AQUA CONSERVANS

CZ 030:2023

Preservative water

DEFINITION

A solution of methylparaben ($C_8H_8O_3$; M_r 152.15) and propylparaben ($C_{10}H_{12}O_3$; M_r 180.20).

Content. 0.085 % to 0.115 % of total $C_8H_8O_3$ and $C_{10}H_{12}O_3$ compounds.

COMPOSITION AND PROCEDURE

Methylparabenum (*0409)*	*0.67* g
Propylparabenum (*0431*)	0.33 g
Aqua purificata (*0008*)	to 1000.0 g

Dissolve methylparaben and propylparaben in boiling purified water. Cool the liquid, make up to 1000.0 g with purified water and filter.

PROPERTIES

Appearance. A clear colourless liquid.

IDENTIFICATION TESTS

A. Heat 0.5 ml briefly in a water bath with 2 ml *Millon's reagent RN;* a red colour appears.

B. The chromatograms obtained in the Parabens test are evaluated (see Purity Tests). There are two spots on the chromatogram of the test solution, one of which corresponds to the location and size of the stain on the chromatogram of reference solution (a) and the other to the spot on the chromatogram of reference solution (b).

PURITY TESTS

Parabens. Thin-layer chromatography (*2.2.27*).

The tested solution. The product being tested.

Reference solution (a). Dissolve 6.7 mg *methylparaben CRL* in *acetone R* and dilute with the acetone to 10 ml.

Reference solution (b). Dissolve 3.3 mg *propylparaben CRL* in *acetone R* and dilute with the acetone to 11 ml.

Reference solution (c). Mix 1 ml of reference solution (a) and 1 ml of reference solution (b).

Stationary phase. Plate with a layer of octadecylsilyl silica gel F254 for TLC R.

Mobile phase. Mixture of volumetric fractions of *glacial acetic acid R, water R* and *methanol R* (1 + 30 + 70).

Application. 2 pl.

Development. Along a 15-cm track.

Drying. In the air.

Detection. Observed under ultraviolet light at 254 nm.

Compliance test: There are two distinctly separated spots on the chromatogram of reference solution (c).

Evaluation. There are two spots on the chromatogram of the tested solution, where the methylparaben stain does not exceed the size and fluorescence quenching intensity of the stain on the chromatogram of reference solution (a) and the propylparaben stain does not exceed the size and fluorescence quenching intensity of the stain on the chromatogram of reference solution (b). No other spots are present.

Chromatograms shall be used for identification test B.

DETERMINATION OF CONTENT

Special part

Mix 25.0 ml in a ground glass stopper flask with 1 ml *concentrated sodium hydroxide RS* and heat for 15 min in a water bath. After cooling, add 25.0 ml *0.0167 mol/l potassium bromide RS,* 2.5 g *potassium bromide R* and 15 ml *3 mol/l hydrochloric acid RS.* Close the flask quickly and allow it to stand in the dark for 15 minutes, stirring occasionally. Then add 1 g *potassium iodide R,* 10 ml *chloroform R,* close the flask and leave the flask standing in the dark for 3 minutes after mixing the mixture. Then re-titrate with *0.1 mol/l thiosulfate RS* to a light yellow colour and after adding 2 ml *starch RS,* titrate again until decolourised.

1 ml 0.0167 mol/l *potassium bromate RS* is equivalent to 2.692 mg of a mixture of $C_8H_8O_3$ and $C_{10}H_{12}O_3$ (2 + 1).

STORAGE

In glass containers, at 15 °C to 25 °C and protected from light.

SHELF LIFE

12 months when stored in dark glass containers at 15 °C to 25 °C and protected from light. Open packaging must be consumed immediately.

ATROPINI SULFATIS OCULOGUTTAE

CZ 034:2023

Eye drops with atropine sulphate

DEFINITION

A sterile solution of atropine sulphate monohydrate ($C_{34}H_{48}N_2O_{10}S.H_2O$; M_r 694.84) with sodium chloride (NaCl; *M*r 58.44) and an antimicrobial preservative.

Content:

* *atropine sulphate monohydrate:* 0.95 % to 1.05%;

* *sodium chloride:* 0.73 % to 0.81%.

* Atropini sulfas monohydricus (*0068*)	* 1.00 g
* Natrii chloridum (*0193*)	* 0.77 g
* Carbethopendecinii bromidum (*CZ 045*)*	* 0.02 g
* Aqua purificata (*0008*) (sterile)**	* to 100.0 g

* In justified cases, a different suitable antimicrobial agent may be used.

* *If needed, it is possible to use *Aqua pro iniectione (0169).*

Dissolve atropine sulphate monohydrate, sodium chloride and carbethopendecinium bromide in 90 g of sterilised purified water (*5.1.1*, steam sterilisation for 15 min at 121 °C). Dilute the solution with sterilised water purified to 100.0 g. Perform membrane filtration (*5.1.1*) and dispense into suitable sterile containers in a class A clean room

PROPERTIES

Appearance. A clear colourless liquid.

IDENTIFICATION TESTS

A. Add 0.2 ml *nitric acid R* to 0.1 ml and evaporate until dry in a water bath. Dissolve the rest in 2 ml *acetone R,* add 0.1 ml *potassium hydroxide* in *ethanol RS;* a purple colour appears (*atropine*).

B. 0.5 ml complies with the alkaloid test (*2.3.1*).

C. Passes test (a) for sulphates (*2.3.1*).

D. Colours flame yellow (*sodium*).

E. Passes test (a) for chlorides (*2.3.1*).

F. Acidify 1 ml with 1.5 ml *dilute sulphuric acid RS,* add 2 ml *chloroform R* and 0.1 ml *potassium permanganate R* solution (1 g/l). After shaking thoroughly, the chloroform layer turns pinkish purple *(quaternary ammonium compound).*

PURITY TESTS

Appearance. The tested preparation is clear **(*2.2.1*) and** colourless **(2.2.2,** *Method II).*

pH (2.2.3). 4.5 to 7.5.

Sterility (2.6.1). Passes the sterility test.

DETERMINATION OF CONTENT
Atropine sulfate monohydrate. Absorption spectrophotometry in the ultraviolet and visible regions (**2.2.25**).
The tested solution. Dilute 1.000 g with *water R* to 50.0 ml in a 50 ml volumetric flask. Transfer 1.0 ml of this solution to a separating funnel, add 0.5 ml of *buffer solution with pH 4.5 RN*, 1.0 ml of saturated solution of *trinitrophenol R* and 10.0 ml *chloroform R*. Shake the mixture thoroughly for 30 seconds. After separation, filter the chloroform layer through a dry filter.
Reference solution Simultaneously prepare a reference solution in the same manner using 1.0 ml of a solution of *atropine sulphate monohydrate CRL* containing 0.2 mg $C_{34}H_{48}N_2O_{10}S.H_2O$ in 1 ml.
Measure the absorbance (2.2.25) of the tested solution and the reference solution at 410 nm against *chloroform R* and calculate the content of $C_{34}H_{48}N_2O_{10}S.H_2O$ as a percentage.

Sodium chloride. To 5.500 g add 40 ml *water R* and 5 ml *diluted sulphuric acid RS*. Titrate with *0.1 mol/l silver nitrate PS* using potentiometric indication of the equivalence point **(2.2.20).**
1 ml of *0.1 mol/l silver nitrate PS* is equivalent to 5.844 mg of NaCl.

STORAGE
See article *Ocularia {1163).*

SHELF LIFE
3 months when stored in sealed glass containers at 15 °C to 25 °C and protected from light.

LABELLING
See article *Ocularia (1163),* paragraph *Oculoguttae.*
The label shall indicate the name of the antimicrobial preservative used.

ERGOTAMINI TARTRAS TRITURATUS

Ergotamine tartrate trituration

DEFINITION
A mixture of ergotamine tartrate ($C_{70}H_{76}N_{10}O_{16}$; M_r 1313.43) with lactose ($C_{12}H_{22}O_{11}$; M_r 342.30).
Content. 0.95 % to 1.05 % of $C_{70}H_{76}N_{10}O_{16}$ compound.

Ergotamini tartras (*0224*)	1.00 g
Lactosum anhydricum (*1061*) seu Lactosum monohydricum (*0187*)	to 100.0 g

In a pre-weighed 150 ml mortar, gradually add anhydrous lactose or lactose monohydrate to the ergotamine tartrate to a total quantity of 100.0 g while stirring thoroughly. Transfer the well-mixed mixture to a wide-mouth dark glass vial with a screw cap.

PROPERTIES
Appearance. A white or almost white crystalline powder.

IDENTIFICATION TESTS
A. Dissolve about 0.2 g in 5.0 ml of a *tartaric acid R* solution (10 g/l). The solution fluoresces blue in the light of a mercury lamp with a radiation maximum at 366 nm. The solution is also used for identity test B.

B. Add 1.0 ml *water R* and 2.0 ml of *Dimethylaminobenzaldehyde RS6* solution to two drops of the solution from identity test A; an intense blue colour will appear.

C. Mix about 0.1 g with 1.0 ml *silver ammonium nitrate RS* and heat in a water bath; a silver mirror (*tartrate;*) appears.

PURITY TESTS

Loss on drying *(2.2.32).* At most 1.5% if anhydrous lactose is used; at most 2.5% if lactose monohydrate is used. 0.500 g is dried for 6 hours in a vacuum at 80 °C.

DETERMINATION OF CONTENT

Absorption spectrophotometry in the ultraviolet and visible regions (*2.2.25*).

The tested solution. Dissolve 0.20 g in a 50 ml graduated flask in a *tartaric acid R* solution (20 g/l) and dilute with it to 50.0 ml. Add 4.0 ml *Dimethylaminobenzaldehyde RS6* to 2.0 ml of this solution, mix and measure the absorbance *(2.2.25)* of the resulting solution at 548 nm against the control solution after 30 min.

Reference solution. Dissolve 0.020 g *ergotamine tartrate CRL* in a 50 ml graduated flask in a *tartaric acid R* solution (20 g/l) and dilute with it to 50.0 ml. Transfer 5.0 ml from this solution to another 50 ml graduated flask and dilute with the same solvent to 50.0 ml. Add 4.0 ml of *Dimethylaminobenzaldehyde RS6 to 2.0 ml of this solution,* mix and measure the absorbance (2.2.25) of the resulting solution at 548 nm against the control solution after 30 min.

Control solution. Add 4.0 ml *of Dimethylaminobenzaldehyde RS6* to 2.0 ml of a *tartaric acid R* solution (20 g/l).

Calculate the content of $C_{70}H_{76}N_{10}O_{16}$ AS A percentage.

SHELF LIFE

6 months when stored in glass containers at 15 °C to 25 °C and protected from light and moisture.

ETHACRIDINI LACTATIS SOLUTIO

CZ 055:2023

Ethacridine lactate solution

DEFINITION

A solution of ethacridine lactate ($C_{18}H_{21}N_3O_4.H_2O$; M_r 361.39).

Content. 90.0 % to 110.0 % of the nominal amount of $C_{18}H_{21}N_3O_4.H_2O$ compound.

COMPOSITION AND PROCEDURE

Solution concentration	**0.1 %**	**1 %**
Ethacridini lactas monohydricus (*1591*)	1.0 g	10.0 g
Aqua purificata (*0008*)	to 1000.0 g	to 1000.0 g

Weigh the required amount of ethacridine lactate into a 1000 ml glass bottle with a ground glass stopper and dissolve in about 500 g of hot purified water. After dissolution, allow it to cool, dilute with purified water to 1000.0 g and mix thoroughly.

PROPERTIES

Appearance. A clear yellow solution.

IDENTIFICATION TESTS

A. Mix 0.2 ml of solution S (see Purity Tests) with 100 ml *water R*. The solution is greenish-yellow and exhibits green fluorescence in ultraviolet light at 365 nm and in daylight. After 5 ml *1 mol/l hydrochloric acid RS* is added the fluorescence disappears *(ethacridine).*

B. To 1 ml of solution S (see Purity Tests), add 1.0 ml *water R*, 0.1 ml *cobalt chloride R* (10 g/l) and 0.1 ml *potassium ferrocyanide R* (50 g/l); a green colour appears.

C. To 5 ml of solution S (see Purity Tests), add 1 ml *1 mol/l sodium hydroxide RS*; a yellow precipitate (*ethacridine*) forms. Filter the mixture and add 2 ml of *diluted sulphuric acid RS* to the colourless filtrate. Heat 0.5 ml of this filtrate for 2 min in a water bath with 1 ml *sulphuric acid R* and after cooling add two drops *guaiacol RSN;* after a while the solution turns light red *(lactate).*

PURITY TESTS

Solution S. Prepare a solution of the tested preparation in *purified water R* so that 100 ml contains about 0.1 g of ethacridine lactate (0.1% will be used directly, 10 ml of 1% solution will be diluted to 100 ml).

pH *(2.2.3).* 5.5 to 7.0; measure solution S.

DETERMINATION OF CONTENT

Absorption spectrophotometry in the ultraviolet and visible regions (*2.2.25*).
The tested solution. Dilute a quantity of the tested solution corresponding to 25 mg ethacridine lactate in a 50ml graduated flask with *carbon dioxide-free water R* to 50.0 ml (25.00 g of 0.1% solution; 2.500 g of 1% solution). Transfer 0.50 ml of this solution to a 10 ml graduated flask, add 0.5 ml *10% hydrochloric acid RSN* and 0.5 ml of *sodium nitrite R* solution (10 g/l) and dilute with *carbon dioxide-free water R* to 10.0 ml. Measure the absorbance of this solution at 515 nm against the control solution.
Reference solution Dissolve 0.025 g *ethacridine lactate monohydrate CRL* in a 50 ml graduated flask in *carbon dioxide-free water R,* heating if necessary, and dilute to 50.0 ml with the same solvent after cooling. Transfer 0.50 ml of this solution to a 10 ml graduated flask, add 0.5 ml of *10% hydrochloric acid RSN* and 0.5 ml of *sodium nitrite R* solution (10 g/l) and dilute with *carbon dioxide-free water R* to 10.0 ml. Measure the absorbance of this solution at 515 nm against the control solution.
Calculate the content of $C_{18}H_{21}N_3O_4.H_2O$ as a percentage.

SHELF LIFE

6 months when stored in dark glass containers at 15 °C to 25 °C and protected from light.

GERANII ETHEROLEUM

GERANII ETHEROLEUM

CZ 066:2023

Geranium essential oil

CAS 8000-46-2

DEFINITION

An essential oil obtained from leaves of various species of the genus *Pelargonium* by distillation with water vapour.

Content. 65.0% to 75.0% of alcohols, expressed as geraniol ($C_{10}H_{18}O$; M_r 154.25).

PROPERTIES

Appearance. A colourless to yellowish or greenish clear liquid, with a characteristic odour.
Solubility. Very soluble in water, miscible with ethanol 96%, ether and fatty oils.

IDENTIFICATION TESTS

Thin-layer chromatography (*2.2.27*).
The tested solution. Dissolve 0.1 g in *96% ethanol R* and dilute to 10 ml.
Reference solution Dissolve 50 mg *geraniol R* in *96% ethanol R* and dilute to 10 ml.
Stationary phase. Plate with a layer of silica gel G for TLC R.
Mobile phase. A mixture of volumetric fractions of *ethyl acetate R* and *toluene R* (5+ 95).
Application. 10 pl.
Development. Along a 12-cm track.
Drying. In the air.
Detection. Spray with *anisaldehyde RS* and dry 5 to 10 min at 100 °C to 105 °C.
Evaluation. The main spot in the chromatogram of the tested solution corresponds approximately to the position and colour of the main spot in the chromatogram of the reference solution. There may be other less intense spots on the test solution chromatogram.

PURITY TESTS

Density *(2.2.5).* 0.884 to 0.905 g/cm^3.

Refractive index *(2.2.6).* 1.462 to 1.474.

Optical rotation *(2.2.7).* -14° to -5°.

Acidity number *(2.5.1).* At most 8.0; Dissolve 5.0 g of the tested substance in 50 ml of the prescribed solvent mixture.

Water in essential oils *(2.8.5).* Meets the test requirements.

Fatty oils and resinous essential oils *(2.8.7).* Meets the test requirements.

Odour and **taste of essential oils** *(2.8.8).* Meets the test requirements.

The residue after the evaporation of essential oils *(2.8.9).* At most 5.0% (0.03 g); Heat 1.00 g for 2 hours in a water bath.

Solubility in ethanol *(2.8.10).* Soluble in three volume parts of *70% ethanol (V/V) R*

DETERMINATION OF CONTENT
Mix 5.0 ml in an acetylation flask with 7.5 ml of *acetic anhydride R* and 1.0 g *anhydrous sodium acetate R* and boil 2 h. Add 20.0 ml *water R* and heat for 15 min in a water bath under a reflux condenser shaking frequently. After cooling, the acetylated essential oil is transferred to a separating funnel and the water layer is removed. Shake the acetylated essential oil with *water R* until the water layer reacts to moistened *blue litmus paper A* with only weak acidity, the water layer is always removed. Dry the acetylated essential oil with *anhydrous sodium sulphate R* and filter.
Mix 1.500 g of acetylated essential oils with 3 ml *96% ethanol R* and 0.1 ml *phenolphthalein RS* and add *0.5 mol/l potassium hydroxide in ethanol VS* drop by drop until a permanent colour appears. Then add 20.0 ml of *0.5 mol/l potassium hydroxide* in *ethanol VS* and boil for 2 h under reflux condenser. After cooling, add 0.5 ml of *phenolphthalein RS* and titrate with *0.5 mol/l hydrochloric acid VSN* until the colour changes. Perform a blind test.

The acetylable component content in percent, expressed as geraniol ($C_{10}H_{18}O$), is calculated according to the formula:

$$x = \frac{a \cdot 7{,}712}{m - a \cdot 0{,}021},$$

where:
a — the difference in consumption of *0.5 mol/l potassium hydroxide* in *ethanol VS* in the test and in the blind test in millilitres;
m - the mass of acetylated essential oils in grams.

STORAGE
In completely filled airtight packaging, protected from light.

HOMATROPINI HYDROBROMIDI OCULOGUTTAE

CZ 070:2023

Eye drops with homatropine hydrobromide

DEFINITION
A sterile solution of homatropine hydrobromide ($C_{16}H_{22}BrNO_3$; M_r 356,26) with sodium chloride (NaCl; M_r 58.44) and an antimicrobial preservative.

Content:
Homatropine hydrobromide: 90.0 % to 110.0 % of the prescribed quantity of $C_{16}H_{22}BrNO$;

sodium chloride: 90.0% to 110.0% of the prescribed amount of NaCl.

COMPOSITION AND PROCEDURE

Solution concentration	**1 %**	**2 %**
Homatropini hydrobromidum (*0500)*	1.00 g	2.00 g
Natrii chloridum (*0193*)	0.73 g	0.57 g
Carbethopendecinii bromidum (*CZ 045*)*	0.02 g	0.02 g
Aqua purificata (*0008*) (sterile)* *	to 100.0 g	to 100.0 g

*In justified cases, a different suitable antimicrobial preservative may be used.

**If needed, it is possible to use Aqua pro iniectione (*0169*).

Dissolve homatropine hydrobromide, sodium chloride and carbethopendecinium bromide in 90 g of sterilised purified water(*5.1.1*, vapour sterilisation 15 min at 121 °C). Top up the solution with sterilised purified water to 100.0 g. Perform membrane filtration (*5.1.1*) and dispense into suitable sterile containers in a class A clean room.

PROPERTIES

Appearance. A clear colourless liquid.

IDENTIFICATION TESTS

A. Add 2 ml of *ammonia diluted by RS1* and 10 ml *ether R* to a quantity of the tested preparation corresponding to 0.02 g of homatropine hydrobromide. After shaking, the ether layer is to separate and evaporate in a water bath until dry. Heat the residue with a solution of 1 ml *mercury chloride R* solution (20 g/l) in *60% ethanol (V/V) R;* a yellow colour appears, which turns brick red *(homatropine).*

B. Add 0.5 ml of *3 mol/l hydrochloric acid RS*, 0.1 ml of *potassium dichromate RS* and 2 ml of *chloroform R* to the amount of test preparation corresponding to 0.01 g of homatropine hydrobromide, and shake; the chloroform layer turns browish yellow (*bromides).*

C. Colours flame yellow *(sodium).*

D. To a quantity of test preparation corresponding to 0.01 g of homatropine hydrobromide add 0.4 ml *silver nitrate RS2* and 2 ml *ammonia diluted by RS1*. Filter and acidify the clear filtrate with 3 ml *dilute nitric acid RS*; a white precipitate (*chlorides)* forms.

E. Add 1 ml of *ammonium thiocyanate RS*, 0.15 ml of a solution of *cobalt chloride R* (10 g/l) in *methanol R* and 2 ml *ether R* to a quantity of the tested preparation corresponding to 0.01 g of homatropine hydrobromide. After shaking the ether layer turns blue *(quaternary ammonium compound).*

PURITY TESTS

Appearance. The tested preparation is clear *(2.2.1)* and colourless *(2.2.2, Method II).*

pH *(2.2.3).* 4.0 to 6.0.

Sterility *(2.6.1).* Passes the sterility test.

DETERMINATION OF CONTENT

Homatropine hydrobromide. Absorption spectrophotometry in the ultraviolet **and** visible regions *(2.2.25).*

The tested solution. Dilute an amount of the tested preparation corresponding to 0.01 g of homatropine hydrobromide in a 50 ml graduated flask with *water R* to 50.0 ml. Transfer 1.0 ml of this solution to a separating funnel, add 0.5 ml of *pH 4.5 buffer solution RN*, 1.0 ml of a saturated solution of *trinitrophenol R*, 10.0 ml *chloroform R* and shake the mixture thoroughly for 30 seconds. After separation, filter the chloroform layer through a dry filter.

Reference solution. Simultaneously prepare a reference solution in the same manner using 1.0 ml of a

solution of *homatropine hydrobromide CRL* containing 0.2 mg C16H22BrNO3 in 1 ml.
Measure the absorbance of the tested solution and the reference solution at 410 nm using *chloroform R* as a compensation liquid and calculate the content of $C_{16}H_{22}BrNO_3$ as a percentage.

Sodium chloride. To a quantity of the tested preparation corresponding to 0.030 g sodium chloride, add 40 ml *water R* and 5 ml of *sulphuric acid diluted in RS.* Titrate with *0.1 mol/l silver nitrate VS* with potentiometric indication of equivalence points *(2.2.20).* Subtract the consumption between two inflection points.
1 ml of *0.1 mol/l silver nitrate VS* is equivalent to 5.844 mg of NaCl.

STORAGE
See article *Ocularia (1163).*

SHELF LIFE

3 months when stored in sealed glass containers at 15 °C to 25 °C and protected from light.

LABELLING
See article *Ocularia (1163),* paragraph *Oculoguttae.*
The label shall indicate the name of the antimicrobial preservative used.

METHYLROSANILINII CHLORIDI SOLUTIO

CZ 086:2023

Methylrosanilinium chloride solution

DEFINITION
A solution of methylrosanilinium chloride ($C_{25}H_{30}ClN_3$; M_r 407.99).
Content. 85.0 % to 105.0 % $C_{25}H_{30}ClN_3$.

bare, glandular on the outside with tiny papillae. The crown is light pink to light purple, weakly symmetrical, bilabiate, with four almost identical tips, the upper tip is larger, often cut out. Stamens are usually stunted.

B. Microscopic evaluation *(2.8.23).* The powdered drug is green to brownish green. It is observed under a microscope in *chloral hydrate RS.* The powdered drug has the following characteristics: stem fragments with an epidermis of polygonal cells, thickened on the outside with a warty cuticle, hypodermis is collenchymal, parenchymatic cells of primary marrow with tiny calcium oxalate crystals; fragments of the leaf epidermis from cells with wavy walls and diacytic vents *(2.8.3);* trichomes short, broadly conical, single-cell to double-celled, warty on the surface; single row three to eight-cell trichomes up to 600 pm long with a slightly warty or grooved cuticle or fragments thereof; glandular hairs with a single to two-cell stem and a single-cell head are up to 40 pm long; glandular hairs (of type *Lamiaceae)* with a head of 55 pm to 70 pm in diameter.

C. Thin-layer chromatography *(2.2.27).*
The tested solution Powder 0.2 g of the drug (355) *(2.9.12)* just before use, shake for a few minutes with 2 ml *dichloromethane R* and filter. Evaporate until dry at a temperature not exceeding 40 °C, dissolve the rest in 0.1 ml *toluene R.*
Reference solution. Dissolve 50 mg of *menthol R,* 20 pl *cineole R,* 10 mg *thymol R* and 10 pl *menthyl acetate R* in *toluene R* and dilute with it to 10 ml.
Stationary phase. Plate with a layer of silica gel GFm for TLC R.
Mobile phase. A mixture of volumetric fractions of *ethyl acetate R* and *toluene R (5+* 95).
Application. 10 pl of comparative solution and 30 pl of test solution, into strips (20 mm x 3 mm).
Development. Along a 15-cm track.
Drying. Air dry until the odour of solvents disappears.
Detection A. Observed under ultraviolet light at 254 nm.

Evaluation A. On the chromatogram of the test solution, there may be a weakly coloured spot approximately corresponding to the position below the thymol spot on the chromatogram of the comparison solution.

Detection B. The layer is sprayed with *anisaldehyde RS* and is observed in daylight while heating for 5 to 10 min at 100 °C to 105 °C.

Evaluation B. On the chromatogram of the comparison solution there are spots in order of ascending *Rp* value in the lower third dark blue (menthol), purplish blue to brown (cineole), pink (thymol), bluish purple (menthyl acetate). On the chromatogram of the test solution, there are stains of menthol (very intense) and cineole (weakly coloured) approximately corresponding to the position and colouring of the stains on the chromatogram of the comparison solution. In the position defined by the spots of cineole and thymol on the chromatogram of the comparison solution, stains may be: light pink (carvone), bluish grey (pulegone), greyish green (isomenthone). In the central part there is a stain approximately corresponding to the position and colouring of the menthyl acetate stain, just below there is a greenish blue spot (menthone), near the front of the mobile phase there is a distinct reddish-purple spot (hydrocarbons); there may be other less intense spots on the chromatogram.

PURITY TESTS

Foreign admixtures *(2.8.2).* At most 3,0 % of the drug showing evidence of Puccinia menthae rust infestation and not more than 5 % of stems not more than 5 mm in diameter.

Loss on drying *(2.2.32).* At most 12.0 %; Dry 2.000 g of the drug **for** 2 hours in a drier at 105 °C.

pH *(2.2.3).* 3.5 **to** 6.0.

Bacterial endotoxins *(2.6.14).* At most 0.25 IU/ml.

DETERMINATION OF CONTENT

Sodium chloride. Dilute 10.0 ml of test preparation 2/3 and 1/2 or 20.0 ml of test preparation 1/3 and 1/5 with about 50 ml of *water R* and 5.0 ml of *nitric acid diluted in RS* and titrate with *0.1 mol/l silver nitrate PS* with potentiometric indication of the equivalence point *(2.2.20).*

1 ml of *0.1 mol/l silver nitrate PS* is equivalent to 5.844 mg of NaCl.

Glucose. Add 0.1 ml of *ammonia diluted in RS1* to 50.0 ml and mix the mixture well.

After 5 min, measure the angle of optical rotation *(2.2.*7) (usually in a 2 dm layer) and calculate the content of C6H12O6 compound in grams per litre of test preparation.

The specific optical rotation values for solutions of different glucose concentrations are given in Table CZ 088-3.

Table CZ 088-3

Glucose concentration (g/1)	17	25	33	40
Specific optical rotation	+52.57	+52.60	+52.65	+52.66

STORAGE

Store at a temperature of up to 25 °C, protected from light and frost.

LABELLING

See Article *Parenteralia (0520),* paragraph *Infusiones.*

The following shall also be indicated on the container label:

- that the solution may only be used if clear;
- the theoretical ion content in mmol/1;
- the theoretical osmolarity of the solution in mosmol/l;
- the theoretical energy value in kJ/1.

NATRU TETRABORATIS GLOBULUS

CZ 089:2023

Vaginal ball with sodium tetraborate

DEFINITION

A vaginal bead made of glycerol–gelatin with sodium decahydrate tetraborate ($Na_2B_4O_7.10H_2O$; M_r 381.37).

Content. 95.0% to 105.0% of the prescribed amount of $Na_2B_4O_7.10H_2O$.

COMPOSITION AND PROCEDURE

Unless otherwise prescribed, it is prepared in the following composition:

Natrii tetraboras decahydricus (*0013*)	0.6 g
Glycerogelatum gelatinae	q.s.

Glycerogelatum gelatinae:

Gelatine (*0330*)	12.5 g
Aqua conservans (*CZ 030*)	25.0 g
Glycerolum 85% (*0497*)	62.5 g

The required amount of gelatin glycerogel is determined by the volume of the chosen form.

Vaginal balls are usually prepared with a weight of 3.6 g.

Allow crumbled gelatine to swell for 15 minutes in a mixture of 85% preservative water and glycerol and heat at a temperature of not more than 65 °C until the gelatine is dissolved. Dissolve the sodium tetraborate decahydrate in the dissolvedn gelatin glycerogel, mix the mixture and remove any foam. Make up with purified water to the required amount, mix the mixture well and pour it into a suitable form while still hot.

PROPERTIES

Appearance. A translucent yellow to light yellow elastic ball, intact smooth surface.

IDENTIFICATION TESTS

A. Dissolve approximately 0.1 g of sodium tetraborate by slightly heating in about 2 ml of *water R*, add 2 ml of *potassium carbonate R* (100 g/l) and heat. After cooling, add 4 ml *potassium hexahydroxoantimonate* and heat again; after a while, a white crystalline precipitate forms. The excretion of the precipitate is accelerated by rubbing a glass rod against the test tube wall (*sodium)*.

B. Moisten an amount corresponding to about 0.2 g of sodium tetraborate in a porcelain dish with 1 ml of *sulphuric acid R*, add 3 ml of *methanol R* and ignite the mixture. The flame is green, especially its edges (*boric acid*).

C. Heat about 1.5 g slowly with 0.5 g *potassium bisulphate R*; the mixture carbonises and a penetrating odor of acrolein develops (*glycerol*).

D. When burning, an odour of burning keratin is present (*gelatine*).

TESTING OF PHARMACEUTICAL FORM

Disintegration test. Perform a disintegration test for rectal and vaginal preparations *(2.9.2).* Evaluate the condition after 60 minutes.

Mass uniformity *(2.9.5).* Passes the mass uniformity test for solid single-dose formulations.

DETERMINATION OF CONTENT

Dissolve 3.000 g by slight heating in 50 ml of *water R.* Dilute the solution with about 50 ml of *water R* and after cooling titrate with *0.5 mol/l hydrochloric acid VSN* with potentiometric indication of the equivalence point *(2.2.20).*

1 ml *0.5 mol/l hydrochloric acid VSN* is equivalent to 95.35 mg $Na_2B_4O_7.10H_2O$.

Calculate the sodium tetraborate content, expressed as a percentage of the declared quantity and in relation to the average mass of one ball, using the formula:

$$\frac{m \cdot z \cdot 100}{n \cdot d};$$

where:

m - the amount of sodium tetraborate found in the weighed mass in grams;
z - average weight of a vaginal ball in grams;
n - weight of the test sample in grams;
d – declared amount of sodium tetraborate in one vaginal ball in grams. STORAGE

Protected from light and freezing, at a temperature of up to 20 °C.

LABELLING
The labelling shall indicate the names of the antimicrobial preservatives used.

SOLUTIO JARISCH

CZ 115:2023

Jarisch solution¨

DEFINITION

A solution of boric acid (H_3BO_3; M_r 61,83) and glycerol ($C_3H_8O_3$; M_r 92,09) in preservative water.

Content:

- *boric acid:* 1.85 % to 2.15 %;
- *glycerol:* 3.16% to 3.68%.

COMPOSITION AND PROCEDURE

Acidum boricum (*0001*)	20.0 g
Glycerolum 85% (*0497*)	40.0 g
Aqua purificata (*0008*)	940.0 g

Dissolve boric acid in boiling purified water. After cooling, add 85% glycerol, top up to 1000.0 g with purified water and filter.

PROPERTIES
Appearance. A clear colourless liquid that turns *blue litmus paper R* red.

IDENTIFICATION TESTS
A. Reduce 5 ml in a porcelain bowl in a water bath, dissolve the rest in 3 ml of *methanol R* and add 0.5 ml of *sulphuric acid R*. When ignited the solution burns with a flame that is green, especially at the edges *(boric acid).*

B. Mix 1 ml with 1 ml of *nitric acid R* and cover the liquid with a layer of 1 ml *potassium dichromate RS;* a purplish blue ring *(glycerol)* forms at the boundary of both layers.

DETERMINATION OF CONTENT
Boric acid. Mix 5.500 g with a solution of 2 g *sorbitol R* in 15 ml of *water R* in pre-neutralised *0.1 mol/l sodium hydroxide VS* using *0.5 ml thymol blue RS* until it turns green. Titrate with a volumetric solution of *0.1 mol/l sodium hydroxide VS* to the same colour.

1 ml of *1 mol/l sodium hydroxide VS* is equivalent to 6.183 mg of H_3BO_3.

Glycerol. Mix 5.000 g in a flask with a ground glass stopper with 50 ml of *water R*, add 0.4 ml of *bromcresol purple RS* and neutralise the liquid with *0.1 mol/l sodium hydroxide VS* until it turns

purple. Then add 1.5 g *sodium periodate R*, close the flask and mix the contents occasionally.
5 minutes after the sodium periodate dissolves, add 1.5 ml *propylene glycol R* and titrate with *0.1 mol/l sodium hydroxide VS* until it turns purple. Correct the determined consumed amount with the result of a blind test.

1 ml of *0.1 mol/l sodium hydroxide VS* is equivalent to 9.209 mg of $C_3H_8O_3$.

SHELF LIFE

6 months when stored in dark glass containers at 15 °C to 25 °C and protected from light.

SOLUTIO JARISCH CUM PARABENIS

CZ 149:2023

Jarisch solution with parabens

DEFINITION

A solution of boric acid (H_3BO_3; M_r 61,83) and glycerol ($C_3H_8O_3$; M_r 92,09) in preservative water.

Content:

- *boric acid:* 1.85 % to 2.15 %;
- *glycerol:* 3.16% to 3.68%.

COMPOSITION AND PROCEDURE

Acidum boricum (*0001*)	20.0 g
Glycerolum 85% (*0497*)	40.0 g
Aqua conservans (*CZ 030*)	940.0 g

Dissolve boric acid in boiling preservative water. After cooling, add 85% glycerol, top up to 1000.0 g with preservative water and filter.

PROPERTIES

Appearance. A clear colourless liquid that turns *blue litmus paper R* red.

IDENTIFICATION TESTS

A. Reduce 5 ml in a porcelain bowl in a water bath, dissolve the rest in 3 ml of *methanol R* and add 0.5 ml of *sulphuric acid R*. When ignited the solution burns with a flame that is green, especially at the edges *(boric acid).*

B. Mix 1 ml with 1 ml of *nitric acid R* and cover the liquid with a layer of 1 ml *potassium dichromate RS;* a purplish blue ring (*glycerol)* forms at the boundary of both layers.

C. Heat 3 ml in a water bath with 1 ml of *Millon's reagent RN;* a red colour appears.

DETERMINATION OF CONTENT

Boric acid. Mix 5.500 g with a solution of 2 g *sorbitol R* in 15 ml of *water R* in pre-neutralised *0.1 mol/l sodium hydroxide VS* using 0.5 ml *thymol blue RS* until it turns green. Titrate with a volumetric solution of *0.1 mol/l sodium hydroxide VS* to the same colour.

1 ml *1 mol/l sodium hydroxide VS* is equivalent to 6.183 mg H_3BO_3.

Glycerol. Mix 5.000 g in a flask with a ground glass stopper with 50 ml of *water R*, add 0.4 ml of *bromcresol purple RS* and neutralise the liquid with *0.1 mol/l sodium hydroxide VS* until it turns purple. Then add 1.5 g *sodium periodate R*, close the flask and mix the contents occasionally.

5 minutes after the sodium periodate dissolves, add 1.5 ml of *propylene glycol R* and titrate with *0.1 mol/l sodium hydroxide VS* until it turns purple. Correct the determined consumed amount with the result of a blind test.
1 ml of *0.1 mol/l sodium hydroxide VS* is equivalent to 9.209 mg of $C_3H_8O_3$.

SHELF LIFE
12 months when stored in dark glass containers at 15 °C to 25 °C and protected from light.

LABELLING
The labelling shall indicate that the product contains antimicrobial preservatives (parabens).

TETRACAINI HYDROCHLORIDI OCULOGUTTAE

CZ 125:2023

Eye drops with tetracaine hydrochloride

DEFINITION

A sterile solution of tetracaine hydrochloride ($C_{15}H_{25}ClN_2O_2$; M_r 300,83) with sodium chloride (NaCl; M_r 58.44) and an antimicrobial preservative.
Content:

- *tetracaine hydrochloride:* 1.90 % to 2.10 %;
- *sodium chloride:* 0.53% to 0.59% NaCl.

COMPOSITION AND PROCEDURE

Tetracaini hydrochloridum (*0057*)	2.00 g
Natrii chloridum (*0193*)	0.56 g
Thiomersalum (*1625*)*	0.002 g
Aqua purificata (*0008*) (sterile)**	to 100.0 g

*In justified cases, a different suitable antimicrobial preservative may be used.

**If needed, it is possible to use Aqua pro iniectione (*0169*).

First, dissolve the thiomersal and then the tetracaine hydrochloride and sodium chloride in 90 g of sterilised purified water (*5.1.1*, steam sterilisation for 15 min at 121 °C) and then dilute the solution with sterilised purified water to 100.0 g. Perform membrane filtration (*5.1.1*) and dispense into suitable sterile containers in a class A clean room.

PROPERTIES

Appearance. A clear colourless liquid.

IDENTIFICATION TESTS

A. Add 0.5 ml of *red fuming nitric acid R* to 0.2 ml and evaporate until dry in a water bath. After cooling, dissolve the rest in 5 ml *acetone R* and add 0.2 ml of *potassium hydroxide* in *ethanol RS;* a purple colour results (*tetracaine*).

B. Colours flame yellow (*sodium*).

C. Add a few drops of *dilute ammonia RS1* to 2 ml and filter the resulting precipitate. Acidify the filtrate with *nitric acid dilute in RS* and add *silver nitrate RS1;* a white curd-like precipitate forms, which after washing with *water R* dissolves easily in *ammonia R (chlorides).*

D. Shake 2 ml with 1 ml of *chloroform R* and 0.1 ml of a freshly prepared solution of *dithizone R*(0.05 g/l) in *chloroform R;* the chloroform layer will turn yellowish orange (*mercury compounds*).

PURITY TESTS

Appearance. The tested preparation is clear *(2.2.1)* and colourless *(2.2.2, Method II).*

pH *(2.2.3).* **5.0 to 6.5.**

Sterility *(2.6.1).* Passes the sterility test.

DETERMINATION OF CONTENT

Tetracaine hydrochloride. To 5.500 g add 0.1 ml of *phenolphthalein RS1*, 10 ml of *water R* and 15 ml of *ether R* and titrate with *0.1 mol/l sodium hydroxide VS* while thoroughly mixing until the water layer turns light red. Correct the determined consumed amount with the result of a blind test. The solution is used to determine sodium chloride.

1 ml of *0.1 mol/l sodium hydroxide VS* is equivalent to 30.08 mg $C_{15}H_{25}ClN_2O_2$.

Sodium chloride. To the titrated solution from the tetracaine hydrochloride determination add 10.0 ml of *sulphuric acid diluted in RS* and titrate with *0.1 mol/l silver nitrate VS* with potentiometric indication of the equivalence point *(2.2.20).* From this consumption, subtract the consumption of *0.1 mol/l sodium hydroxide VS* determined by titration of tetracaine hydrochloride.

1 ml of *0.1 mol/l silver nitrate VS* is equivalent to 5.844 mg of NaCl.

STORAGE

See article *Ocularia (1163).* Protect from light.

SHELF LIFE

3 months when stored in sealed glass containers at 15 °C to 25 °C and protected from light.

LABELLING

See article *Ocularia (1163),* paragraph *Oculoguttae.*

The label shall indicate the name of the antimicrobial preservative used.