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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 <sup>a</sup> | 0.38                    | —                        | —                            |
| Acetazolamide related compound D              | 0.43                    | 0.70                     | 2.0                          |
| Aminothiadiazole mercaptan <sup>a,b</sup>     | 0.55                    | —                        | —                            |
| Acetamidothiadiazole <sup>a,c</sup>           | 0.77                    | —                        | —                            |



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