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

Terbutaline Tablets

General Notices

Action and use

Beta$_2$-adrenoceptor agonist; bronchodilator.

DEFINITION

Terbutaline Tablets contain Terbutaline Sulfate.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of terbutaline sulfate $(C_{12}H_{19}NO_3)_2,H_2SO_4$

90.0 to 110.0% of the stated amount.

IDENTIFICATION

A. Shake a quantity of the powdered tablets containing 20 mg of Terbutaline Sulfate with 50 mL of 0.1M *sodium hydroxide* for 10 minutes, dilute to 100 mL with 0.1M *sodium hydroxide* and filter. Dilute 20 mL of the filtrate to 50 mL with 0.1M *sodium hydroxide*. The *light absorption* of the resulting solution, Appendix II B, in the range 230 to 350 nm exhibits a maximum only at 296 nm.
B. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Shake a quantity of the powdered tablets containing 10 mg of Terbutaline Sulfate with 4 mL of a mixture of equal volumes of *ethanol* (*96%*) and *water* for 10 minutes, centrifuge and use the clear solution.
(2) 0.25% w/v of *terbutaline sulfate 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 2 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air, allow to stand for a few minutes in an atmosphere saturated with *diethylamine* and spray with *diazotised nitroaniline solution*.

MOBILE PHASE

5 volumes of *formic acid*, 25 volumes of *cyclohexane* and 65 volumes of *propan-2-ol*.

CONFIRMATION

The spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2) and the principal spot in the chromatogram obtained with solution (3) appears as a single compact spot.

Related substances

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

(1) Shake a quantity of the powdered tablets containing 75 mg of Terbutaline Sulfate with 35 mL of the mobile phase for 15 minutes, add sufficient of the mobile phase to produce 50 mL, mix and filter (Whatman GF/C paper is suitable).
(2) Dilute 1 volume of solution (1) to 50 volumes with the mobile phase and further dilute 1 volume to 10 volumes with the mobile phase.
(3) 0.00045% w/v of *terbutaline sulfate BPCRS* and 0.00015% w/v of *terbutaline impurity C BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil BDS C18 5µm 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 276 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1) allow the chromatography to proceed for 6 times the retention time of the principal peak.

MOBILE PHASE

Prepare a 0.05M solution of *ammonium formate* by dissolving 3.15 g of *ammonium formate* in 980 mL of *water*, adjust the pH to 3.0 by the addition of about 8 mL of *anhydrous formic acid* and add sufficient *water* to produce 1000 mL. Dissolve 4.23 g of *sodium hexanesulfonate* in 770 mL of the ammonium formate solution and add 230 mL of *methanol*.

When the chromatograms are recorded under the prescribed conditions the retention times are about 9 minutes for terbutaline impurity C and about 11 minutes for terbutaline sulfate.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution factor* between the peaks due to terbutaline sulfate and terbutaline impurity C is at least 2.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to terbutaline impurity C is not greater than twice the area of the peak due to terbutaline impurity C in the chromatogram obtained with solution (3) (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) (0.2%);

the sum of the areas of any such peaks is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (0.4%).

Disregard any peaks with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with solution (2) (0.02%) and any peaks with a retention time of less than 2.5 minutes.

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Shake a quantity of the powdered tablets containing 15 mg of Terbutaline Sulfate with 20 mL of 0.05M *sulfuric acid* for 15 minutes, add 1.6 mL of 1.5M *sodium acetate* and sufficient *water* to produce 25 mL and filter (Whatman GF/C paper is suitable).
(2) Dissolve 30 mg of *terbutaline sulfate BPCRS* in 40 mL of 0.05M *sulfuric acid*, add 3.2 mL of 1.5M *sodium acetate* and add sufficient *water* to produce 50 mL.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the content of $(C_{12}H_{19}NO_3)_2,H_2SO_4$ in the tablets from the chromatograms obtained and using the declared content of $(C_{12}H_{19}NO_3)_2,H_2SO_4$ in *terbutaline sulfate BPCRS*.