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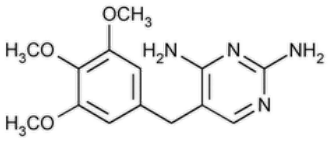
Trimethoprim



$C_{14}H_{18}N_4O_3$ 290.32

2,4-Pyrimidinediamine, 5-[(3,4,5-trimethoxyphenyl)methyl]-.

2,4-Diamino-5-(3,4,5-trimethoxybenzyl)pyrimidine CAS RN®: 738-70-5; UNII: AN164J8Y0X.

» Trimethoprim contains not less than 98.5 percent and not more than 101.0 percent of $C_{14}H_{18}N_4O_3$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers. Store at room temperature.

USP Reference standards ⟨11⟩—
USP Trimethoprim RS

Identification—

Change to read:

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

Solution: 1 in 100.

Medium: chloroform.

B: Transfer about 100 mg of it, accurately weighed, to a 100-mL volumetric flask, and dissolve in 25 mL of alcohol. Dilute quantitatively and stepwise with sodium hydroxide solution (1 in 250) to obtain a 1 in 50,000 solution: the UV absorption spectrum of this solution exhibits maxima and minima only at the same wavelengths as that of a similar solution of USP Trimethoprim RS, concomitantly measured; and the respective absorptivities, calculated on the dried basis for the test sample only, at the wavelength of maximum absorbance at about 287 nm do not differ by more than 3.0%.

Melting range ⟨741⟩**:** between 199° and 203°.

Loss on drying ⟨731⟩—Dry it in vacuum at 105° for 4 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩**:** not more than 0.1%.

Chromatographic purity—

Buffer solution—Prepare a 10 mM sodium perchlorate solution in water, adjust with phosphoric acid to a pH of 3.6, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and methanol (7:3). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Resolution solution—Dissolve accurately weighed quantities of USP Trimethoprim RS and diaveridine; and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having known concentrations of about 10 µg per mL and 5 µg per mL, respectively.

Test solution—Transfer about 25.0 mg of Trimethoprim, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column that contains base-deactivated packing L1. The flow rate is 1.3 mL per minute. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between the peaks for trimethoprim and diaveridine is not less than 2.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Inject a volume (about 20 µL) of the *Test solution* into the chromatograph, record the chromatogram for not less than 11 times the retention time of the trimethoprim peak, and measure all of the peak responses. Calculate the percentage of each impurity in the portion of Trimethoprim taken by the formula:

$$100\{Fr_i/[\Sigma(Fr_i) + Fr_T]\}$$

in which F is a relative response factor, and is equal to 0.5 for any peak having a relative retention time of 0.9, 2.3, 2.7, or 10.3, and is equal to

1.0 for all other peaks; r_i is the peak response for each impurity; and r_T is the peak response for trimethoprim obtained from the *Test solution:* not more than 0.1% of any individual impurity is found; and not more than 0.2% of total impurities is found.

Assay—Transfer about 300 mg of Trimethoprim, accurately weighed, to a conical flask, add 60 mL of glacial acetic acid, and titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 29.03 mg of $C_{14}H_{18}N_4O_3$.

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

Topic/Question	Contact	Expert Committee
TRIMETHOPRIM	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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