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Dacarbazine Injection

General Notices

Action and use

Cytotoxic alkylating agent.

DEFINITION

Dacarbazine Injection is a sterile solution of Dacarbazine in Water for Injections. It is prepared by dissolving Dacarbazine for Injection in the requisite amount of Water for Injections.

The injection complies with the requirements stated under Parenteral Preparations.

STORAGE

Dacarbazine Injection 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.

DACARBAZINE FOR INJECTION

DEFINITION

Dacarbazine for Injection is a sterile material consisting of Dacarbazine with or without excipients. It is supplied in a sealed container.

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

Content of dacarbazine, $C_6H_{10}N_6O$

90.0 to 110.0% of the stated amount.

CHARACTERISTICS

A white or very pale yellow powder.

IDENTIFICATION

A. Dissolve a quantity of the contents of the sealed container containing 0.1 g of Dacarbazine in 200 mL of 0.1M *mixed phosphate buffer pH 7.0*, dilute with the buffer solution to 250 mL and dilute 3 mL to 200 mL with the same buffer solution.

The *light absorption* of the resulting solution, Appendix II B, in the range 230 to 350 nm exhibits two maxima, at 237 nm and 330 nm.

B. In the test for 5-aminoimidazole-4-carboxamide hydrochloride, the principal peak in the chromatogram obtained with solution (2) corresponds to that in the chromatogram obtained with solution (3).

TESTS

5-Aminoimidazole-4-carboxamide hydrochloride

Carry out the method for *liquid chromatography*, Appendix III D protected from light, using the following solutions in low-actinic glassware.

(1) Dissolve a quantity of the contents of the sealed container containing 0.20 g of Dacarbazine in 40 mL of 0.1M *acetic acid* and add sufficient 0.1M *acetic acid* to produce 50 mL.
(2) Dilute 1 volume of solution (1) to 100 volumes with 0.1M *acetic acid*.
(3) 0.004% w/v of *dacarbazine BPCRS* in 0.1M *acetic acid*.
(4) 0.0024% w/v of *5-aminoimidazole-4-carboxamide hydrochloride* in 0.1M *acetic acid*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used using the mobile phase described below. Inject each sample within 1 hour of preparation.

MOBILE PHASE

0.005M *dioctyl sodium sulfosuccinate* in a mixture of 3 volumes of *glacial acetic acid*, 87 volumes of *water* and 110 volumes of *methanol*.

LIMITS

The area of any peak corresponding to 5-aminoimidazole-4-carboxamide hydrochloride in the chromatogram obtained with solution (1) is not greater than the area of the peak in the chromatogram obtained with solution (4) (0.6%).

Related substances

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

(1) Dissolve a quantity of the contents of the sealed container containing 0.20 g of Dacarbazine in 40 mL of 0.25M *acetic acid* and add sufficient 0.25M *acetic acid* to produce 50 mL.
(2) 0.0040% w/v of *2-azahypoxanthine BPCRS* in 0.25M *acetic acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (20 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (Nucleosil C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 254 nm.
(f) Inject 20 µL of each solution within 1 hour of preparation.
(g) After use the column should be thoroughly flushed with *methanol* to remove dacarbazine which does not elute with the mobile phase.

MOBILE PHASE

0.005M *dioctyl sodium sulfosuccinate* in a mixture of 1.5 volumes of *glacial acetic acid* and 98.5 volumes of *water*.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1%);

not more than one such peak has an area greater than half the area of the peak in the chromatogram obtained with solution (2) (0.5%);

the sum of the areas of all such peaks is not greater than three times the area of the peak in the chromatogram obtained with solution (2) (3%).

Uniformity of content

Sealed containers containing 200 mg or less of Dacarbazine comply with the requirements stated under Parenteral Preparations, Powders for Injections or Infusions. Use the individual results obtained in the Assay.

ASSAY

Carry out the following procedure protected from light. Dissolve the contents of one container in 0.1M *hydrochloric acid* and dilute with sufficient 0.1M *hydrochloric acid* to produce a final solution containing 0.0008% w/v of Dacarbazine. Measure the *absorbance* of the resulting solution at the maximum at 323 nm, Appendix II B. Calculate the content of $C_6H_{10}N_6O$ in the sealed container taking 1090 as the value of A(1%, 1 cm) at the maximum at 323 nm.

Repeat the procedure with a further nine sealed containers and calculate the average content of $C_6H_{10}N_6O$ per container from the 10 individual results thus obtained.

STORAGE

The sealed container should be protected from light and stored at a temperature of 2° to 8°.