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Co-trimazine Injection

General Notices

Trimethoprim and Sulfadiazine Injection

Action and use

Dihydrofolate reductase inhibitor + sulfonamide antibacterial.

DEFINITION

Co-trimazine Injection is a sterile suspension in Water for Injections containing Trimethoprim and Sulfadiazine in the proportion one part to five parts.

PRODUCTION

Co-trimazine Injection is prepared by the addition, with aseptic precautions, of sterile Trimethoprim to a solution of sulfadiazine sodium previously sterilised by *filtration*. The solution of sulfadiazine sodium is prepared by the interaction of Sulfadiazine and Sodium Hydroxide.

The injection complies with the requirements stated under Parenteral Preparations and with the following requirements.

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

90.0 to 110.0% of the stated amount.

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

90.0 to 110.0% of the stated amount.

CHARACTERISTICS

A suspension of an almost white solid in a pale straw-coloured solution.

IDENTIFICATION

A. The light absorption, Appendix II B, in the range 250 to 325 nm of the solution obtained in the Assay for trimethoprim exhibits a maximum only at 271 nm.
B. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions.
(1) Ensure that the injection is homogeneous by gently inverting the container several times. To 2.5 mL of the well mixed injection add 4 mL of *hydrochloric acid* and dilute to 50 mL with 1.4M *methanolic ammonia*.
(2) 2.0% w/v of *sulfadiazine BPCRS* in 1.4M *methanolic ammonia*.
(3) 0.4% w/v of *trimethoprim BPCRS* in 1.4M *methanolic ammonia*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating silica gel F_{254}.
(b) Use the mobile phase as described below.
(c) Apply 1 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

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

CONFIRMATION

In the chromatogram obtained with solution (1):

one of the principal spots in the chromatogram obtained with solution (1) corresponds to the principal spot in the chromatogram obtained with solution (2);

the other principal spot corresponds to the principal spot in the chromatogram obtained with solution (3).

C. To 5 mL of the filtrate obtained in the Assay for sulfadiazine add 10 mL of *water* and 5 mL of *thiobarbituric acid-citrate buffer*, mix and heat on a water bath for 30 minutes. A pink colour is produced.

Alkalinity

pH, 10.0 to 10.5, Appendix V L.

ASSAY

For trimethoprim

Extract the *chloroform* solution reserved in the Assay for sulfadiazine with three quantities, of 100, 50 and 50 mL, of 1M *acetic acid* and dilute the combined extracts to 500 mL with 1M *acetic acid*. To 5 mL add 35 mL of 1M *acetic acid* and sufficient *water* to produce 200 mL and measure the *absorbance* of the resulting solution at the maximum at 271 nm, Appendix II B. 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

Disperse the trimethoprim evenly throughout the injection by gently inverting the container several times, avoiding the formation of foam. Transfer a quantity of the injection containing the equivalent of 2 g of Sulfadiazine to a separating funnel containing 50 mL of 0.1M *sodium hydroxide* and extract with two quantities, of 100 mL and 50 mL, of *chloroform*, washing the extract with the same 25 mL quantity of 0.1M *sodium hydroxide*. Reserve the combined chloroform extracts for the Assay for trimethoprim.

Dilute the combined aqueous solutions and washings to 250 mL with *water*, filter and dilute 5 mL of the filtrate to 200 mL with *water*. Dilute 10 mL of this solution to 100 mL with *water*. To 3 mL of the resulting solution add 1 mL of *2M 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, add sufficient *water* to produce 25 mL and measure the *absorbance* of the resulting solution at 538 nm, Appendix II B. Repeat the operation using 3 mL of a solution prepared by dissolving 0.2 g of *sulfadiazine BPCRS* in 50 mL of 0.1M *sodium hydroxide*, adding sufficient *water* to produce 200 mL, diluting 5.0 mL of the resulting solution to 250 mL with *water* and beginning at the words ‘add 1 mL of *2M hydrochloric acid*…’. Calculate the content of $C_{10}H_{10}N_4O_2S$ in the injection from the absorbances obtained using the declared content of $C_{10}H_{10}N_4O_2S$ in *sulfadiazine BPCRS*.

When trimethoprim and sulfadiazine injection is prescribed or demanded, Co-trimazine Injection shall be dispensed or supplied.