

## 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 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

**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*

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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 *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.]

- USP Vincristine Sulfate (Assay) RS •(RB 1–Jul-2011)