

Vinblastine Sulfate for Injection

DEFINITION

Change to read:

Vinblastine Sulfate for Injection (IRA 1-Nov-2011) 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

- **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 USP Vincristine Sulfate RS and USP Vinblastine Sulfate RS in water prepared as follows. Transfer USP Vincristine Sulfate RS to a suitable volumetric flask, and dissolve in *Standard solution* to obtain a solution having 0.4 mg/mL each of USP Vincristine Sulfate RS and USP Vinblastine Sulfate RS in water.
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
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 ($C_{46}H_{58}N_4O_9 \cdot H_2SO_4$) 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 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:

$$\text{Result} = [r_U/(\Sigma r_U + 25r_S)] \times 100$$

r_U = peak response of each impurity appearing after the solvent peak from *Sample solution A*
 r_S = peak response of vinblastine from *Sample solution B*

Calculate the percentage of total impurities:

$$\text{Result} = [\Sigma r_U/(\Sigma r_U + 25r_S)] \times 100$$

r_U = peak response of each impurity appearing after the solvent peak from *Sample solution A*
 r_S = peak response of vinblastine from *Sample solution B*

2 Vinblastine

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*, and store in a refrigerator.

Change to read:

- **LABELING:** The label states: •“For Intravenous Use Only–Fatal If Given By Other Routes.” •(IRA 1–Nov-2011) 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. •For Intravenous Use Only–Fatal If Given By Other Routes.” •(IRA 1–

Nov-2011)

- **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.]