Vincristine Sulfate

Change to read:

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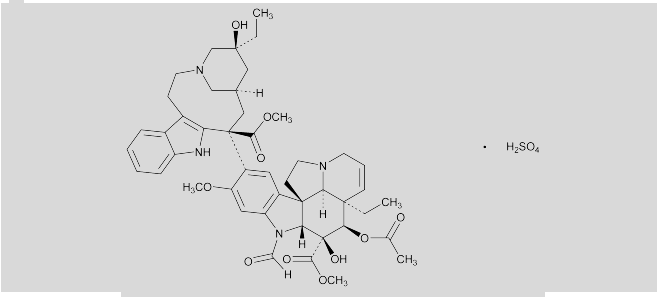

•(RB 1-Jul-2011)

$C_{46}H_{56}N_4O_{10} \cdot H_2SO_4$ 923.04
Vincaleukoblastine, 22-oxo-, sulfate (1:1) (salt);
Leurocristine sulfate (1:1) (salt) [2068-78-2].

DEFINITION

Vincristine Sulfate contains NLT 95.0% and NMT 105.0% of $C_{46}H_{56}N_4O_{10} \cdot H_2SO_4$, calculated on the dried basis.
[**CAUTION—**Handle Vincristine Sulfate with great care because it is a potent cytotoxic agent.]

IDENTIFICATION

Change to read:

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
  •**Standard:** Proceed as directed in the chapter using either USP Vincristine Sulfate RS or USP Vincristine Sulfate (Assay) RS. If USP Vincristine Sulfate (Assay) RS is used, dissolve a portion of it in a mixture of methylene chloride and methanol (3:1). Transfer the supernatant to an open container, and evaporate it at room temperature under nitrogen.
  Acceptance criteria: Meets the requirements• (RB 1-Jul-2011)
- **B. IDENTIFICATION TESTS—GENERAL,** *Sulfate* ⟨**191**⟩
  Sample solution: 100 mg/mL
  Acceptance criteria: Meets the requirements

ASSAY

Change to read:

- **PROCEDURE**
  Solution A: Diethylamine and water (1:59). Adjust with phosphoric acid to a pH of 7.5.
  Mobile phase: Methanol and *Solution A* (70:30)
  Standard solution: •1.2 mg/mL• (RB 1-Jul-2011) of USP Vincristine Sulfate RS •or Vincristine Sulfate (Assay) RS• (RB 1-Jul-2011) in water
  System suitability solution: 1 mg/mL of • • (RB 1-Jul-2011) USP Vinblastine Sulfate RS in the •*Standard solution*• (RB 1-Jul-2011)
  Sample solution: •1.2 mg/mL• (RB 1-Jul-2011) of Vincristine Sulfate in water. Equilibrate a portion of Vincristine Sulfate for 30 min in ambient humidity. Using another portion of the equilibrated specimen, determine the loss on drying as directed for USP Vincristine Sulfate RS.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 297 nm
  Precolumn: Porous silica gel packing
  Guard column: 2- to 5-cm; packing L1
  Column: 4.6-mm × 25-cm; packing L7
  Flow rate: 1.5 mL/min
  Injection size: 10 µL
  System suitability
  Samples: *System suitability solution* and *Standard solution*
  Suitability requirements
  Resolution: NLT 4.0 between vincristine sulfate and vinblastine sulfate, *System suitability solution*. [NOTE—For a particular column, the resolution may be increased by increasing the proportion of water in the *Mobile phase*.]
  Relative standard deviation: NMT 2.0%, *Standard solution*
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of vincristine sulfate ($C_{46}H_{56}N_4O_{10} \cdot H_2SO_4$) in the portion of Vincristine Sulfate 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 the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0% on the dried basis

IMPURITIES

- **ORGANIC IMPURITIES**
  Solution A: Diethylamine and water (3:197). Adjust with phosphoric acid to a pH of 7.5.
  Solution B: Methanol
  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	38	62
12	38	62
27	8	92
29	38	62
34	38	62

Standard solution, System suitability solution, and **System suitability:** Proceed as directed in the *Assay*.
Sample solution A: Proceed as directed for the *Sample solution* in the *Assay*.
Sample solution B: 0.04 mg/mL of vincristine sulfate from *Sample solution A* in water
Chromatographic system: Proceed as directed in the *Assay*, except to use a *Flow rate* of 2 mL/min and 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 Vincristine Sulfate taken:

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

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

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Calculate the percentage of total impurities in the portion of Vincristine Sulfate taken:

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

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

Acceptance criteria
Individual impurities: NMT 1.0%
Total impurities: NMT 4.0%

SPECIFIC TESTS

- **pH** ⟨**791**⟩
Sample solution: 1 mg/mL
Acceptance criteria: 3.5–4.5
- **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°/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°)
Acceptance criteria: It loses NMT 12.0% of its weight.

ADDITIONAL REQUIREMENTS

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

Change to read:

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

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