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

Famotidine Tablets

General Notices

Action and use

Histamine H_2 receptor antagonist; treatment of peptic ulceration.

DEFINITION

Famotidine Tablets contain Famotidine.

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

Content of famotidine, $C_8H_{15}N_7O_2S_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the peak in the chromatogram obtained with solution (2).
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 40 mg of Famotidine with 4 mL of *glacial acetic acid* with the aid of ultrasound, dilute to 10 mL with the same solvent, centrifuge and use the clear supernatant liquid.
(2) 0.4% w/v of *famotidine BPCRS* in *glacial acetic acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}* (Fischer Silica Gel GF plates are suitable).
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air and examine immediately under *ultraviolet light (254 nm)*.

MOBILE PHASE

2 volumes of 13.5M *ammonia*, 20 volumes of *toluene*, 25 volumes of *methanol* and 40 volumes of *ethyl acetate*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds to that in the chromatogram obtained with solution (2).

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 phosphate buffer pH 4.5, at a temperature of 37°, as the medium prepared in the following manner. Dissolve 13.61 g of *potassium dihydrogen orthophosphate* in *water*, adjust the pH of the solution with *orthophosphoric acid* or 1M *potassium hydroxide* as necessary and add sufficient *water* to produce 1000 mL.

PROCEDURE

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

(1) Withdraw a sample of the medium, filter and centrifuge at 2000 revolutions per minute for 20 minutes. Dilute, if necessary, with the dissolution medium to produce a solution expected to contain 0.001% w/v of Famotidine.
(2) 0.001% w/v of *famotidine BPCRS* in the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Inertsil ODS-2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.4 mL per minute.
(d) Use a column temperature of 40°.
(e) Use a detection wavelength of 275 nm.
(f) Inject 50 µL of each solution.

MOBILE PHASE

7 volumes of *acetonitrile* and a mixture of 93 volumes of 0.1M *sodium acetate* containing 0.1% v/v of *triethylamine* the pH adjusted to 6.0 with *glacial acetic acid*.

DETERMINATION OF CONTENT

Calculate the total content of famotidine, $C_8H_{15}N_7O_2S_3$, in the medium using the declared content of $C_8H_{15}N_7O_2S_3$ in *famotidine BPCRS*.

Related substances

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

Solution A: 0.05M *potassium dihydrogen orthophosphate* adjusted to pH 6.0 with 1M *potassium hydroxide*.

(1) Add 200 mL of solution A to a quantity of whole tablets containing 0.2 g of Famotidine, mix with the aid of ultrasound for 5 minutes, add about 200 mL of *methanol*, shake for 60 minutes and add sufficient solution A to produce 500 mL.
(2) Dilute 1 volume of solution (1) to 100 volumes with solution A.
(3) Dilute 1 volume of solution (1) to 10 volumes with solution A and dilute 1 volume of the resulting solution to 50 volumes with solution A.
(4) Add 40 mL of *acetonitrile* to a mixture of 2 mg of each of *famotidine impurity C BPCRS*, *famotidine degradation impurity 1 BPCRS* (famotidine impurity F) and *famotidine impurity D EPCRS* (famotidine degradation impurity 2) mix with the aid of ultrasound for 2 minutes, cool, add 40 mL of *methanol* and sufficient solution A to produce 200 mL. Dilute 1 volume of the resulting solution to 5 volumes with solution A.
(5) Dissolve 8 mg of *famotidine BPCRS* in 15 mL of solution A with the aid of ultrasound, cool and add sufficient solution A to produce 20 mL (solution B); to 1 mL of this solution add 0.05 mL of *hydrogen peroxide solution (10 vol)* (generates famotidine degradation impurity 3).
(6) Dilute 1 volume of solution B with 100 volumes of solution A and further dilute a suitable volume with an equal volume of solution (4).

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Dissolution may be used.

When the chromatograms are recorded under the prescribed conditions, the relative retention(s) with reference to famotidine (retention time about 5 minutes) are: famotidine degradation impurity 3, about 0.4; famotidine impurity F, about 0.6; famotidine impurity C, about 0.7; and famotidine impurity D, about 1.2.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (6):

the *resolution* between the peaks due to famotidine impurity C and famotidine is at least 1.4;

the *resolution* between the peaks due to famotidine and famotidine impurity D is at least 1.4.

If this resolution is not achieved adjust the content of *acetonitrile* or decrease the concentration of sodium acetate in the mobile phase.

LIMITS

In the chromatogram obtained with solution (1):

the areas of any peaks corresponding to impurities C, D, or F are not greater than the areas of the corresponding peaks in the chromatogram obtained with solution (4) (0.5% of each);

the area of any peak corresponding to famotidine degradation impurity 3 is not greater than the area of the peak in the chromatogram obtained with solution (2) (1%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.2%).

the sum of the areas of any *secondary peaks* is not greater than 2.5 times the principal peak in the chromatogram obtained with solution (2) (2.5%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (3) (0.05%).

ASSAY

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

Solution A: 0.05M *potassium dihydrogen orthophosphate* adjusted to pH 6.0 with 1M *potassium hydroxide*.

(1) Add 200 mL of solution A to a quantity of whole tablets containing 0.2 g of Famotidine, mix with the aid of ultrasound for 5 minutes, add about 200 mL of *methanol*, shake for 60 minutes and add sufficient solution A to produce 500 mL. Dilute 1 volume of this solution to 5 volumes with solution A.
(2) Dissolve 8 mg of *famotidine BPCRS* in 4 mL of *methanol*, mix with the aid of ultrasound for 5 minutes and add sufficient solution A to produce 20 mL. Dilute 1 volume of this solution to 5 volumes with solution A.

CHROMATOGRAPHIC CONDITIONS

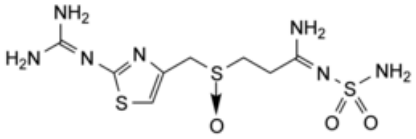
The chromatographic conditions described under Dissolution may be used.

DETERMINATION OF CONTENT

Calculate the content of $C_8H_{15}N_7O_2S_3$ in the tablets using the declared content of $C_8H_{15}N_7O_2S_3$ in *famotidine BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities C, D, and F listed under Famotidine and the following:



3. 3-[2-(Diaminomethyleneamino)-1,3-thiazol-4-ylmethylsulfinyl]-*N*-sulfamoylpropanamidine.