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Acetazolamide for Injection

DEFINITION

Acetazolamide for Injection is prepared from Acetazolamide with the aid of sodium hydroxide. It is suitable for parenteral use. The contents of each container, when constituted as directed in the labeling, yield a solution containing NLT 95.0% and NMT 110.0% of the labeled amount of acetazolamide ($C_4H_6N_4O_3S_2$).

IDENTIFICATION

Change to read:

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

Sample: Dissolve 500 mg in 5 mL of water, add 2 drops of hydrochloric acid, and allow the mixture to stand for about 15 min. Filter through a fine sintered-glass funnel, wash with several small portions of water, and dry under vacuum over silica gel for 3 h.

Acceptance criteria: Meets the requirements

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

• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sodium*:** Meets the requirements

ASSAY

• **Procedure**

Mobile phase: Dissolve 4.1 g of anhydrous sodium acetate in 950 mL of water, add 20 mL of methanol and 30 mL of acetonitrile, and mix. Adjust with glacial acetic acid to a pH of 4.0.

Standard solution: 0.1 mg/mL of USP Acetazolamide RS prepared as follows. Transfer USP Acetazolamide RS to a suitable volumetric flask, add 0.5 N sodium hydroxide equivalent to 10% of the final volume, and dilute with water to volume.

Sample solution: Nominally 0.1 mg/mL of acetazolamide from Acetazolamide for Injection prepared as follows. Dissolve the contents of one container of Acetazolamide for Injection in a volume of water corresponding to the volume of solvent specified in the labeling. Dilute with water as needed.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4.6-mm × 25-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetazolamide ($C_4H_6N_4O_3S_2$) in the portion of Acetazolamide for Injection taken:

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

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

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

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

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

Acceptance criteria: 95.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩:** Meets the requirements

IMPURITIES

• **Organic Impurities**

Buffer: 6.8 g/L of monobasic potassium phosphate in water

Mobile phase: Acetonitrile and *Buffer* (10:90)

System suitability solution: 0.16 µg/mL each of USP Acetazolamide Related Compound D RS and USP Acetazolamide Related Compound E RS in *Mobile phase*

Standard stock solution: 0.1 mg/mL of USP Acetazolamide RS prepared as follows. Transfer a weighed amount of USP Acetazolamide RS to a suitable volumetric flask and add acetonitrile equivalent to 10% of the final volume and *Buffer* equivalent to 20% of the final volume. Sonicate to dissolve and dilute with *Buffer* to volume.

Standard solution: 0.8 µg/mL of USP Acetazolamide RS from *Standard stock solution* in *Mobile phase*

Sample solution: Nominally 0.4 mg/mL of acetazolamide from Acetazolamide for Injection prepared as follows. Dissolve the contents of one container of Acetazolamide for Injection in water corresponding to the volume of solvent specified in the labeling. Dilute with *Mobile phase* as needed.

Chromatographic system

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

Mode: LC

Detector: 265 nm

Column: 4.6-mm × 15-cm; 3.5-µm packing L11

Flow rate: 1.0 mL/min

Injection volume: 25 µL

Run time: NLT 3.5 times the retention time of acetazolamide

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between acetazolamide related compound E and acetazolamide related compound D, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Acetazolamide for Injection 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 acetazolamide from the *Standard solution*

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

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

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard any impurity peak less than 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Acetazolamide related compound E[a]	0.38	—	—
Acetazolamide related compound D	0.43	0.70	2.0
Aminothiadiazole mercaptan[a,b]	0.55	—	—
Acetamidothiadiazole[a,c]	0.77	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Acetazolamide	1.0	—	—
Mercaptothiadiazole analog[a,d]	1.4	—	—
Chlorothiadiazole analog[a,e]	2.2	—	—
Acetazolamide dimer[a,f]	2.8	—	—
Any unspecified degradation product	—	1.0	0.20
Total degradation products	—	—	3.0

[a] This process impurity is controlled in the drug substance. It is included in the table for identification only and is not to be reported in the total degradation products.

[b] 5-Amino-1,3,4-thiadiazole-2-thiol.

[c] *N*-(1,3,4-Thiadiazol-2-yl)acetamide.

[d] *N*-(5-Mercapto-1,3,4-thiadiazol-2-yl)acetamide.

[e] *N*-(5-Chloro-1,3,4-thiadiazol-2-yl)acetamide.

[f] *N*,*N*′-{5,5′-[(Hydrosulfonylamino)sulfonyl]*bis*(1,3,4-thiadiazole-5,2-diyl)}diacetamide.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: Freshly prepared solution (1 in 10)

Acceptance criteria: 9.0–10.0

• **Bacterial Endotoxins Test** ⟨85⟩**:** It contains NMT 0.5 USP Endotoxin Units/mg of acetazolamide.

• **Injections and Implanted Drug Products** ⟨1⟩, *Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and Clarity of Solutions***:** Meets the requirements at the time of use

• **Sterility Tests** ⟨71⟩**:** Meets the requirements

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements* ⟨659⟩, *Injection Packaging, Packaging for constitution*, preferably in containers of Type III glass, and store at room temperature.

• **Labeling** ⟨7⟩, *Labels and Labeling for Injectable Products***:** Meets the requirements

• **USP Reference Standards** ⟨11⟩

USP Acetazolamide RS

USP Acetazolamide Related Compound D RS

5-Amino-1,3,4-thiadiazole-2-sulfonamide.

$C_2H_4N_4O_2S_2$ 180.21

USP Acetazolamide Related Compound E RS

5-Acetamido-1,3,4-thiadiazole-2-sulfonic acid potassium salt.

$C_4H_4KN_3O_4S_2$ 261.32

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

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

Chromatographic Database Information: Chromatographic Database

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