This text was updated in Ph. Eur. 11.6 (effective 01/01/2025)

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

Eye Preparations

General Notices

(Ph. Eur. monograph 1163)

Eye Preparations comply with the requirements of the European Pharmacopoeia. These requirements are reproduced in the British Pharmacopoeia.

Ph Eur

DEFINITION

Eye preparations are sterile preparations intended for application to the eyeball and/or to the conjunctiva, or for insertion into the conjunctival sac, to deliver active substances for a local effect.

They are liquid, semi-solid or solid preparations containing one or more active substances in a suitable vehicle. They may contain excipients, for example to adjust the tonicity or viscosity of the preparation, to adjust or stabilise the pH, to increase the solubility of the active substances, to stabilise the preparation or to provide adequate antimicrobial properties. The excipients do not adversely affect the intended medicinal action of the preparation or, at the concentrations used, cause toxicity or undue local irritation.

With the exception of veterinary medicinal products, preparations specifically intended for use in the injured eye or during surgical procedures are, unless otherwise justified and authorised, free from preservatives and supplied in single-dose containers.

Where applicable, containers for eye 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 eye preparations may be distinguished:

— eye drops;

— eye lotions;

— powders for eye drops and powders for eye lotions;

— semi-solid eye preparations;

— ophthalmic inserts.

PRODUCTION

During the development of an eye preparation, it shall be demonstrated that the antimicrobial activity of the preparation as such or, if necessary, after the addition of a suitable preservative or preservatives or the selection of an appropriate container, provides adequate protection against adverse effects that may arise from microbial contamination or proliferation during the storage and use of the preparation. For eye preparations provided in multidose containers, it must be demonstrated that the antimicrobial properties of the preparation are maintained throughout the entire shelf-life, including the in-use period. A suitable test method together with criteria for judging the preservative properties of the formulation are provided in general chapter *5.1.3. Efficacy of antimicrobial preservation*.

The need for and efficacy of any added preservatives, as well as their compatibility with the other ingredients in the preparation, shall be demonstrated to the satisfaction of the competent authority.

Eye preparations that do not contain antimicrobial preservatives and whose formulations do not provide acceptable antimicrobial efficacy are supplied either in single-dose containers or in multidose containers that prevent microbial contamination of the contents after opening.

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

Eye 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*.

Liquid eye preparations examined under suitable conditions of visibility are practically free from visible particles.

Recommendations on testing for visible particles are given in general chapter 5.17.2.

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

TESTS

Sterility (*2.6.1*)

Eye preparations comply with the test.

Applicators supplied separately also comply with the test. Using aseptic technique, remove the applicator from its package and transfer it to a tube of culture medium, immersing it completely. Incubate and interpret the results as described in the test.

STORAGE

Unless otherwise justified and authorised, store in a sterile, tamper-evident container.

LABELLING

The label states the name of any added preservative.

EYE DROPS

DEFINITION

Eye drops are sterile liquid eye preparations intended for instillation into the eye. They are formulated as solutions, emulsions or suspensions.

Examined under suitable conditions of visibility, eye drops that are solutions are practically clear and practically free from particles.

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 remains sufficiently stable to enable the correct dose to be delivered.

Eye drops supplied in multidose containers allow successive drops of the preparation to be administered. The containers contain at most 10 mL of the preparation, unless otherwise justified and authorised.

TESTS

Particulate contamination: sub-visible particles (*2.9.53*)

Unless otherwise justified and authorised, eye drops specifically intended for use in surgical procedures, as a first-aid treatment or for the treatment of the injured eye comply with the following limits using Method 1 or Method 2.

Method 1 (light obscuration particle count test)

The average number of particles present in the containers or units tested does not exceed 1000 per millilitre for particles equal to or greater than 10 µm in size and does not exceed 100 per millilitre for particles equal to or greater than 25 µm in size.

Method 2 (microscopic particle count test)

The average number of particles present in the containers or units tested does not exceed 3000 per container for particles equal to or greater than 10 µm in size and does not exceed 300 per container for particles equal to or greater than 25 µm in size.

In the case of emulsions, colloidal dispersions or liposomal preparations, these limits may be higher.

Particulate contamination: visible particles (*2.9.20*)

Eye drops examined under suitable conditions of visibility are practically free from visible particles.

Recommendations on testing for visible particles are given in general chapter 5.17.2.

Particle size

Unless otherwise justified and authorised, eye drops that are suspensions comply with the following test.

Introduce a suitable quantity of the suspension into a counting cell or, using a micropipette, onto a slide, as appropriate, and scan under a microscope an area corresponding to 10 µg of the active substance. For practical reasons, it is recommended to start by scanning the whole sample at low magnification (e.g. 50 ×) in order to identify the particles greater than 25 µm in size. These larger particles can then be measured at a higher magnification (e.g. 200 × to 500 ×). For each 10 µg of active substance, not more than 20 particles are greater than 25 µm in size, and not more than 2 of these particles are greater than 50 µm in size. None of the particles is greater than 90 µm in size.

LABELLING

The label states, for multidose containers, the period within which the preparation is to be used after opening. This period does not exceed 4 weeks, unless otherwise justified and authorised.

EYE LOTIONS

DEFINITION

Eye lotions are sterile aqueous liquid eye preparations intended for rinsing or bathing the eye or for impregnating eye dressings.

Examined under suitable conditions of visibility, eye lotions are practically clear and practically free from particles.

Multidose containers contain at most 200 mL of preparation unless otherwise justified and authorised.

TESTS

Particulate contamination: sub-visible particles (*2.9.53*)

Unless otherwise justified and authorised, eye lotions specifically intended for use in surgical procedures, as a first-aid treatment and for the treatment of the injured eye comply with the following limits using Method 1 or Method 2.

Method 1 (light obscuration particle count test)

For preparations supplied in containers with a nominal volume of less than or equal to 100 mL, the average number of particles present in the containers or units tested does not exceed 6000 per container for particles equal to or greater than 10 µm in size and does not exceed 600 per container for particles equal to or greater than 25 µm in size.

For preparations supplied in containers with a nominal volume of more than 100 mL, the average number of particles present in the containers or units tested does not exceed 25 per millilitre for particles equal to or greater than 10 µm in size and does not exceed 3 per millilitre for particles equal to or greater than 25 µm in size.

Method 2 (microscopic particle count test)

For preparations supplied in containers with a nominal volume of less than or equal to 100 mL, the average number of particles present in the containers or units tested does not exceed 3000 per container for particles equal to or greater than 10 µm in size and does not exceed 300 per container for particles equal to or greater than 25 µm in size.

For preparations supplied in containers with a nominal volume of more than 100 mL, the average number of particles present in the containers or units tested does not exceed 12 per millilitre for particles equal to or greater than 10 µm in size and does not exceed 2 per millilitre for particles equal to or greater than 25 µm in size.

Particulate contamination: visible particles (*2.9.20*)

Eye lotions examined under suitable conditions of visibility are practically free from visible particles.

Recommendations on testing for visible particles are given in general chapter 5.17.2.

LABELLING

The label states:

— where applicable, that the contents are to be used on one occasion only;

— for multidose containers, the period within which the preparation is to be used after opening. This period does not exceed 4 weeks, unless otherwise justified and authorised.

POWDERS FOR EYE DROPS AND POWDERS FOR EYE LOTIONS

DEFINITION

Powders for the preparation of eye drops and eye lotions are sterile solid eye preparations intended to be dissolved or dispersed in the prescribed liquid at the time of administration. They may contain additional excipients to prevent aggregation of the particles.

After dissolution or dispersion, they comply with the requirements for eye drops or eye lotions, as appropriate.

TESTS

Uniformity of dosage units (*2.9.40*)

Powders for eye drops and eye lotions supplied in single-dose containers 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, powders for eye drops and eye lotions supplied in single-dose containers and having a content of active substance of less than 2 mg or less than 2 per cent of the total mass comply with the requirements under Test B. If the preparation contains more than one active substance, the requirement applies only to those substances that correspond to the above conditions.

Uniformity of mass (*2.9.5*)

Powders for eye drops and eye lotions supplied in single-dose containers comply with the test. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

SEMI-SOLID EYE PREPARATIONS

DEFINITION

Semi-solid eye preparations are sterile eye preparations intended for application to the conjunctiva or the eyelids. They are creams, gels or ointments with a homogeneous appearance.

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

Semi-solid eye preparations are supplied in small, sterilised, suitably designed single-dose or multidose containers fitted or provided with a sterilised cannula. The containers contain at most 10 g of preparation, unless otherwise justified and authorised. The containers must be well-closed to prevent microbial contamination and are of such a shape as to facilitate administration without contamination.

TESTS

Particle size

Semi-solid eye preparations containing dispersed solid particles comply with the following test.

On a slide, gently spread a quantity of preparation corresponding to at least 10 µg of active substance as a thin layer. Scan the whole area of the sample under a microscope. For practical reasons, it is recommended to start by scanning the whole sample at a low magnification (e.g. 50 ×) in order to identify the particles greater than 25 µm in size. These larger particles can then be measured at a higher magnification (e.g. 200 x to 500 ×). For each 10 µg of active substance, not more than 20 particles are greater than 25 µm in size, and not more than 2 of these particles are greater than 50 µm in size. None of the particles is greater than 90 µm in size.

LABELLING

The label states, for multidose containers, the period within which the preparation is to be used after opening. This period does not exceed 4 weeks, unless otherwise justified and authorised.

OPHTHALMIC INSERTS

DEFINITION

Ophthalmic inserts are sterile, solid or semi-solid single-dose eye preparations of a size and shape suitable for insertion in the conjunctival sac. They generally consist of a reservoir of active substance embedded in a matrix or bounded by a rate-

controlling membrane. The active substance, which is more or less soluble in lacrymal fluid, is released over a given period of time.

Ophthalmic inserts are supplied in sterile single-dose packaging.

TESTS

Uniformity of dosage units (*2.9.40*)

Ophthalmic inserts comply with the test or, where justified and authorised, with the test for uniformity of content 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*)

Ophthalmic inserts comply, where applicable, with the requirements under Test A.

Release of active substance(s)

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

LABELLING

The label states:

— where applicable, the total quantity of active substance per insert;

— where applicable, the dose released per unit time.