Interim Revision Announcement
Official: May 1, 2021

Sulfamethoxazole

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$C_{10}H_{11}N_3O_3S$ 253.28
Benzenesulfonamide, 4-amino-*N*-(5-methyl-3-isoxazolyl)-;
N^1-(5-Methyl-3-isoxazolyl)sulfanilamide [723-46-6]; UNII: JE42381TNV.

DEFINITION

Sulfamethoxazole contains NLT 98.0% and NMT 102.0% of sulfamethoxazole ($C_{10}H_{11}N_3O_3S$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K ▲or 197A▲ (IRA 1-May-2021)

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

ASSAY

Change to read:

- **Procedure**

Buffer: 13.6 g/L of potassium dihydrogen phosphate adjusted with a 20-g/L solution of potassium hydroxide to a pH of 5.3

Mobile phase: Methanol and *Buffer* (30:70)

Standard solution: 0.1 mg/mL ▲▲ (IRA 1-May-2021) of USP Sulfamethoxazole RS ▲▲ (IRA 1-May-2021) in *Mobile phase*. Sonicate at 45° with intermittent shaking to dissolve before final dilution.

▲**System suitability solution:** 0.1 mg/mL each of USP Sulfamethoxazole RS and USP Sulfamethoxazole Related Compound A RS in *Mobile phase*. Sonicate at 45° with intermittent shaking to dissolve before final dilution. ▲ (IRA 1-May-2021)

Sample solution: 0.1 mg/mL of Sulfamethoxazole in *Mobile phase*. Sonicate at 45° with intermittent shaking to dissolve before final dilution.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4-mm × 25-cm; 5-µm packing L7

Flow rate: 0.9 mL/min

Injection volume: 20 µL

System suitability

Samples: ▲*System suitability solution* and▲ (IRA 1-May-2021) *Standard solution*

[NOTE—The relative retention times for sulfamethoxazole and sulfamethoxazole related compound A are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 3.5 between sulfamethoxazole and sulfamethoxazole related compound A, ▲*System suitability solution*▲ (IRA 1-May-2021)

Relative standard deviation: NMT 0.73%, ▲*Standard solution*▲ (IRA 1-May-2021)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of sulfamethoxazole ($C_{10}H_{11}N_3O_3S$) in the portion of Sulfamethoxazole taken:

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

r_U = peak response of sulfamethoxazole from the *Sample solution*

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

● **RESIDUE ON IGNITION** ⟨281⟩**:** NMT 0.1%

Change to read:

● **ORGANIC IMPURITIES**

Buffer, Mobile phase, ▲**System suitability solution,**▲ (IRA 1-May-2021) and **Chromatographic system:** Proceed as directed in the *Assay*.

▲▲ (IRA 1-May-2021)

Peak identification solution: 1 µg/mL each of USP Sulfamethoxazole Related Compound A RS, USP Sulfamethoxazole Related Compound B RS, USP Sulfamethoxazole Related Compound C RS, USP Sulfanilic Acid RS, and USP Sulfanilamide RS in *Mobile phase*. Sonicate, if necessary, to dissolve before final dilution.

▲**Sensitivity solution:** 0.3 µg/mL of USP Sulfamethoxazole RS in *Mobile phase*. Sonicate, if necessary, to dissolve before final dilution.▲ (IRA 1-May-2021)

Standard solution: 1 µg/mL each of USP Sulfamethoxazole RS and USP Sulfamethoxazole Related Compound F RS in *Mobile phase*. Sonicate, if necessary, to dissolve before final dilution.

Sample solution: 1 mg/mL of Sulfamethoxazole in *Mobile phase*. Sonicate at 45° with intermittent shaking to dissolve before final dilution.

System suitability

Samples: *System suitability solution*, ▲*Sensitivity solution*,▲ (IRA 1-May-2021) and *Standard solution*

Suitability requirements

Resolution: NLT 3.5 between sulfamethoxazole and sulfamethoxazole related compound A, ▲▲ (IRA 1-May-2021) *System suitability solution*

Relative standard deviation: NMT 5.0% ▲each▲ (IRA 1-May-2021) for sulfamethoxazole ▲and sulfamethoxazole related compound F,▲ (IRA 1-May-2021) *Standard solution*

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (IRA 1-May-2021)

Analysis

Samples: *Peak identification solution*, *Standard solution*, and *Sample solution*

Calculate the percentage of sulfamethoxazole related compound F in the portion of Sulfamethoxazole taken:

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

r_U = peak response of sulfamethoxazole related compound F from the *Sample solution*

r_S = peak response of sulfamethoxazole related compound F from the *Standard solution*

C_S = concentration of USP Sulfamethoxazole Related Compound F RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any ▲other▲ (IRA 1-May-2021) individual impurity in the portion of Sulfamethoxazole taken:

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

r_U = peak response of any ▲other▲ (IRA 1-May-2021) individual impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.03%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Sulfanilic acid	0.26	0.10
Sulfanilamide	0.35	0.10
Sulfamethoxazole related compound F	0.45	0.10
Sulfamethoxazole related compound C	0.50	0.10
Sulfamethoxazole	1.0	—
Sulfamethoxazole related compound A	1.2	0.10
Sulfamethoxazole related compound B	2.1	0.10

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any individual unspecified impurity	—	0.10
Total impurities	—	0.30

SPECIFIC TESTS

- **Loss on Drying** ⟨731⟩

  Analysis: Dry at 105° for 4 h.

  Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

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

Change to read:

- **USP Reference Standards** ⟨11⟩

  USP Sulfamethoxazole RS

  USP Sulfamethoxazole Related Compound A RS

  N-{4-[*N*-(5-Methylisoxazol-3-yl)sulfamoyl]phenyl}acetamide.

  $C_{12}H_{13}N_3O_4S$ 295.31

  USP Sulfamethoxazole Related Compound B RS

  4-Amino-*N*-{4-[*N*-(5-methylisoxazol-3-yl)sulfamoyl]phenyl}benzenesulfonamide.

  $C_{16}H_{16}N_4O_5S_2$ 408.45

  USP Sulfamethoxazole Related Compound C RS

  5-Methylisoxazol-3-amine.

  $C_4H_6N_2O$ ▲98.11▲ (IRA 1-May-2021)

  USP Sulfamethoxazole Related Compound F RS

  4-Amino-*N*-(3-methylisoxazol-5-yl)benzenesulfonamide.

  $C_{10}H_{11}N_3O_3S$ 253.28

  USP Sulfanilamide RS

  4-Aminobenzenesulfonamide.

  $C_6H_8N_2O_2S$ 172.20

  USP Sulfanilic Acid RS

  4-Aminobenzenesulfonic acid.

  $C_6H_7NO_3S$ 173.19

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