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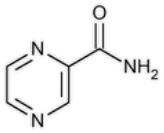
# Pyrazinamide

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-pyrazinamide-notice-20210430.



$C_5H_5N_3O$ 123.12

Pyrazinecarboxamide CAS RN®: 98-96-4; UNII: 2KNI5N06TI.

**DEFINITION**

***Change to read:***

Pyrazinamide contains NLT ▲98.0%▲ (USP 1-May-2021) and NMT ▲102.0%▲ (USP 1-May-2021) of pyrazinamide ($C_5H_5N_3O$), calculated on the anhydrous basis.

**IDENTIFICATION**

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197M

***Change to read:***

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2021)

***Delete the following:***

▲• **C. Procedure**

**Sample:** 20 mg

**Analysis:** Boil the *Sample* with 5 mL of 5 N sodium hydroxide.

**Acceptance criteria:** The odor of ammonia is perceptible.▲ (USP 1-May-2021)

**ASSAY**

***Change to read:***

• **Procedure**

▲**Mobile phase:** Transfer 2.0 g of tetrabutyl ammonium hydrogen sulphate to a 1000-mL volumetric flask. Add 800 mL of water and sonicate to dissolve. Add 2.0 mL of ammonia water, 25 percent and mix. Adjust with 10% phosphoric acid to a pH of 6.8, and dilute with water to volume. Pass through a suitable filter of 0.45-µm pore size.

**Diluent:** Water

**System suitability solution:** 0.01 mg/mL of USP Pyrazinamide RS and 0.001 mg/mL of USP Pyrazinamide Related Compound A RS in *Diluent*

**Standard stock solution:** 1.0 mg/mL of USP Pyrazinamide RS in *Diluent*

**Standard solution:** 0.02 mg/mL of USP Pyrazinamide RS in *Diluent*, from *Standard stock solution*

**Sample stock solution:** 1.0 mg/mL of Pyrazinamide in *Diluent*

**Sample solution:** 0.02 mg/mL of Pyrazinamide in *Diluent*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 269 nm

**Column:** 4.6-mm × 15-cm; 5-µm packing L1

**Column temperature:** 25°

**Flow rate:** 1.0 mL/min

**Injection volume:** 20 µL

**Run time:** NLT 4.0 times the retention time of pyrazinamide

**System suitability**

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

**Suitability requirements**

**Resolution:** NLT 3.0 between pyrazinamide and pyrazinamide related compound A, *System suitability solution*

**Tailing factor:** NMT 3.0, *Standard solution*

**Relative standard deviation:** NMT 1.0%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of pyrazinamide ($C_5H_5N_3O$) in the portion of Pyrazinamide taken:

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

$r_U$ = peak response of pyrazinamide from the *Sample solution*

$r_S$ = peak response of pyrazinamide from the *Standard solution*

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

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

**Acceptance criteria:** 98.0%–102.0% on the anhydrous basis▲ (USP 1-May-2021)

**IMPURITIES**

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

***Change to read:***

• **▲Organic Impurities**

**Mobile phase:** Transfer 6.8 g of potassium dihydrogen phosphate to a 1000-mL volumetric flask. Add 800 mL of water and 1.84 g of sodium hydroxide and dissolve. Adjust with dilute phosphoric acid to a pH of 3.0, and dilute with water to volume. Add 10 mL of acetonitrile and 1 mL of tetrahydrofuran and mix.

**Diluent:** Water

**System suitability solution:** 0.08 mg/mL of USP Pyrazinamide RS and 0.004 mg/mL of USP Pyrazinamide Related Compound B RS in *Diluent*

**Standard solution:** 0.0002 mg/mL each of USP Pyrazinamide RS and USP Pyrazinamide Related Compound A RS and 0.0004 mg/mL of USP Pyrazinamide Related Compound B RS in *Diluent*

**Sample solution:** 0.4 mg/mL of Pyrazinamide in *Diluent*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 270 nm

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

**Column temperature:** 30°

**Flow rate:** 2.0 mL/min

**Injection volume:** 40 µL

**Run time:** NLT 5.2 times the retention time of pyrazinamide

**System suitability**

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

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

**Suitability requirements**

**Resolution:** NLT 4.0 between pyrazinamide and pyrazinamide related compound B, *System suitability solution*

**Relative standard deviation:** NMT 10.0%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate separately the percentage of pyrazinamide related compound A, pyrazinamide related compound B, and any unspecified impurity in the portion of Pyrazinamide taken:

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

$r_U$ = peak response of pyrazinamide related compound A, pyrazinamide related compound B, or any unspecified impurity from the *Sample solution*

$r_S$ = peak response of pyrazinamide, pyrazinamide related compound A, or pyrazinamide related compound B from the *Standard solution*

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

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

**Acceptance criteria:** See *Table 1*. The reporting threshold is 0.003%.

**Table 1**

| Name | Relative Retention Time | Acceptance Criteria, NMT (%) |
|---|---|---|
| Pyrazinamide related compound A[a] | 0.56 | 0.05 |
| Pyrazinamide | 1.0 | — |
| Pyrazinamide related compound B[b] | 1.52 | 0.10 |
| Any unspecified impurity | — | ▲0.05▲ (RB 1-May-2021) |
| Total impurities | — | ▲0.2▲ (RB 1-May-2021) |

[a] Pyrazinecarboxylic acid.

[b] Pyrazinecarbonitrile.

▲ (USP 1-May-2021)

## SPECIFIC TESTS

***Delete the following:***

▲• **Melting Range or Temperature** ⟨741⟩**:** 188°–191°▲ (USP 1-May-2021)

• **Water Determination** ⟨921⟩, *Method I***:** NMT 0.5%

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

***Change to read:***

• **USP Reference Standards** ⟨11⟩

USP Pyrazinamide RS

▲ USP Pyrazinamide Related Compound A RS

Pyrazinecarboxylic acid.

$C_5H_4N_2O_2$ 124.10

USP Pyrazinamide Related Compound B RS

Pyrazinecarbonitrile.

$C_5H_3N_3$ 105.10▲ (USP 1-May-2021)

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| PYRAZINAMIDE | Documentary Standards Support | SM12020 Small Molecules 1 |

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM12020 Small Molecules 1 |

**Chromatographic Database Information:** Chromatographic Database

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