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Pantoprazole Gastro-resistant Tablets

General Notices

Gastro-resistant Pantoprazole Tablets

Action and use

Proton pump inhibitor; treatment of peptic ulcer disease.

DEFINITION

Pantoprazole Gastro-resistant Tablets contain Pantoprazole Sodium Sesquihydrate. 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 pantoprazole, $C_{16}H_{15}F_2N_3O_4S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the powdered tablets containing the equivalent of 50 mg of pantoprazole with 10 mL of *acetone*, filter (Whatman GF/C is suitable) and evaporate to dryness. Dry the residue at 60° for 30 minutes. The *infrared absorption spectrum* Appendix II A, is concordant with the reference spectrum of pantoprazole sodium *(RS 488)*.

TESTS

Dissolution

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

First stage (pH 4.5)

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 100 revolutions per minute.
(b) Use as the medium 700 mL of *0.05M phosphate buffer solution pH 4.5*.

PROCEDURE

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

(1) After 45 minutes, withdraw a sample of the medium, and filter the aliquot (0.45-µm PVDF is suitable). Dilute 1 volume of the filtrate to 5 volumes with *water*, and further dilute, if necessary, with sufficient *water* to produce a solution expected

to contain about 0.00057% w/v of pantoprazole. Proceed immediately to the final stage.
(2) 0.0006% w/v of *pantoprazole sodium BPCRS* in *water*.
(3) 0.0018% w/v of *pantoprazole sodium BPCRS* and 0.0002% w/v of *pantoprazole impurity A BPCRS* in *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4 mm) 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 an autosampler temperature of 5°.
(f) Use a detection wavelength of 290 nm.
(g) Inject 50 µL of each solution.

MOBILE PHASE

35 volumes of *acetonitrile* and 65 volumes of 0.01M *dipotassium hydrogen phosphate trihydrate*, previously adjusted to pH 7.0 with a 20% v/v solution of *orthophosphoric acid*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and pantoprazole is at least 1.5.

DETERMINATION OF CONTENT

Calculate the total content of $C_{16}H_{15}F_2N_3O_4S$ in the medium using the declared content of $C_{16}H_{15}F_2N_3O_4S$ in *pantoprazole sodium BPCRS*.

LIMITS

The amount of pantoprazole released is not more than 10% of the stated amount.

Final stage (about pH 6.8)

Mix 1 volume of 10M *sodium hydroxide* with 99 volumes of *0.05M phosphate buffer solution pH 4.5* (solution A).

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 100 revolutions per minute.
(b) Within 5 minutes of completion of the first stage, add to the vessel 200 mL of solution A, previously held and maintained at 37°.

PROCEDURE

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

(1) After 45 minutes, withdraw a sample of the medium, and filter the aliquot (0.45-µm PVDF is suitable). Dilute 1 volume of the filtrate to 5 volumes with *water*, and further dilute, if necessary, with sufficient *water* to produce a solution expected to contain about 0.00044% w/v of pantoprazole.
(2) 0.00047% w/v of *pantoprazole sodium BPCRS* in *water*.
(3) 0.0018% w/v of *pantoprazole sodium BPCRS* and 0.0002% w/v of *pantoprazole impurity A BPCRS* in *water*.

CHROMATOGRAPHIC CONDITIONS

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

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and pantoprazole is at least 1.5.

DETERMINATION OF CONTENT

Calculate the total content of $C_{16}H_{15}F_2N_3O_4S$ in the medium using the declared content of $C_{16}H_{15}F_2N_3O_4S$ in *pantoprazole sodium BPCRS*.

LIMITS

The amount of pantoprazole released is not less than 65% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 40 volumes of mobile phase B and 60 volumes of mobile phase A.

(1) Shake a quantity of whole tablets containing the equivalent of 0.16 g of pantoprazole in 50 mL, mix with the aid of ultrasound and dilute to produce 100 mL. Dilute 5 volumes to 20 volumes.
(2) Dilute 1 volume of solution (1) to 20 volumes. Dilute 1 volume of this solution to 10 volumes.
(3) 0.05% w/v of *pantoprazole for system suitability EPCRS*.
(4) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (12.5 cm × 4 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Kromasil C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use a column temperature of 40°.
(e) Use an autosampler temperature of 5°.
(f) Use a detection wavelength of 290 nm.
(g) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 0.174% w/v solution of *disodium hydrogen orthophosphate*, previously adjusted to pH 7.0 with *orthophosphoric acid*.

Mobile phase B 48 volumes of mobile phase A and 52 volumes of *acetonitrile*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-3	60	40	isocratic
3-43	60→40	40→60	linear gradient
43-48	40→60	60→40	linear gradient
48-55	60	40	re-equilibration

When the chromatograms are recorded under the prescribed conditions the retention times relative to pantoprazole (retention time about 16 minutes) are: impurity C, about 0.4; impurity A, about 0.8; impurity D + F, about 1.3; impurity E, about 2.0 and impurity B, about 2.2.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to pantoprazole and impurity D + F is greater than 3.0.

LIMITS

Identify any peak in the chromatogram obtained with solution (1) due to impurity C using the chromatogram obtained with solution (3) and multiply the area of this peak by a correction factor of 0.6.

In the chromatogram obtained with solution (1):

the area of any peak due to impurity A and impurity D + F (combined peak area) is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.5% of each);

the area of any other *secondary peak* is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

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

Prepare a solution containing equal volumes of *acetonitrile* and 0.001M *sodium hydroxide* (solution B).

(1) Shake 10 tablets with 50 mL of solution B, mix with the aid of ultrasound and dilute to 100 mL with solution B. Centrifuge and dilute the supernatant liquid with solution B to give a solution containing the equivalent of 0.004% w/v of pantoprazole.
(2) 0.0045% w/v of *pantoprazole sodium BPCRS* in solution B.
(3) 0.0045% w/v of *pantoprazole sodium BPCRS* and 0.0005% w/v of *pantoprazole impurity A BPCRS* in solution B.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used with an injection volume of 20 µL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and pantoprazole is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{16}H_{15}F_2N_3O_4S$ in the tablets from the chromatograms obtained and using the declared content of $C_{16}H_{15}F_2N_3O_4S$ in *pantoprazole sodium BPCRS*.

LABELLING

The quantity of the active ingredient is stated in terms of the equivalent amount of pantoprazole.

IMPURITIES

The impurities limited by this monograph include those listed under Pantoprazole Sodium Sesquihydrate.