Acamprosate Gastro-resistant Tablets

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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Acamprosate Gastro-resistant Tablets

Acamprosate Calcium Gastro-resistant Tablets

Acamprosate Gastro-resistant Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of acamprosate calcium, $C_{10}H_{20}CaN_2O_8S_2$.

Usual strengths. 333 mg; 666 mg.

Identification

A. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

B. The powdered tablets give reaction (A) of calcium salts (2.3.1).

Tests

Dissolution (2.5.2).
A. Apparatus No. 1 (Basket),
Medium. 900 ml of *0.1 M hydrochloric acid*,
Speed and time. 180 rpm and 120 minutes.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate, if necessary, with the dissolution medium to obtain a solution containing 0.037 per cent w/v of Acamprosate Calcium.

Reference solution. Dissolve a weighed quantity of *acamprosate calcium IPRS* in the dissolution medium and dilute with the dissolution medium to obtain a solution having a known concentration similar to the test solution.

Chromatographic system
- a stainless steel column 10 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (4 µm), (Such as Synergi Hydro RP),
- mobile phase: a mixture of 90 volumes of a buffer solution prepared by dissolving 156 mg of *sodium perchlorate*, and 190 mg of *tetrabutylammonium perchlorate* in 1000 ml of *water* and 10 volumes of *methanol*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 205 nm,
- injection volume: 20 µl.

Inject the reference solution and the test solution.

Calculate the content of $C_{10}H_{20}CaN_2O_8S_2$ in the medium.

Complies with the acceptance criteria given under acid stage.

B. Apparatus No. 1 (Basket),
Medium.900 ml of buffer pH 6.8 prepared by diluting 150 ml of *2 M sodium hydroxide* to 1000 ml with *0.1 M citric acid*, adjusted to pH 6.8 with *0.5 M citric acid*,

Speed and time.180 rpm and 60 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate, if necessary, with the dissolution medium to obtain a solution containing 0.037 per cent w/v of Acamprosate Calcium.

Reference solution. A0.037 per cent w/v solution of *acamprosate calcium IPRS* in the dissolution medium.

- Use the chromatographic system as described under in test A.

Inject the reference solution and the test solution.

Calculate the content of $C_{10}H_{20}CaN_2O_8S_2$ in the medium.

Q. Not less than 75 per cent of the stated amount of $C_{10}H_{20}CaN_2O_8S_2$.

Acamprosate impurity A (Homotaurine). Determine by liquid chromatography (2.4.14).

Test solution. Remove the tablet coating of 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 0.333 g of Acamprosate Calcium in *borate buffer solution pH 10.4* for 10 minutes and dilute to 50.0 ml with *borate buffer solution pH 10.4*, filter. Dilute 3.0 ml of the filtrate to 20.0 ml with *borate buffer solution pH 10.4*. Transfer 3.0 ml of the solution to a 25 ml ground-glass-stoppered tube, add 0.15 ml of a freshly prepared 0.5 per cent w/v solution of *fluorescamine* in *acetonitrile*. Shake immediately and vigorously for 30 seconds. Place in a water-bath at 50° for 30 minutes. Cool under a stream of cold water. filter.

Reference solution. A 0.0001 per cent w/v solution of *acamprosate impurity A IPRS* (3-Amino-1-propanesulphonic acid) in *borate buffer solution pH 10.4*. Treat 3.0 ml of the solution in the same way as the test solution.

Chromatographic system

- pre-column: a stainless steel column 7.5 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5µm),
- column: a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5µm) (Such as Hypersil ODS)
- mobile phase: 10 volumes of *acetonitrile*, 10 volumes of *methanol* and 80 volumes of *0.1 M phosphate buffer pH 6.5*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 261 nm,
- injection volume: 20 µl.

The relative retention time with reference to acamprosate impurity A, for fluorescamine is about 4 minutes. *[NOTE – Acamprosate is not detected]*.

Inject the reference solution and the test solution. Run the chromatogram 6 times the retention time of acamprosate impurity A. In the chromatogram obtained with the test solution, the area of any peak corresponding to acamprosate impurity A is not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.1 per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Weigh and powder 20 tablets. Disperse a quantity of powder containing 0.333 g of Acamprosate Calcium in the mobile phase, with the aid of ultrasound and dilute to 200.0 ml with the mobile phase. Dilute 5.0 ml of the solution to 25.0 ml with the mobile phase, filter.

Reference solution. A 0.033 per cent w/v solution of *acamprosate calcium IPRS* in the mobile phase.

Chromatographic system

- pre-column: a stainless steel column 7.5 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5µm),
- column: a stainless steel column 10 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5µm) (Such as Hypersil ODS 2),
- mobile phase: a mixture of 90 volumes of a buffer solution prepared by dissolving 156 mg of *sodium perchlorate* and 380 mg of *tetrabutylammonium perchlorate* in 1000 ml of *water* and 10 volumes of *methanol,*
- flow rate: 1 ml per minute,
- spectrophotometer set at 205 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{10}H_{20}CaN_2O_8S_2$.in the tablets.

Storage. Store protected from light and moisture, at a temperature not exceeding 30º.