Vinblastine Sulfate for Injection

DEFINITION

Change to read:

Vinblastine Sulfate for Injection contains NLT 90.0% and NMT 110.0% of the labeled amount of vinblastine sulfate (C_{26}H_{38}N_{4}O_{9}·H_{2}SO_{4}).

CAUTION—Handle Vinblastine Sulfate for Injection with great care because it is a potent cytotoxic agent.

IDENTIFICATION

A. INFRARED ABSORPTION (197K)

Acceptance criteria: Meets the requirements

B. IDENTIFICATION TESTS—GENERAL, Sulfate (191) Sample solution: 100 mg/mL in water

Acceptance criteria: Meets the requirements

ASSAY

PROCEDURE

Solution A: Diethylamine and water (14:986). Adjust with phosphoric acid to a pH of 7.5.

Solution B: Acetonitrile and methanol (20:80)

Mobile phase: Solution A and Solution B (38:62)

Standard solution: 0.4 mg/mL of USP Vinblastine Sulfate RS in water

System suitability solution: 0.4 mg/mL each of vincristine sulfate and vinblastine sulfate in water prepared as follows. Transfer USP Vincristine Sulfate RS or USP Vin- cristine Sulfate (Assay) RS to a suitable volumetric flask, and dissolve, and with phosphoric acid to a pH of 7.5. Sample solution A: 1 mg/mL. Insert the stopper, shake to mix, and combine the solutions from the five containers.

Sample solution: 0.4 mg/mL of vinblastine sulfate in water, from the Sample stock solution

Chromatographic system

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 262 nm

Pre-column: Packed with porous silica gel; installed between the pump and the injector

Column: 4.6-mm × 15-cm; packing L1

Flow rate: 2 mL/min

Injection size: 20 µL

System suitability

Samples: Standard solution and System suitability solution

Suitability requirements

Resolution: NLT 4.0 between vincristine and vinblastine, System suitability solution

Relative standard deviation: NMT 2.0%, Standard solution

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of vinblastine sulfate (C_{26}H_{38}N_{4}O_{9}·H_{2}SO_{4}) in the portion of Vinblastine Sulfate for Injection taken:

\[ \text{Result} = \left( \frac{r_0}{r_1} \right) \times \left( \frac{C_1}{C_0} \right) \times 100 \]

[\text{\(C_0\) = nominal concentration of vinblastine sulfate in the Sample solution (mg/mL)}

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

UNIFORMITY OF DOSAGE UNITS (905)

Procedure for content uniformity

Buffer: Dissolve 13.61 g of sodium acetate in 900 mL of water in a 1000-mL volumetric flask. Adjust with glacial acetic acid to a pH of 5.0 while stirring, and dilute with water to volume.

Standard solution: 40 µg/mL of USP Vinblastine Sulfate RS in Buffer

Sample solution: Dissolve the contents of one container of Vinblastine Sulfate for Injection in Buffer to obtain a solution having a concentration of 40–50 µg/mL.

Instrumental conditions

(See Spectrophotometry and Light-Scattering (851).)

Mode: UV

Analytical wavelength: 269 nm

Cell: 1 cm

Blank: Buffer

Analysis

Samples: Standard solution and Sample solution

Concomitantly determine the absorbances of the Sample solution and the Standard solution, and calculate the percentage of vinblastine sulfate (C_{26}H_{38}N_{4}O_{9}·H_{2}SO_{4}) in the portion of Vinblastine Sulfate for Injection taken:

\[ \text{Result} = \left( \frac{A_0}{A_1} \right) \times \left( \frac{C_1}{C_0} \right) \times 100 \]

[\text{\(A_0\) = absorbance of the Sample solution}

[\text{\(A_1\) = absorbance of the Standard solution}

[\text{\(C_1\) = concentration of USP Vinblastine Sulfate RS in the Standard solution (mg/mL)}

[\text{\(C_0\) = nominal concentration of vinblastine sulfate in the Sample solution (mg/mL)}

Acceptance criteria: Meets the requirements

IMPURITIES

ORGANIC IMPURITIES

Mobile phase, System suitability solution, and System suitability: Prepare as directed in the Assay.

Sample solution A: Use the Sample solution, prepared as directed in the Assay.

Sample solution B: 16 µg/mL of vinblastine sulfate in water, from Sample solution A

Chromatographic system: Proceed as directed in the Assay, except to use an injection size of 200 µL.

Analysis

Samples: Sample solution A and Sample solution B

Calculate the percentage of each impurity in the portion of Vinblastine Sulfate for Injection taken:

\[ \text{Result} = \left[ \frac{r_0}{(\Sigma r_i + 25r_0)} \right] \times 100 \]

[r_0 = peak response of each impurity appearing after the solvent peak from Sample solution A

[r_i = peak response of vinblastine from Sample solution B

Calculate the percentage of total impurities:

\[ \text{Result} = \left[ \frac{\Sigma r_i}{(\Sigma r_i + 25r_0)} \right] \times 100 \]

[r_0 = peak response of each impurity appearing after the solvent peak from Sample solution A

[r_i = peak response of vinblastine from Sample solution B

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Acceptance criteria
Individual impurities: NMT 2.0%
Total impurities: NMT 5.0%

SPECIFIC TESTS
• **Bacterial Endotoxins Test (85):** It contains NMT 10.0 USP Endotoxin Units/mg of vinblastine sulfate.
• **Sterility Tests (71):** Meets the requirements
• **Constituted Solution:** At the time of use, it meets the requirements for Intravenous Use Only—Fatal If Given By Other Routes.
• **Completeness of Solution (641):** A 10-mg portion (Note—No Loss on Drying determination is needed for) dissolves in 10 mL of Water for Injection to yield a clear solution.
• **Other Requirements:** It meets the requirements for Intravenous Use Only—Fatal If Given By Other Routes.

ADDITIONAL REQUIREMENTS
• **Packaging and Storage:** Preserve as described in Intravenous Use Only—Fatal If Given By Other Routes. When dispensed, the container or syringe (holding the individual dose prepared for administration to the patient) must be enclosed in an overwrap bearing the statement: “Do Not Remove Covering Until Moment of Injection.”

Change to read:

• **Labeling:** The label states: “For Intravenous Use Only—Fatal If Given By Other Routes.”