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

Acamprosate Gastro-resistant Tablets

General Notices

Gastro-resistant Acamprosate Tablets

Action and use

Treatment of alcoholism.

DEFINITION

Acamprosate Gastro-resistant Tablets contain Acamprosate Calcium. They are covered with a gastro-resistant coating or prepared from granules or particles covered with a gastro-resistant coating.

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

Content of acamprosate calcium, $C_{10}H_{20}CaN_2O_8S_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. 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).
B. The powdered tablets yield reaction A characteristic of *calcium salts*, Appendix VI.

TESTS

Dissolution

Carry out the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

First stage

(a) Use Apparatus 1, rotating the basket at 180 revolutions per minute.
(b) Use 900 mL of 0.1M *hydrochloric acid*, at a temperature of 37°, as the medium.

PROCEDURE

(1) After 2 hours, withdraw a 20-mL sample of the medium, filter through a 0.45-µm filter and dilute, if necessary, to produce a solution expected to contain 0.037% w/v of Acamprosate Calcium.
(2) 0.00185% w/v of *acamprosate calcium BPCRS* in 0.1M *hydrochloric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm x 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (4 µm) (Synergi Hydro RP is suitable).
(b) Use isocratic elution using 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 205 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

To 850 mL of a solution containing 140.5 mg of *sodium perchlorate* and 170.95 mg of *tetrabutylammonium perchlorate* add 100 mL of *methanol R2* and dilute to 1000 mL with *water*.

DETERMINATION OF CONTENT

Calculate the total content of $C_{10}H_{20}CaN_2O_8S_2$ in the medium using the declared content of $C_{10}H_{20}CaN_2O_8S_2$in *acamprosate calcium BPCRS*.

LIMITS

The amount of Acamprosate Calcium released is not more than 5% of the stated amount.

Final stage

Buffer pH 6.8 Add 150 mL of 2M *sodium hydroxide* in sufficient 0.1M *citric acid* to produce 1000 mL, adjust the pH to 6.8, if necessary, with 0.5M *citric acid*.

(a) Use Apparatus 1, rotating the basket at 180 revolutions per minute.
(b) Replace the 0.1M *hydrochloric acid* in the vessel with 900 mL of buffer pH 6.8, previously held and maintained at 37°.

PROCEDURE

(1) After 2 hours, withdraw a 20-mL sample of the medium, filter through a 0.45-µm filter and dilute, if necessary, to produce a solution expected to contain 0.037% w/v of Acamprosate Calcium.
(2) 0.037% w/v of *acamprosate calcium BPCRS* in buffer pH 6.8.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under the first stage may be used.

DETERMINATION OF CONTENT

Calculate the total content of $C_{10}H_{20}CaN_2O_8S_2$ in the medium using the declared content of $C_{10}H_{20}CaN_2O_8S_2$in *acamprosate calcium BPCRS*.

LIMITS

The amount of Acamprosate Calcium released is not less than 75% (Q) of the stated amount.

Impurity A (homotaurine)

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

(1) Remove the tablet coating from 5 tablets by stirring with three 50-mL quantities of *acetone*. Allow the cores to dry at room temperature. Stir a quantity of the powdered tablets containing 333 mg of Acamprosate Calcium with 50 mL of *borate buffer solution pH 10.4* for 10 minutes and filter through a 0.45-µm filter. Dilute 3 mL of this solution to 20 mL with *borate buffer solution pH 10.4*. Place 3.0 mL of the solution obtained in a 25-mL ground-glass-stoppered tube. Add 0.15 mL of a freshly prepared 0.5% w/v solution of *fluorescamine* in *acetonitrile*. Shake immediately and vigorously for 30 seconds. Place in a water-bath at 50° for 30 min. Cool under a stream of cold water. Filter the supernatant liquid through a suitable filter.

(2) Dissolve 10 mg of *acamprosate impurity A EPCRS* in *borate buffer solution pH 10.4* and dilute to 100.0 mL with the same solvent. Dilute 1.0 mL of the solution to 100.0 mL *with* *borate buffer solution pH 10.4*. Treat 3.0 mL of this solution in the same way as solution (1).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) with a stainless steel pre-column (7.5 cm × 4.6 mm) both packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS is suitable).
(b) Use isocratic elution using 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 261 nm.
(f) Inject 20 µL of each solution.
(g) Allow the chromatography to proceed for 6 times the retention time of impurity A.

MOBILE PHASE

10 volumes of *acetonitrile*, 10 mL of *methanol* and 80 volumes of *0.1M phosphate buffer solution pH 6.5*.

When the chromatograms are recorded under the prescribed conditions the retention time of fluorescamine is about 4 minutes and impurity A is about 8 minutes. Acamprosate is not detected.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

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

(1) Weigh and powder 20 tablets. Shake, with the aid of ultrasound, a quantity of the powdered tablets containing 333 mg of Acamprosate Calcium with 150 mL of mobile phase, dilute to 200 mL and filter through a 0.45-µm filter. Dilute 1 volume of the resulting solution to 5 volumes.
(2) 0.033% w/v of *acamprosate calcium BPCRS* in mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) with a stainless steel pre-column (7.5 cm × 4.6 mm) both packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS2 is suitable).
(b) Use isocratic elution using 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 205 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

To 850 mL of a solution containing 140.5 mg of *sodium perchlorate* and 342 mg of *tetrabutylammonium perchlorate* add 100 mL of *methanol R2* and dilute to 1000 mL with *water*.

SYSTEM SUITABILITY

Inject solution (2) five times. The test is not valid unless the relative standard deviation of the area of the principal peak is at most 2.0%.

DETERMINATION OF CONTENT

Calculate the content of $C_{10}H_{20}CaN_2O_8S_2$ in the tablets from the chromatogram obtained and using the declared content of $C_{10}H_{20}CaN_2O_8S_2$ in *acamprosate calcium BPCRS*.