Vinblastine Sulfate for Injection

DEFINITION

Vinblastine Sulfate for Injection is Vinblastine Sulfate suitable for parenteral use. It contains NLT 90.0% and NMT 110.0% of the labeled amount of vinblastine sulfate ($C_{46}H_{58}N_4O_9 \cdot H_2SO_4$).

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

IDENTIFICATION

- **A. INFRARED ABSORPTION ⟨197K⟩**
  Sample: Use material previously dried in a vacuum at 60° for 16 h.
  Acceptance criteria: Meets the requirements
- **B. IDENTIFICATION TESTS—GENERAL,** *Sulfate* **⟨191⟩**
  Sample solution: 100 mg/mL in water
  Acceptance criteria: Meets the requirements

ASSAY

Change to read:

- **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 Vincristine Sulfate (Assay) RS •(RB 1-Jul-2011) to a suitable volumetric flask, and dissolve in *Standard solution*.
  Sample stock solution: Pipet a suitable volume of water into each of five containers of Vinblastine Sulfate for Injection to obtain a solution in each having a concentration of 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
  Precolumn: 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: *System suitability solution* and *Standard 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 ($C_{46}H_{58}N_4O_9 \cdot H_2SO_4$) in the portion of Vinblastine Sulfate for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Vinblastine Sulfate RS in the *Standard solution* (mg/mL)
C_U = 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 ($C_{46}H_{58}N_4O_9 \cdot H_2SO_4$) in the portion of Vinblastine Sulfate for Injection taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Vinblastine Sulfate RS in the *Standard solution* (mg/mL)
C_U = 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 from *Sample solution A* in water
  Chromatographic system: Proceed as directed in the *Assay*, except 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:

$$\text{Result} = [r_{UA}/(\Sigma r_{UA} + 25r_{UB})] \times 100$$

r_{UA} = peak response of each impurity appearing after the solvent peak from *Sample solution A*
r_{UB} = peak response of vinblastine from *Sample solution B*

Calculate the percentage of total impurities:

$$\text{Result} = [(\Sigma r_{UA}/(\Sigma r_{UA} + 25r_{UB})] \times 100$$

r_{UA} = peak response of each impurity appearing after the solvent peak from *Sample solution A*
r_{UB} = peak response of vinblastine from *Sample solution B*

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 *Injections* ⟨1⟩*, Constituted Solutions*.
- **COMPLETENESS OF SOLUTION ⟨641⟩:** A 10-mg portion dissolves in 10 mL of Water for Injection to yield a clear solution.
- **OTHER REQUIREMENTS:** It meets the requirements for *Injections* ⟨1⟩*, Labeling*.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve as described in *Injections* ⟨1⟩*, Containers for Sterile Solids*, in a refrigerator.
- **LABELING:** The label states: "Fatal if Given Intrathecally. For Intravenous Use Only." 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. Fatal If Given Intrathecally. For Intravenous Use Only."

Change to read:

- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Endotoxin RS
  USP Vinblastine Sulfate RS
  USP Vincristine Sulfate RS
  [NOTE—No *Loss on Drying* determination is needed for USP Vincristine Sulfate RS.]
  •USP Vincristine Sulfate (Assay) RS•(RB 1-Jul-2011)