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Zidovudine Infusion

General Notices

Zidovudine Concentrate for Intravenous Infusion

Action and use

Nucleoside reverse transcriptase inhibitor; antiviral (HIV).

DEFINITION

Zidovudine Infusion is a sterile solution containing Zidovudine. It is prepared by diluting Zidovudine Concentrate for Infusion in a suitable diluent in accordance with the manufacturer's instructions.

The infusion complies with the requirements stated under Parenteral Preparations.

STORAGE

Zidovudine Infusion should be used immediately after preparation but, in any case, within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instructions.

ZIDOVUDINE CONCENTRATE FOR INFUSION

DEFINITION

Zidovudine Concentrate for Infusion is a sterile solution consisting of Zidovudine with or without excipients. It is supplied in a sealed container.

The contents of the sealed container comply with the requirements for Concentrates for Injections or Infusions stated under Parenteral Preparations and with the following requirements.

Content of zidovudine, $C_{10}H_{13}N_5O_4$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions protected from light.
(1) Dilute a volume of the contents of the sealed container in sufficient *methanol (50%)* to produce a solution containing 0.1% w/v of Zidovudine.
(2) 0.1% w/v of *zidovudine BPCRS* in *methanol (50%)*.

CHROMATOGRAPHIC CONDITIONS

(a) Use precoated *silica gel F_{254}* plates (Merck silica gel 60 F_{254} plates are suitable).
(b) Use the mobile phase described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 12 cm.
(e) After removal of the plate, dry it in air and immediately examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

3 volumes of *glacial acetic acid*, 10 volumes of *methanol* and 90 volumes of *dichloromethane*.

CONFIRMATION

The chromatogram obtained with solution (1) shows a principal spot corresponding in position, colour and size to the principal spot in the chromatograms obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (1) shows a principal peak with the same retention time as the principal peak due to zidovudine in the chromatogram obtained with solution (2).

TESTS

Acidity or alkalinity

pH of a solution containing 0.01% w/v of Zidovudine, 3.5 to 7.0, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase protected from light.

(1) Dilute a volume of the contents of the sealed container to produce a solution containing 0.1% w/v of Zidovudine.
(2) Dilute 1 volume of solution (1) to 500 volumes.
(3) 0.01% w/v of *zidovudine impurity standard BPCRS*.
(4) 0.003% w/v of *thymine*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Spherisorb ODS2 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 265 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

20 volumes of *methanol* and 80 volumes of *water*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3):

the chromatogram closely resembles the reference chromatogram supplied with *zidovudine impurity standard BPCRS*;

the *resolution* between the peaks due to zidovudine and zidovudine impurity B is at least 1.5.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to Impurity C (thymine) is not greater than the area of the principal peak in the chromatogram obtained with solution (4) (3.0%);

the area of any peak with a relative retention time of 2.8 (Impurity G) is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the area of any peak corresponding to Impurity G and any other *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained solution (2) (1.0%).

Disregard any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in mobile phase protected from light.

(1) Dilute a volume of the contents of the sealed container to produce a solution containing 0.02% w/v of Zidovudine.
(2) 0.02% w/v of *zidovudine BPCRS*.
(3) 0.01% w/v of *zidovudine impurity standard BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to zidovudine and zidovudine impurity B is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of $C_{10}H_{13}N_5O_4$ in the infusion from the chromatograms obtained using the declared content of $C_{10}H_{13}N_5O_4$ in *zidovudine BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities B, C, E and G listed under Zidovudine.