Vinblastine Sulfate

\[
\text{C}_{46}\text{H}_{58}\text{N}_{4}\text{O}_{9} \cdot \text{H}_2\text{SO}_4 \quad 909.07
\]

Vincaleukoblastine, sulfate (1:1) (salt); Vincaleukoblastine sulfate (1:1) (salt) \[143-67-9\].

**DEFINITION**
Vinblastine Sulfate contains NLT 96.0% and NMT 102.0% of \( \text{C}_{46}\text{H}_{58}\text{N}_{4}\text{O}_{9} \cdot \text{H}_2\text{SO}_4 \), corrections being applied for loss in weight.

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

**IDENTIFICATION**

- **A. INFRARED ABSORPTION (197K)**
  - Analysis: The sample specimen and Reference Standard are previously dried in vacuum at 60° for 16 h.
  - Acceptance criteria: Meets the requirements

- **B. IDENTIFICATION TESTS—GENERAL, Sulfate (191)**
  - Sample: 100 mg/mL in water
  - Acceptance criteria: Meets the requirements

**ASSAY**

**Change to read:**

- **PROCEDURE 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 solution: 0.4 mg/mL of Vinblastine Sulfate in water

**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: System suitability solution and Standard solution

**Suitability requirements**

- Resolution: NLT 4.0 between the vincristine and vinblastine, System suitability solution
- Relative standard deviation: NMT 2.0%, Standard solution

**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 in the Assay.
  - Sample solution B: 16 μg/mL of vinblastine sulfate in water from Sample solution A

**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

**Analysis**

- **Samples:** Standard solution and Sample solution
  - Calculate the percentage of vinblastine sulfate \( (\text{C}_{46}\text{H}_{58}\text{N}_{4}\text{O}_{9} \cdot \text{H}_2\text{SO}_4) \) in the portion of Vinblastine Sulfate taken:
  
  \[
  \text{Result} = \left( \frac{\text{r}_U}{\text{r}_S} \right) \times \left( \frac{\text{C}_U}{\text{C}_S} \right) \times 100
  \]

  - \( \text{r}_U \) = peak response from the Sample solution
  - \( \text{r}_S \) = peak response from the Standard solution
  - \( \text{C}_S \) = concentration of USP Vinblastine Sulfate RS in the Standard solution (mg/mL)
  - \( \text{C}_U \) = concentration of Vinblastine Sulfate in the Sample solution (mg/mL)

  **Acceptance criteria:** 96.0%–102.0%, corrections being applied for loss in weight

**SPECIFIC TESTS**

- **PH (791)**
  - Sample: 1.5 mg/mL in water
  - Acceptance criteria: 3.5–5.0

- **Loss on Drying**

(See Thermal Analysis (891).) [NOTE—In this procedure, perform weighings rapidly with minimum exposure of the substances to air.]

- **Sample:** 10 mg
- **Analysis:** Determine the percentage of volatile substances by thermogravimetric analysis on an appropriately calibrated instrument. Heat the Sample at the rate of \( 5^\circ/\text{min} \) between ambient temperature and 200° in an atmosphere of nitrogen at a flow rate of 40 mL/min. From the thermogram, determine the accumulated loss.
in weight between ambient temperature and a point on the plateau before decomposition is indicated (at about 160°C).

Acceptance criteria: It loses NMT 15.0% of its weight.

- **STERILITY Tests (71):** Where the label states that Vinblastine Sulfate is sterile, it meets the requirements.

- **Bacterial Endotoxins Test (85):** Where the label states that Vinblastine Sulfate is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 10.0 USP Endotoxin Units/mg of vinblastine sulfate.

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in tight, light-resistant containers, in a freezer.

- **Labeling:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

**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.**

  - USP Vincristine Sulfate (Assay) RS (88 1-Jul-2011)