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

Glycopyrronium Bromide Cream

General Notices

NOTE: This monograph has been developed to cover unlicensed formulations.

Action and use

Anticholinergic; used in the treatment of hyperhidrosis.

DEFINITION

Glycopyrronium Bromide Cream contains Glycopyrronium Bromide in a suitable basis.

The cream complies with the requirements stated under Topical Semi-solid Preparations and with the following requirements. Where appropriate, the cream also complies with the requirements stated under Unlicensed Medicines.

Content of glycopyrronium bromide, $C_{19}H_{28}BrNO_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Place a quantity of the cream containing 5 mg of Glycopyrronium Bromide into a ground-glass-stoppered centrifuge tube, add 50 mL of *water*, heat at 60° for 15 minutes and allow to cool. Shake the cooled solution for 15 minutes and then centrifuge at 3000 rpm for 15 minutes. Carefully remove the lower layer using a pipette and filter using a 0.45-µm PTFE syringe filter.
(2) 0.01% w/v of *glycopyrronium bromide BPCRS* in *water*.
(3) Equal volumes of solutions (1) and (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 30 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air, spray with a solution containing 10 volumes of *potassium iodide solution*, 10 volumes of *potassium iodobismuthate solution*, 12 volumes of *glacial acetic acid* and 67 volumes of *water*.

MOBILE PHASE

20 volumes of *glacial acetic acid*, 20 volumes of *water* and 60 volumes of *butan-1-ol*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) appears as 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 retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

TESTS

Related substances

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

(1) Place a quantity of the cream containing 5 mg of Glycopyrronium Bromide into a ground-glass-stoppered centrifuge tube, add 20 mL of mobile phase A, heat at 60° for 10 minutes and allow to cool. Mix the cooled solution using a vortex mixer for 1 minute and then centrifuge at 3000 rpm for 15 minutes. Carefully remove the lower layer using a pipette and filter using a 0.45-µm PTFE syringe filter.
(2) Dilute 1 volume of solution (1) to 100 volumes; further dilute 1 volume to 10 volumes.
(3) 0.05% w/v of *glycopyrronium for peak identification EPCRS* (contains impurities E and I).
(4) Dilute a mixture containing 1 volume of a 0.1% w/v solution of *benzaldehyde* (impurity F) and 2 volumes of a 0.05% w/v solution of *glycopyrronium bromide BPCRS* to 100 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Inertsil ODS-3 is suitable).
(b) Use gradient 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 215 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A Dissolve 0.25 g of *sodium heptanesulfonate* in 615 mL of a 0.163% w/v solution of *anhydrous sodium sulfate*; add 3 mL of a 0.515% w/v solution of *sulfuric acid*, 150 mL of *methanol R2* and 235 mL of *acetonitrile R1*.

Mobile phase B *acetonitrile R1*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-20	100	0	isocratic
20-30	100 → 50	0 → 50	linear gradient
30-45	50	50	isocratic
45-47	50 → 100	50 → 0	linear gradient
47-55	100	0	re-equilibration

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to glycopyrronium (retention time about 11 minutes) are: impurity E, about 0.7; impurity F (benzaldehyde), about 0.8; impurity I, about 2.3.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity F and glycopyrronium is at least 5.0.

LIMITS

Use the chromatogram obtained with solution (3) and the chromatogram supplied with *glycopyrronium for peak identification EPCRS* to identify the peaks due to impurities E and I.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity I is not greater than three times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any peak corresponding to impurity E is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.1%);

the sum of the areas of all the *secondary peaks* is not greater than five times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (2) (0.1%) and any peak due to bromide.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase A as described under Related substances.

(1) Place a weighed quantity of the cream containing 2 mg of Glycopyrronium Bromide into a ground-glass-stoppered centrifuge tube, add 20 mL of mobile phase A, heat at 60° for 10 minutes and allow to cool. Mix the cooled solution using a vortex mixer for 1 minute and then centrifuge at 3000 rpm for 15 minutes. Carefully remove the lower layer using a pipette and filter using a 0.45-µm PTFE syringe filter.
(2) 0.01% w/v of *glycopyrronium bromide BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used but using isocratic elution and mobile phase A.

SYSTEM SUITABILITY

The Assay is not valid unless the *symmetry factor* of the principal peak in the chromatogram obtained with solution (2) is between 0.8 and 2.0.

DETERMINATION OF CONTENT

Calculate the content of $C_{19}H_{28}BrNO_3$ in the cream using the declared content of $C_{19}H_{28}BrNO_3$ in *glycopyrronium bromide BPCRS*.

IMPURITIES

With the exception of impurity N, the impurities limited by the requirements of this monograph include those listed under Glycopyrronium Bromide.