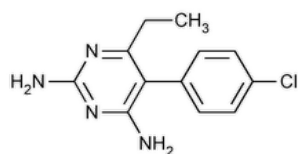


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# Pyrimethamine

## Change to read:



$C_{12}H_{13}ClN_4$  248.71

2,4-Pyrimidinediamine, 5-(4-chlorophenyl)-6-ethyl-

2,4-Diamino-5-( $\blacktriangle$ 4 $\blacktriangle$  (USP 1-May-2024) -chlorophenyl)-6-ethylpyrimidine CAS RN<sup>®</sup>: 58-14-0; UNII: Z3614QOX8W.

## Change to read:

### DEFINITION

Pyrimethamine contains  $\blacktriangle$ NLT 98.0% and NMT 102.0% $\blacktriangle$  (USP 1-May-2024) of pyrimethamine ( $C_{12}H_{13}ClN_4$ ) calculated on the dried basis.

### IDENTIFICATION

#### Change to read:

• **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:**  $\blacktriangle$ 197A or  $\blacktriangle$  (USP 1-May-2024) 197K

• **B. IDENTIFICATION TESTS—GENERAL (191), Chemical Identification Tests, Chloride**

**Sample solution:** Mix about 100 mg of Pyrimethamine with 500 mg of [anhydrous sodium carbonate](#), and ignite the mixture. Cool, add 5 mL of hot water, heat for 5 min on a steam bath, filter, and neutralize the filtrate with [nitric acid](#).

**Acceptance criteria:** Meets the requirements

• **C.** 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

**Solution A:** Add 1 mL of [phosphoric acid](#) to [water](#) and dilute with [water](#) to 1000 mL.

**Mobile phase:** [Acetonitrile](#) and *Solution A* (17:83)

**Standard solution:** 0.02 mg/mL of [USP Pyrimethamine RS](#) in *Solution A*

**Sample solution:** 0.02 mg/mL of Pyrimethamine in *Solution A*

##### Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

**Mode:** LC

**Detector:** UV 210 nm

**Column:** 2.0-mm  $\times$  10-cm; 3- $\mu$ m packing [L11](#)

**Flow rate:** 0.3 mL/min

**Injection volume:** 5  $\mu$ L

##### System suitability

**Sample:** *Standard solution*

##### Suitability requirements

$\blacktriangle$  (USP 1-May-2024)

**Tailing factor:** NMT 1.8

**Relative standard deviation:** NMT  $\blacktriangle$ 0.73% $\blacktriangle$  (USP 1-May-2024)

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of pyrimethamine (C<sub>12</sub>H<sub>13</sub>ClN<sub>4</sub>) in the portion of Pyrimethamine taken:

Result = (r<sub>U</sub>/r<sub>S</sub>) × (C<sub>S</sub>/C<sub>U</sub>) × 100

r<sub>U</sub> = peak response of pyrimethamine from the Sample solution

r<sub>S</sub> = peak response of pyrimethamine from the Standard solution

C<sub>S</sub> = concentration of [USP Pyrimethamine RS](#) in the Standard solution (mg/mL)

C<sub>U</sub> = concentration of Pyrimethamine in the Sample solution (mg/mL)

Acceptance criteria: ▲98.0%–102.0%▲ (USP 1-May-2024) on the dried basis

IMPURITIES

• [RESIDUE ON IGNITION \(281\)](#): NMT 0.1%

Delete the following:

▲• [ORDINARY IMPURITIES \(466\)](#)▲ (USP 1-MAY-2024)

Add the following:

▲• ORGANIC IMPURITIES

Solution A: 2.72 g/L of [potassium phosphate monobasic](#) in [water](#). Adjust with 25% [ammonium hydroxide](#) to a pH of 8.0.

Solution B: [Acetonitrile](#)

Mobile phase: See [Table 1](#).

Table 1

| Time (min) | Solution A (%) | Solution B (%) |
|------------|----------------|----------------|
| 0          | 65             | 35             |
| 6          | 65             | 35             |
| 20         | 40             | 60             |
| 30         | 55             | 45             |
| 35         | 65             | 35             |
| 40         | 65             | 35             |

Diluent: Solution A and Solution B (50:50)

Sensitivity solution: 0.0005 mg/mL of [USP Pyrimethamine RS](#) in Diluent

Standard solution: 0.001 mg/mL of [USP Pyrimethamine RS](#) in Diluent. Sonicate to dissolve.

Sample solution: 1 mg/mL of Pyrimethamine in Diluent. Sonicate to dissolve.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing [L1](#)

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Samples: Sensitivity solution and Standard solution

[NOTE—The relative retention times in [Table 2](#) are provided as information that could aid in peak assignment.]