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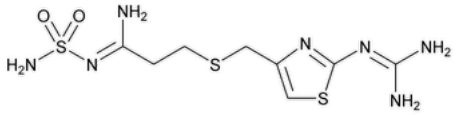
Famotidine



$C_8H_{15}N_7O_2S_3$ 337.45

Propanimidamide, *N'*-(aminosulfonyl)-3-[[[2-[(diaminomethylene)amino]-4-thiazolyl]methyl]thio]-;
[1-Amino-3-[[[2-[(diaminomethylene)amino]-4-thiazolyl]methyl]thio]propylidene]sulfamide;
3-[[2-(Diaminomethyleneamino)thiazol-4-yl]methylthio]-*N'*-sulfamoylpropanimidamide CAS RN®: 76824-35-6; UNII: 5QZO15J2Z8.

DEFINITION

Famotidine contains NLT 98.5% and NMT 101.0% of famotidine ($C_8H_{15}N_7O_2S_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy* 197A, 197K, or 197M▲ (CN 1-May-2020)

ASSAY

• **Procedure**

Sample: Dissolve 250 mg of Famotidine in 80 mL of glacial acetic acid.

Analysis: Titrate with 0.1 N perchloric acid VS (see *Titrimetry* ⟨541⟩), using a suitable anhydrous electrode system. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 16.87 mg of $C_8H_{15}N_7O_2S_3$.

Acceptance criteria: 98.5%–101.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Buffer: 1.882 g/L of sodium 1-hexanesulfonate in water, adjusted with acetic acid to a pH of 3.5

Solution A: Acetonitrile, methanol, and *Buffer* (94:6:900)

Solution B: Acetonitrile

Mobile phase: See *Table 1*. [Note—If necessary, adjust the *Mobile phase* to achieve a retention time of 19–23 min for the famotidine peak and a maximum of 48 min for the famotidine related compound E peak.]

Table 1

Time (min)	Solution A (%)	Solution B (%)	Flow Rate (mL/min)
0	100	0	1
23	96	4	1
27	96	4	2
47	78	22	2
48	100	0	2
54	100	0	1

Standard stock solution: 0.5 mg/mL of USP Famotidine RS in *Solution A*

Standard solution: 0.5 µg/mL of USP Famotidine RS in *Solution A*

System suitability stock solution: 0.25 mg/mL of USP Famotidine Related Compound D RS in methanol

System suitability solution: Transfer 1 mL of the *System suitability stock solution* and 0.5 mL of the *Standard stock solution* into a 100-mL volumetric flask, and dilute with *Solution A* to volume.

Sample solution: 0.5 mg/mL of Famotidine in *Solution A*

Identification solution: 0.5 mg/mL of USP Famotidine RS and 1.5 µg/mL of each of USP Famotidine Related Compound B RS, USP Famotidine Related Compound C RS, USP Famotidine Related Compound D RS, USP Famotidine Related Compound E RS, and USP Famotidine Related Compound F RS in *Solution A*

[NOTE—To address the poor solubility of USP Famotidine Related Compound F RS in *Solution A*, it may be first dissolved in a minimal amount of 0.1 N sodium hydroxide.]

Chromatographic system

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

Mode: LC

Detector: UV 265 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: See *Table 1*.

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 3.5 between famotidine and famotidine related compound D

Analysis

Samples: *Standard solution*, *Sample solution*, and *Identification solution*

Chromatograph the *Identification solution*, and identify the components on the basis of their relative retention times, given in *Table 2*. Calculate the percentage of each impurity in the portion of Famotidine taken:

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

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

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

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

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

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Famotidine	1.0	—	—
Famotidine related compound D[a]	1.1	1.0	0.3
Famotidine related compound C[b]	1.2	0.53	0.3
Famotidine cyanoamidine[c]	1.4	0.71	0.2
Famotidine related compound F[d]	1.5	0.59	0.1
Famotidine amidine[e]	1.6	0.53	0.2
Famotidine related compound B[f]	2.0	0.40	0.3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Famotidine related compound E[g]	2.1	1.0	0.3
Any other individual impurity	—	1.0	0.1
Total impurities	—	—	1.0

[a] Famotidine propanamide.

[b] Famotidine sulfamoyl propanamide.

[c] *N*-Cyano-3-[[2-(diaminomethyleneamino)thiazol-4-yl]methylthio]propanimidamide.

[d] Famotidine propionic acid.

[e] 3-[[2-(Diaminomethyleneamino)thiazol-4-yl]methylthio]propanimidamide.

[f] Famotidine dimer.

[g] Famotidine disulfide.

SPECIFIC TESTS

• **Loss on Drying ⟨731⟩**

Analysis: Dry a sample at a pressure not exceeding 5 mm of mercury at 80° for 5 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

• **USP Reference Standards ⟨11⟩**

USP Famotidine RS

USP Famotidine Related Compound B RS

3,5-Bis[2-[[2-[(diaminomethylene)amino]thiazol-4-yl]methylthio]ethyl]-4*H*-1,2,4,6-thiatriazine 1,1-dioxide.

$C_{16}H_{23}N_{11}O_2S_5$ 561.73

USP Famotidine Related Compound C RS

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

$C_8H_{15}ClN_6O_3S_3$ 374.88

USP Famotidine Related Compound D RS

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

$C_8H_{13}N_5OS_2$ 259.35

USP Famotidine Related Compound E RS

2,2'-[4,4'-Disulfanediylbis(methylene)bis(thiazole-4,2-diyl)]diguanidine.

$C_{10}H_{14}N_8S_4$ 374.53

USP Famotidine Related Compound F RS

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

$C_8H_{12}N_4O_2S_2$ 260.34

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

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

Chromatographic Database Information: Chromatographic Database

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