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Famotidine Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-famotidine-tabs-20230728.

DEFINITION
Famotidine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$).

IDENTIFICATION

• **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

Standard solution: 4 mg/mL of USP Famotidine RS in glacial acetic acid

Sample solution: Transfer a portion of finely powdered Tablets, equivalent to about 40 mg of famotidine, to a 10-mL volumetric flask. Dissolve in glacial acetic acid with the aid of sonication, dilute with glacial acetic acid to volume, and centrifuge to get a clear liquid.

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 10 µL

Developing solvent system: Ethyl acetate, methanol, toluene, and ammonium hydroxide (40:25:20:2)

Analysis: Allow the spots to dry, and develop the plate in a paper-lined chromatographic chamber equilibrated with *Developing solvent system* for about 1 h before use. Allow the chromatogram to develop until the solvent front has moved about 15 cm. Remove the plate, air-dry, and examine the plate under short-wavelength UV light.

Acceptance criteria: The principal spot from the *Sample solution* corresponds in appearance and R_F value to that of the *Standard solution*.

• **B.** The retention time of the major peak in the *Sample solution* corresponds to that in the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: Dissolve 13.6 g of sodium acetate trihydrate in 750 mL of water. Add 1 mL of triethylamine, adjust with glacial acetic acid to a pH of 6.0, and dilute with water to 1 L.

Mobile phase: Acetonitrile and *Buffer* (7:93)

Diluent: Dissolve 6.8 g of potassium phosphate, monobasic in 750 mL of water, adjust with 1 M potassium hydroxide to a pH of 6.0, and dilute with water to 1 L.

System suitability stock solution: Transfer 10 mg of famotidine to a 50-mL volumetric flask. Add 1 mL of 0.1 N hydrochloric acid, heat at 80° for 30 min, and cool to room temperature. Add 2 mL of 0.1 N sodium hydroxide, heat at 80° for 30 min, cool to room temperature, and neutralize by adding 1 mL of 0.1 N hydrochloric acid. Dilute with *Diluent* to volume. Transfer 10 mL of this solution to a separate 50-mL volumetric flask containing 5 mg of famotidine dissolved in 8 mL of methanol. Dilute with *Diluent* to volume. Transfer 25 mL of this solution to a 50-mL volumetric flask, and dilute with *Diluent* to volume. [Note—This solution is stable for up to 1 month.]

System suitability solution: Transfer 1–1.5 mL of the *System suitability stock solution* to a suitable container, add 1 drop of hydrogen peroxide solution, and mix well.
[Note—Prepare fresh daily.]

Standard solution: Transfer 10 mg of USP Famotidine RS to a 100-mL volumetric flask, add 20 mL of methanol, and sonicate for 5 min. Dilute with *Diluent* to volume.

Sample solution: Transfer NLT 10 Tablets to a 1-L volumetric flask. Add 200 mL of *Diluent*, and swirl to erode the Tablets. Add 200 mL of methanol, and stir by mechanical means at 300 rpm for 1 h. Dilute with *Diluent* to volume, mix, and filter. Quantitatively dilute a portion of the clear filtrate with *Diluent* to obtain a solution containing about 0.1 mg/mL of famotidine.

Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 15-cm; packing L1

Column temperature: 40°

Flow rate: 1.4 mL/min

Injection size: 50 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

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[NOTE—Identify peaks using *Table 1*.]

Resolution: NLT 1.3 between the famotidine sulfamoyl propanamide and famotidine peaks, and NLT 1.3 between the famotidine and famotidine propanamide peaks, *System suitability solution*

Capacity factor: NLT 2.0 for the famotidine peak, *System suitability solution*

Relative standard deviation: Less than 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Famotidine RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of famotidine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

▲Test 1▲ (RB 1-Aug-2023)

Medium: pH 4.5, 0.1 M phosphate buffer (13.6 g/L of potassium phosphate, monobasic); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Determine the amount of $C_8H_{15}N_7O_2S_3$ dissolved using one of the following methods.

Spectrophotometric method

Standard solution: USP Famotidine RS in *Medium* in a concentration similar to the one expected in the *Sample solution*

Sample solution: Pass a portion of the sample under test through a suitable filter.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 265 nm

Chromatographic method

Buffer, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 0.14 mg/mL of USP Famotidine RS in *Medium*. Dilute this solution with *Medium* to obtain a solution containing (*L*/900) mg/mL, where *L* is the Famotidine Tablet label claim, in mg.

Sample solution: Pass a portion of the solution under test through a suitable filter.

System suitability

Sample: *Standard solution*

Suitability requirements

Capacity factor: Greater than 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the amount of famotidine ($C_8H_{15}N_7O_2S_3$) dissolved:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Famotidine RS in the *Standard solution* (mg/mL)

L = label claim, mg/Tablet

V = volume of *Medium*, 900 mL

Tolerances: NLT 75% (*Q*) of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$) is dissolved.

For Tablets labeled as chewable

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Proceed as directed for either of the methods specified above, except for the following:

Time: 45 min

Tolerances: NLT 80% (*Q*) of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$) is dissolved.

For Tablets labeled as film-coated

Proceed as directed for either of the methods specified above, except for the following:

Time: 30 min

Tolerances: NLT 80% (*Q*) of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$) is dissolved.

▲**Test 2:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: pH 4.5 phosphate buffer (Dissolve 13.6 g of potassium phosphate, monobasic in 1000 mL of water, and adjust with 1 N sodium hydroxide or 1 N hydrochloric acid to a pH of 4.5.); 500 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: 0.02 mg/mL of USP Famotidine RS in *Medium*. Sonicate to dissolve.

[NOTE—It is recommended to maintain the water bath temperature at 10°–15° during sonication.]

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding first few milliliters of filtrate. Dilute with *Medium*, if necessary, to obtain a concentration similar to that of the *Standard solution*.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 265 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount famotidine ($C_8H_{15}N_7O_2S_3$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times D \times (1/L) \times 100$$

A_U = UV absorbance from the *Sample solution*

A_S = UV absorbance from the *Standard solution*

C_S = concentration of USP Famotidine RS in the *Standard solution* (mg/mL)

V = volume of *Medium*, 500 mL

D = dilution factor for the *Sample solution*

L = label claim (mg/Tablet)

Tolerances: NLT 80% (*Q*) of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$) is dissolved.▲ (RB 1-Aug-2023)

• **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩**:** Meet the requirements

IMPURITIES

• **ORGANIC IMPURITIES**

Mobile phase, Diluent, System suitability solution, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak area of each impurity from the *Sample solution*

r_S = peak area of famotidine from the *Standard solution*

C_S = concentration of USP Famotidine RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of famotidine in the *Sample solution* (mg/mL)

F = relative response factor for each impurity (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria NMT (%)
Famotidine sulfoxide[a]	0.4	1.0	1.0
Famotidine propionic acid (famotidine related compound F)[b]	0.7	1.0	0.5
Famotidine sulfamoyl propanamide (famotidine related compound C)[c]	0.8	1.0	0.5
Famotidine	1.0	—	—
Famotidine propanamide (famotidine related compound D)[d]	1.2	1.3	0.5
Total impurities	—	—	1.5

[a] 3-[[2-(Diaminomethyleneamino)thiazol-4-yl]methylsulfinyl]-*N*'-sulfamoylpropanimidamide.

[b] 3-[[2-(Diaminomethyleneamino)thiazol-4-yl]methylthio]propanoic acid.

[c] 3-[[2-(Diaminomethyleneamino)thiazol-4-yl]methylthio]-*N*-sulfamoylpropanamide.

[d] 3-[[2-(Diaminomethyleneamino)thiazol-4-yl]methylthio]propanamide.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Store at controlled room temperature.

Add the following:

▲• **Labeling:** When more than one *Dissolution* test is given, the labeling states the test used only if *Test 1* is not used.▲ (RB 1-Aug-2023)

• **USP Reference Standards** ⟨11⟩

USP Famotidine RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
FAMOTIDINE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

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