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Vinblastine Injection

General Notices

Vinblastine Sulphate Powder for Injection
Vinblastine Sulphate Solution for Injection

Action and use

Vinca alkaloid cytotoxic.

DEFINITION

Vinblastine Injection is a sterile solution of Vinblastine Sulfate in Water for Injections. It is supplied as a ready-to-use solution or it is prepared by dissolving Vinblastine Sulfate Powder for Injection in accordance with the manufacturer's instructions.

The injection complies with the requirements stated under Parenteral Preparations.

STORAGE

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

VINBLASTINE SULFATE POWDER FOR INJECTION

DEFINITION

Vinblastine Sulfate Powder for Injection is a sterile material prepared from Vinblastine Sulfate. It may contain excipients. I 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 vinblastine sulfate, $C_{46}H_{58}N_4O_9,H_2SO_4$

92.5 to 107.5% of the stated amount of anhydrous vinblastine sulfate.

IDENTIFICATION

A. In the test for Related substances, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (3).
B. To 1 mg of the powder being examined, add 0.2 mL of a freshly prepared 1% w/v solution of *vanillin* in *hydrochloric acid*. A pink colour is produced in about 1 minute (distinction from vincristine sulfate).

C. Yield the reactions characteristic of *sulfates*, Appendix VI.

TESTS

Acidity

pH of a solution containing the equivalent of 0.15% w/v of anhydrous vinblastine sulfate, 3.5 to 5.0, Appendix V L.

Clarity of solution

Dissolve the contents of a sealed container in 10 mL of *carbon dioxide-free water*. The resulting solution is *clear*, Append IV A.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Keep the solutions in ice before use.

(1) Dissolve the contents of a sealed container in sufficient *water* to produce a solution containing the equivalent of 0.1% w/v of anhydrous vinblastine sulfate.
(2) 0.1% w/v each of *vinblastine sulfate EPCRS* and *vincristine sulfate EPCRS* in *water*.
(3) 0.1% w/v of *vinblastine sulfate EPCRS* in *water*.
(4) Dilute 1 volume of solution (1) to 50 volumes with *water*.
(5) Dilute 1 volume of solution (4) to 20 volumes with *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octylsilyl silica gel for chromatography* (5 µm) (Zorbax C8 is suitable). Place a guard column packed with a suitable silica gel placed between the pump and the injection device.
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 262 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 3 times the retention time of the peak due to vinblastine.

MOBILE PHASE

12 volumes of *acetonitrile*, 38 volumes of a 1.5% v/v solution of *diethylamine* adjusted to pH 7.5 with *orthophosphoric aci* and 50 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions the retention times of vincristine sulfate and vinblastine sulfate are about 12.5 and 17.5 minutes respectively.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2) the *resolution* between the peaks due to vinblastine and vincristine is at least 4.0.

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 (4) (2%);

the sum of the areas of all the *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (4) (5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

Loss on drying

When dried at 60° at a pressure not exceeding 0.7 kPa for 16 hours, lose not more than 17.0% of their weight. Use 0.5 g.

Uniformity of content

The content of anhydrous vinblastine sulfate in each of 10 individual containers as determined in the Assay is not less tha 90.0% and not more than 110.0% of the average except that in one container the content may be not less than 80.0% an not more than 120.0% of the average.

ASSAY

Dissolve the contents of a sealed container in a suitable volume of *methanol* and dilute with sufficient *methanol* to produc a solution containing 0.004% w/v of anhydrous vinblastine sulfate. Measure the *absorbance* of the resulting solution at th maximum at 267 nm, Appendix II B. Calculate the content of $C_{46}H_{58}N_4O_9,H_2SO_4$ in the sealed container taking 185 as the value of A(1%, 1 cm) at the maximum at 267 nm. Repeat the procedure with a further nine sealed containers. Calculate the average content of $C_{46}H_{58}N_4O_9,H_2SO_4$ per container from the 10 individual results thus obtained.

LABELLING

The label of the sealed container states (1) the weight of anhydrous vinblastine sulfate contained in it; (2) when reconstituted, that the preparation is for intravenous use only, it is fatal if given by other routes.

VINBLASTINE SULFATE SOLUTION FOR INJECTION

DEFINITION

Vinblastine Sulfate Solution for Injection is a sterile solution containing Vinblastine Sulfate. It may contain excipients. It is supplied as a ready-to-use solution.

The contents of the sealed container comply with the requirements for Parenteral Preparations and with the following requirements.

Content of vinblastine sulfate, $C_{46}H_{58}N_4O_9,H_2SO_4$

92.5 to 107.5% of the stated amount of anhydrous vinblastine sulfate.

IDENTIFICATION

A. In the test for Related substances the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (3).
B. To a quantity of the injection containing 1 mg of Vinblastine Sulfate add 0.2 mL of a freshly prepared 1% w/v solution of *vanillin* in *hydrochloric acid*. A pink colour is produced in about 1 minute (distinction from vincristine sulfate).
C. Yield the reactions characteristic of *sulfates*, Appendix VI.

TESTS

Acidity

The pH of the injection is 3.5 to 5.0, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Keep the solutions in ice before use.

(1) Dilute the injection with *water*, if necessary, to produce a solution containing the equivalent of 0.1% w/v of anhydrous vinblastine sulfate.
(2) 0.1% w/v each of *vinblastine sulfate EPCRS* and *vincristine sulfate EPCRS* in *water*.
(3) 0.1% w/v of *vinblastine sulfate EPCRS* in *water*.
(4) Dilute 1 volume of solution (1) to 50 volumes with *water*.
(5) Dilute 1 volume of solution (4) to 20 volumes with *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *end-capped octylsilyl silica gel for chromatography* (5 µm) (Zorbax C8 is suitable). Place a guard column packed with a suitable silica gel placed between the pump and the injection device.
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.0 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 262 nm.
(f) Inject 20 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 3 times the retention time of the peak due to vinblastine.

MOBILE PHASE

12 volumes of *acetonitrile*, 38 volumes of a 1.5% v/v solution of *diethylamine* adjusted to pH 7.5 with *orthophosphoric acid* and 50 volumes of *methanol*.

When the chromatograms are recorded under the prescribed conditions the retention times of vincristine sulfate and vinblastine sulfate are about 12.5 and 17.5 minutes respectively.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (2) the *resolution* between the peaks due to vinblastine and vincristine is at least 4.0.

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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 (4) (2%);

the sum of the areas of all the *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (4) (5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

ASSAY

Dilute a quantity of the injection with *methanol* to produce a solution containing 0.004% w/v of anhydrous vinblastine sulfate. Measure the *absorbance* of the resulting solution at the maximum at 267 nm, Appendix II B using *methanol (96%)* in the reference cell. Calculate the content of $C_{46}H_{58}N_4O_9,H_2SO_4$ in the injection using a 0.004% w/v solution of *vinblastine sulfate EPCRS* in *methanol (96%)* and the declared content of *vinblastine sulfate EPCRS*.

LABELLING

The label of the sealed container states (1) the concentration of anhydrous vinblastine sulfate and volume contained in it; (2) that the preparation is for intravenous use only, it is fatal if given by other routes.