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

Alverine Capsules

General Notices

Action and use

Smooth muscle relaxant; antispasmodic.

DEFINITION

Alverine Capsules contain Alverine Citrate.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of alverine citrate, $C_{20}H_{27}N,C_6H_8O_7$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the contents of the capsules containing 0.12 g of Alverine Citrate with 5 mL of *methanol* for 5 minutes, filter through a 0.45-µm PTFE filter, evaporate the filtrate to dryness under a stream of nitrogen using a warm water bath and dry the residue for 1 hour at 50° under vacuum. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of alverine citrate (*RS 409*).

TESTS

Dissolution

Comply with the requirements for Monographs of the British Pharmacopoeia in the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

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

(1) After 45 minutes withdraw a 20-mL sample of the medium and filter through a 0.45-µm filter, discarding the first 10 mL of the filtrate. Dilute, if necessary, with 0.1M *hydrochloric acid* to produce a solution expected to contain about 0.006% w/v of Alverine Citrate.
(2) 0.006% w/v of *alverine citrate BPCRS* in 0.1M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

DETERMINATION OF CONTENT

Calculate the total content of alverine citrate, $C_{20}H_{27}N,C_6H_8O_7$, in the medium from the chromatograms obtained and using the declared content of $C_{20}H_{27}N,C_6H_8O_7$ in *alverine citrate BPCRS*.

Related substances

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

(1) Add 80 mL of *methanol* to a quantity of the mixed contents of the capsules containing 0.6 g of Alverine Citrate. Mix with the aid of ultrasound for 1 hour, allow to cool to room temperature, add sufficient *methanol* to produce 100 mL, mix and filter (Whatman GF/C is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with *methanol* and dilute 1 volume of the resulting solution to 5 volumes with *methanol*.
(3) *alverine citrate impurity standard solution BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil BDS C18 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.
(g) Allow the chromatography to proceed for 4 times the retention time of alverine.

MOBILE PHASE

0.01M *sodium dodecyl sulfate* in a mixture of 45 volumes of *water* and 55 volumes of *acetonitrile*, adjusting the pH of the mixture to 3.0 with *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) closely resembles the reference chromatogram supplied with *alverine citrate impurity standard solution BPCRS*.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to alverine citrate impurity A, is not greater than the area of the corresponding peak in the chromatogram obtained with solution (3) (0.2%);

the area of any peak corresponding to alverine citrate impurity C is not greater than the area of the corresponding peak in the chromatogram obtained with solution (3) (0.5%);

the area of any peak corresponding to alverine citrate impurity D is not greater than the area of the corresponding peak in the chromatogram obtained with solution (3) (0.5%);

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 all *secondary peaks* is not greater than 7 times the area of the principal peak in the chromatogram obtained with solution (2) (1.4%).

Disregard any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

(1) To a quantity of the mixed contents of the capsules containing 0.6 g Alverine Citrate add 100 mL of *methanol*, mix with the aid of ultrasound for 1 hour and add sufficient *methanol* to produce 500 mL. Stir vigorously for 10 minutes and filter (Cellulose nitrate filter 0.45 µm is suitable). Dilute 1 volume of the filtrate to 2 volumes with *water*.
(2) Dilute 1 volume of a 0.6% w/v solution of *alverine citrate BPCRS* in *methanol* to 10 volumes with *water*.
(3) *alverine citrate impurity standard solution BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained closely resembles the reference chromatogram supplied with *alverine citrate impurity standard solution BPCRS*.

DETERMINATION OF CONTENT

Calculate the content of $C_{20}H_{27}N,C_6H_8O_7$ in the capsules using the declared content of $C_{20}H_{27}N,C_6H_8O_7$ in *alverine citrate BPCRS*.

STORAGE

Alverine Capsules should be stored in a dry place and not above 25°.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, C and D listed under Alverine Citrate.