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

Betaxolol Eye Drops, Suspension

General Notices

Action and use

Beta-adrenoceptor antagonist.

DEFINITION

Betaxolol Eye Drops, Suspension are a sterile suspension of Betaxolol Hydrochloride in Purified Water containing suitabl binding and suspending agents.

The eye drops comply with the requirements stated under Eye Preparations and with the following requirements.

Content of betaxolol, $C_{18}H_{29}NO_3$

90.0 to 110.0% of the stated amount.

The eye drops should be shaken vigorously before carrying out the following tests.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Dilute the eye drops with *water* to produce a solution containing the equivalent of 0.1% w/v of betaxolol. Shake 1 mL of the solution with 4 mL of *water*, 0.1 mL of 13.5M *ammonia* and 2 mL of *chloroform*, centrifuge and use the chloroform layer.
(2) Prepare solution (2) in the same manner as solution (1) but using a 0.1% w/v solution of *betaxolol hydrochloride BPCRS* in place of the eye drops.
(3) Equal volumes of solution (1) and solution (2).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel* (Merck silica gel 60 plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with a solution prepared by dissolving 5 g of *iodine* and 10 g of *potassium iodide* in sufficient *water* to produce 100 mL and mixing 20 mL of the resulting solution with 30 mL of *water* and 50 mL of 2 M *acetic acid*. Examine the plate immediately; spots due to betaxolol appear brown.

MOBILE PHASE

30 volumes of a solution prepared by diluting 1 volume of 13.5M *ammonia* to 50 volumes with *propan-2-ol* immediately before use and 70 volumes of *chloroform*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) shows a single, compact spot.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (1) shows a principal peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Particle size

Examine using an automated light obscuration instrument such as that described in Appendix XIII A. Not less than 99.5% of the particles are less than 25 µm, not less than 99.95% are less than 50 µm and none exceeds 75 µm.

Acidity or alkalinity

pH, 6.5 to 7.5, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) Dilute a suitable volume of the eye drops with sufficient of the mobile phase to produce a solution containing the equivalent of 0.02% w/v of betaxolol, centrifuge and use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 100 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Spherisorb ODS-2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Dissolve 3 g of *sodium dodecyl sulfate* in 450 mL of the following solution. 45 volumes of a buffer solution prepared as described below and 55 volumes of *acetonitrile*. To prepare the buffer solution add 5 mL of *orthophosphoric acid* to 990 m of *water*, adjust the pH to 3.0 with 2M *ammonia* and add sufficient *water* to produce 1000 mL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2), the *column efficiency*, determined on the pea due to betaxolol is at least 8000 *theoretical plates* per metre and the *symmetry factor* of the principal peak is not more tha 2.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of not more than one *secondary peak* is greater than 0.3 times the area of the principal peak in the chromatogra obtained with solution (2) (0.3%).

Bound betaxolol

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute a weighed quantity of the eye drops with sufficient of the mobile phase to produce a solution containing the equivalent of 0.01 % w/v betaxolol. Mix with the aid of ultrasound for 15 minutes and allow to cool. Centrifuge at a speed 2000 revolutions per minute for 10 minutes and use the supernatant liquid.
(2) Centrifuge the eye drops at a speed of 25,000 revolutions per minute for 30 minutes and dilute a weighed quantity o the supernatant liquid with sufficient of the mobile phase to produce a solution expected to contain the equivalent of 0.01% w/v of betaxolol.
(3) 0.012% w/v *betaxolol hydrochloride BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (Spherisorb ODS-2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

45 volumes of *acetonitrile* and 55 volumes of *water* containing 0.71% w/v *anhydrous disodium hydrogen orthophosphate* and 0.91% w/v of *dimethylamine hydrochloride*, adjusted to pH 3.0 with *orthophosphoric acid*.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the eye drops, Appendix V G, and calculate the content of $C_{18}H_{29}O_3$, weight in volume, in solutions (1) and (2) using the declared content of $C_{18}H_{29}O_3$ in *betaxolol hydrochloride BPCRS*. Calculate the content of bound betaxolol from the difference between the contents of betaxolol found in solutions (1) and (2).

LIMITS

45.0 to 65.0% of the stated content of betaxolol

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase.

(1) Dilute a weighed quantity of the eye drops to produce a solution containing the equivalent of 0.01% w/v of betaxolol. Mix thoroughly and centrifuge.
(2) 0.012% w/v of *betaxolol hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Bound betaxolol may be used.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the eye drops, Appendix V G, and calculate the content of $C_{18}H_{29}NO_3$, weight in volume, using the declared content of $C_{18}H_{29}NO_3$ in *betaxolol hydrochloride BPCRS*.

STORAGE

Betaxolol Eye Drops, Suspension should be protected from light.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of betaxolol.