Edition: BP 2025 (Ph. Eur. 11.6 update)

# Co-trimazine Tablets

General Notices

Trimethoprim and Sulfadiazine Tablets

**Action and use**

Dihydrofolate reductase inhibitor + sulfonamide antibacterial.

## DEFINITION

Co-trimazine Tablets contain Trimethoprim and Sulfadiazine in the proportion one part to five parts.

*The tablets comply with the requirements stated under Tablets and with the following requirements.*

**Content of trimethoprim, $C_{14}H_{18}N_4O_3$**

92.5 to 107.5% of the stated amount.

**Content of sulfadiazine, $C_{10}H_{10}N_4O_2S$**

92.5 to 107.5% of the stated amount.

## IDENTIFICATION

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.

(1) Shake a quantity of the finely powdered tablets containing 0.2 g of Sulfadiazine with sufficient 1.4M *methanolic ammonia* to produce 100 mL, centrifuge and use the supernatant liquid.
(2) Shake a quantity of the finely powdered tablets containing 0.2 g of Trimethoprim with sufficient 1.4M *methanolic ammonia* to produce 100 mL, centrifuge and use the supernatant liquid.
(3) 0.2% w/v solution of *sulfadiazine BPCRS* in 1.4M *methanolic ammonia*.
(4) 0.2% w/v solution of *trimethoprim BPCRS* in 1.4M *methanolic ammonia*.
(5) Mix equal volumes of solutions (3) and (4).

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel $GF_{254}$*.
(b) Use the mobile phase as described below.
(c) Apply 5 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in a current of air, spray with a 0.1% w/v solution of *4-dimethylaminobenzaldehyde* in a mixture of 1 mL of *hydrochloric acid* and 100 mL of *ethanol (96%)*, allow to dry and spray with *dilute potassium iodobismuthate solution*.

MOBILE PHASE

5 volumes of *water*, 15 volumes of *dimethylformamide* and 75 volumes of *ethyl acetate*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (5) shows two clearly separated spots.

CONFIRMATION

The spot in the chromatogram obtained with solution (1) with an Rf value of about 0.7 corresponds to the principal spot in the chromatogram obtained with solution (3) and the spot in the chromatogram obtained with solution (2) with an Rf value of about 0.3 corresponds to the principal spot in the chromatogram obtained with solution (4).

## ASSAY

Weigh and finely powder 20 tablets.

***For trimethoprim***

Extract the combined chloroform extracts from the Assay for sulfadiazine with four 50-mL quantities of a 5% v/v solution of 6M *acetic acid*. Wash the combined aqueous extracts with 5 mL of *chloroform*, discard the chloroform layer and dilute to 250 mL with a 5% v/v solution of 6M *acetic acid*. Dilute 20 mL to 100 mL with *water*. Determine the *absorbance* of the resulting solution at the maximum at 271 nm, Appendix II B, and calculate the content of $C_{14}H_{18}N_4O_3$ taking 204 as the value of A(1%, 1 cm) at the maximum at 271 nm.

***For sulfadiazine***

Transfer a quantity of the powdered tablets containing 0.125 g of Sulfadiazine to a separating funnel containing 20 mL of 0.1M *sodium hydroxide* and extract with four 50-mL quantities of *chloroform*. Wash each chloroform extract with the same two 10-mL quantities of 0.1M *sodium hydroxide*. Combine the aqueous washings and the aqueous layer from the separating funnel and reserve the combined chloroform extracts for the Assay for trimethoprim. Dilute the combined aqueous solutions to 250 mL with *water*, filter and dilute 10 mL of the filtrate to 200 mL with *water*. To 2 mL of the resulting solution add 0.5 mL of 4M *hydrochloric acid* and 1 mL of a 0.1% w/v solution of *sodium nitrite* and allow to stand for 2 minutes. Add 1 mL of a 0.5% w/v solution of *ammonium sulfamate* and allow to stand for 3 minutes. Add 1 mL of a 0.1% w/v solution of *N-(1-naphthyl)-ethylenediamine dihydrochloride*, allow to stand for 10 minutes and dilute to 25 mL with *water*. Measure the *absorbance* of the resulting solution at the maximum at 538 nm, Appendix II B, using in the reference cell a solution prepared at the same time and in the same manner using 2 mL of *water* and beginning at the words ‘add 0.5 mL of 4M *hydrochloric acid*...’. Calculate the content of $C_{10}H_{10}N_4O_2S$ from the *absorbance* obtained by repeating the operation with 2 mL of a 0.0025% w/v solution of *sulfadiazine BPCRS* in 0.0005M *sodium hydroxide* and beginning at the words ‘add 0.5 mL of 4M *hydrochloric acid*…’.

When trimethoprim and sulfadiazine tablets are prescribed or demanded, Co-trimazine Tablets shall be dispensed or supplied.