutical product;

2) name(s) of the active ingredient(s); international nonproprietary names (INN) should be used whenever possible;

3) amount of active ingredient(s) in a dose unit and the number of dose units in the container or the amount of active ingredient(s) in suitable dose volume and the volume of the container;

4) where applicable, the name of any added antimicrobial agent;

5) batch (lot) number assigned by the manufacturer;

6) expiry date and, when required, the date of manufacture;

7) any special storage conditions or handling precautions that may be necessary;

8) directions for use, warnings and precautions that may be necessary;

9) name and address of the manufacturer or the person responsible for placing the product on the market.

Requirements for specific types of rectal preparations

Suppositories

Definition

Suppositories are solid single-dose preparations intended for rectal application. They are prepared by moulding or compression. The shape, volume and consistency of suppositories are suitable for rectal application.

Suppositories contain one or more active ingredients dispersed or dissolved in a suitable basis that may be soluble or dispersible in water or may melt at body temperature. When prepared by moulding, suppository bases such as macrogols, gelatinous mixtures consisting of, for example, gelatin, water and glycerol, hydrogenated vegetable oils, hard fat or cocoa butter are usually employed.

Excipients such as diluents, adsorbents, surface-active agents preferably of nonionic type, lubricants, antimicrobial preservatives and colouring matter authorized by the appropriate national or regional authority may be added when necessary.

Manufacture

It is common to use a suppository base in which the active ingredient(s) does not dissolve in order to avoid problems associated with partition between the molten or softened base and the rectal liquid. The release of the active ingredient(s) may in case of a suspension be dependent on sedimentation of the solid particles in the molten or softened base to the interface of the rectal liquid. The particle size of the active ingredient(s) should therefore be optimized to take both sedimentation and dissolution in the rectal liquid into account.

In the manufacture of suppositories containing dispersed active ingredient(s) measures are taken to ensure a suitable and controlled particle size.

When prepared by moulding the medicated mass, sufficiently liquefied by heating, is poured into suitable moulds. The suppositories solidify on cooling. In certain cases it is also possible to cold-mould by compression in a suitable press.

The softening time is determined according to the text *Softening time determination of lipophilic suppositories*, published in the Supplementary information section.

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

Packaging must be adequate to protect suppositories from light, excessive heat, moisture and damage due to handling and transportation. It is necessary to ensure that the suppositories can be released from the packaging easily and without damage.

Visual inspection

Suppositories are elongated, smooth and have a uniform texture and appearance.

Evidence of physical and/or chemical instability is demonstrated by noticeable changes in:

– surface texture or form;

– colour and odour.

Disintegration

Suppositories comply with *5.4 Disintegration test for suppositories and rectal capsules* unless intended for sustained release.

Uniformity of mass

Suppositories comply with *5.2 Uniformity of mass for single-dose preparations*.

Uniformity of content

If applicable, suppositories comply with *5.1 Uniformity of content for single-dose preparations*. If the suppository has more than one active ingredient the requirement applies only to those active ingredients that fall into the category specified in the test. If the test for uniformity of content is prescribed the test for uniformity of mass is not required.

Containers

Suppositories should be supplied in a well-closed container. The container material should not adversely affect the quality of the preparation, nor should it allow diffusion into or across the container material or yield foreign substances into the preparation.

Rectal capsules

Definition

Rectal capsules are solid, single-dose preparations generally similar to soft capsules as defined in the monograph on *Capsules*,

except that they may have a lubricating coating. The contents of rectal capsules are usually solutions or suspensions of the active ingredient(s) in non-aqueous liquids, e.g. vegetable oil, or in semi-solid mixtures of suitable excipients.

Manufacture

See the manufacturing instructions for soft capsules. Other considerations for rectal capsules include the study of and suitable controls for pH, leakage and pellicle formation.

A suitable test is carried out to demonstrate the appropriate release of the active ingredient(s) from rectal capsules.

Visual inspection

Rectal capsules are of elongated shape, smooth and have a uniform external appearance.

Unpack and inspect at least 20 rectal capsules. They should be smooth and undamaged. Evidence of physical instability is demonstrated by gross changes in physical appearance, including hardening or softening, cracking, swelling, mottling or discoloration of the shell.

Disintegration

Rectal capsules comply with *5.4 Disintegration test for suppositories and rectal capsules* unless intended for sustained release.

Uniformity of mass

Rectal capsules comply with the requirements for capsules in *5.2 Uniformity of mass for single-dose preparations*.

Uniformity of content

Rectal capsules comply with *5.1 Uniformity of content for single-dose preparations*. If the rectal capsule has more than one active ingredient the requirement applies only to those active ingredients that fall into the category specified in the test. If the test for uniformity of content is prescribed the test for uniformity of mass is not required.

Rectal solutions, emulsions and suspensions

Definition

Rectal solutions, emulsions and suspensions (also called enemas) are liquid preparations intended for rectal application to obtain a local or systemic effect, or they may be intended for diagnostic purposes. They contain one or more active ingredients dissolved or dispersed in water, glycerol, macrogols, vegetable oil or mixtures thereof.

Rectal emulsions may show evidence of phase separation but are readily redispersed on shaking. Rectal 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.

They may contain excipients, for example, to adjust the viscosity of the preparation, to adjust or stabilize pH, to increase the solubility of the active ingredient(s) and to stabilize the preparation. The excipients do not, at the concentrations used, cause undue local irritation.

Rectal solutions, emulsions and suspensions are supplied in single-dose 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 the preparation complies with the requirements for rectal solutions or rectal suspensions as appropriate.

Disintegration

Tablets for rectal solutions or suspensions comply with the following test: Place one tablet in a 250 mL beaker containing 200 mL of water R at 15–25 °C. Repeat the operation on five additional tablets. The tablets comply with the test if each of the six tablets used in the test dissolves or disintegrates within 3 minutes, unless otherwise specified in the individual monograph.

Labelling

The label states:

– the method of preparing the rectal solution or suspension;

– when necessary, conditions and duration of storage of the final preparation.

Semi-solid rectal preparations

Definition

Semi-solid rectal preparations are ointments, creams or gels intended for local treatment in the rectum.

They are usually supplied as single-dose preparations in containers adapted to deliver the preparation to the rectum or are accompanied by a suitable applicator.

Semi-solid rectal preparations comply with the requirements for *Topical semi-solid dosage forms*.

Manufacture

When supplied in multidose containers the expected reproducibility of the delivery of the intended volume must be ensured.