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 \((\text{C}_{46}\text{H}_{58}\text{N}_{4}\text{O}_{9} \cdot \text{H}_{2}\text{SO}_{4})\). [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)

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 Vinblastine Sulfate (Assay) RS 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 taken to a suitable volume. 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 each impurity appearing after the solvent peak from Sample solution B

\[
\text{Result} = \left(\frac{r_{\text{UA}}}{r_{\text{UB}}} - 1\right) \times (C_{\text{L}}/C_{\text{U}}) \times 100
\]

\(r_{\text{UA}}\) = peak response from the Sample solution
\(r_{\text{UB}}\) = peak response from the Standard solution

Acceptance criteria: NLT 10.0% each total impurities:

\[
\text{Result} = \left(\frac{r_{\text{UA}}}{r_{\text{UB}}} - 1\right) \times 100
\]

\(r_{\text{UA}}\) = peak response of each impurity appearing after the solvent peak from Sample solution A
\(r_{\text{UB}}\) = 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)