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Famotidine Injection

DEFINITION

Famotidine Injection is a sterile, concentrated solution of Famotidine. It contains NLT 90.0% and NMT 110.0% of the labeled amount of famotidine ($C_8H_{15}N_7O_2S_3$). It may contain suitable preservatives.

IDENTIFICATION

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

ASSAY

• **Procedure**

Buffer: 13.8 g/L of monobasic sodium phosphate

Mobile phase: Methanol, water, and *Buffer* (5:32:3). Adjust with 1 N sodium hydroxide to a pH of 5.3.

Diluent: Dissolve 1.36 g of monobasic potassium phosphate in 800 mL of water, adjust with 1 N sodium hydroxide to a pH of 7.0, and dilute with water to 1 L.

Standard solution

If benzyl alcohol is present: 0.1 mg/mL of USP Famotidine RS and 0.09 mg/mL of USP Benzyl Alcohol RS in *Diluent*

If benzyl alcohol is not present: 0.1 mg/mL of USP Famotidine RS in *Diluent*

Sample solution: Transfer a volume of Injection, equivalent to 20 mg of famotidine based on the label claim, to a 200-mL volumetric flask, and dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 5-µm packing L3

Flow rate: 1 mL/min

Injection size: 30 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0% for the famotidine peak

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 Injection taken:

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

r_U = peak response of famotidine 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 = nominal concentration of famotidine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

OTHER COMPONENTS

• **Content of Benzyl Alcohol** (if present)

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

System suitability stock solution: Proceed as directed in the *Organic Impurities* test.

System suitability solution: Transfer 25 mL of *System suitability stock solution* to a 50-mL volumetric flask. Add 1 drop (approximately 20 mg) of USP Benzyl Alcohol RS, and dilute with *Diluent* to volume.

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.3 between adjacent peaks of benzyl alcohol and famotidine propionic acid; the benzyl alcohol peak is resolved from the solvent front, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benzyl alcohol in the portion of Injection taken:

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

r_U = peak area of benzyl alcohol from the *Sample solution*

r_S = peak area of benzyl alcohol from the *Standard solution*

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

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

Acceptance criteria: The content of benzyl alcohol meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩*, Specific Tests, Vehicles and added substances*.

IMPURITIES

• **Organic Impurities**

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

System suitability stock solution: Transfer 10 mg of USP Famotidine RS to a 50-mL volumetric flask. Add 1 mL of 0.1 N hydrochloric acid. Heat at 80° for 30 min. Allow to cool, add 2 mL of 0.1 N sodium hydroxide, and heat at 80° for an additional 30 min. Allow to cool, and neutralize by adding 1 mL of 0.1 N hydrochloric acid. Dilute with *Diluent* to volume (*Solution A*). Transfer 5 mg of USP Famotidine RS to a separate 50-mL volumetric flask, add 8 mL of methanol, and sonicate to dissolve. Add 10 mL of *Solution A*, and dilute with *Diluent* to volume.

System suitability solution

If benzyl alcohol is present: Transfer 25 mL of *System suitability stock solution* to a 50-mL volumetric flask. Add 1 drop (approximately 20 mg) of USP Benzyl Alcohol RS, and dilute with *Diluent* to volume.

If benzyl alcohol is not present: Transfer 25 mL of *System suitability stock solution* to a 50-mL volumetric flask, and dilute with *Diluent* to volume.

System suitability

Sample: *System suitability solution*

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.3 between adjacent peaks of famotidine propionic acid, famotidine sulfamoyl propanamide, famotidine, and famotidine propanamide for each pair of peaks

Analysis

Sample: *Sample solution*

Calculate the percentage of the total of famotidine propionic acid, famotidine sulfamoyl propanamide, and famotidine propanamide in the portion of Injection taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = sum of the peak areas for famotidine propionic acid, famotidine sulfamoyl propanamide, and famotidine propanamide from the *Sample solution*

r_T = sum of the peak areas for famotidine, famotidine propionic acid, famotidine sulfamoyl propanamide, and famotidine propanamide from the *Sample solution*

Acceptance criteria

Total impurities: NMT 5.0%

Table 1

Name	Relative Retention Time
Benzyl alcohol (if present)	0.4
Famotidine propionic acid (famotidine related compound F)[a]	0.7
Famotidine sulfamoyl propanamide (famotidine related compound C)[b]	0.8
Famotidine	1.0
Famotidine propanamide (famotidine related compound D)[c]	1.3

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

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

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

SPECIFIC TESTS

- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩:** 5.0–5.6
- **Particulate Matter in Injections ⟨788⟩:** Meets the requirements for small-volume injections
- **Bacterial Endotoxins Test ⟨85⟩:** NMT 16.67 USP Endotoxin Units/mg of famotidine
- **Other Requirements:** It meets the requirements under *Container Content for Injections ⟨697⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in single-dose or multiple-dose containers, preferably of Type I glass. Store in a refrigerator.
- **Labeling:** It meets the requirements under *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*. Label it to indicate that the Injection is to be diluted with a suitable parenteral vehicle prior to administration. Label it to indicate the name and the quantity of any added preservative.
- **USP Reference Standards ⟨11⟩**

  USP Benzyl Alcohol RS

  USP Famotidine RS

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

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

Chromatographic Database Information: Chromatographic Database

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