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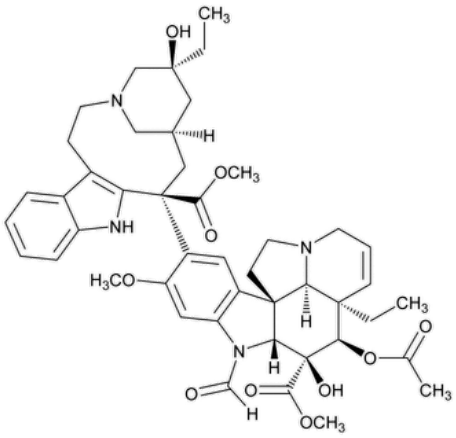
Vincristine Sulfate



• H_2SO_4

$C_{46}H_{56}N_4O_{10} \cdot H_2SO_4$ 923.04

Vincaleukoblastine, 22-oxo-, sulfate (1:1) (salt);

Leurocristine sulfate (1:1) (salt) CAS RN®: 2068-78-2; UNII: T5IRO3534A.

DEFINITION

Vincristine Sulfate contains NLT 95.0% and NMT 105.0% of vincristine sulfate ($C_{46}H_{56}N_4O_{10} \cdot H_2SO_4$), calculated on the dried basis.

[**Caution—**Handle vincristine sulfate with great care because it is a potent cytotoxic agent.]

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K

▲▲ (USP 1-Dec-2020)

• **B. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Sulfate***

Sample solution: 100 mg/mL

Acceptance criteria: Meets the requirements

• **C.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

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 of USP Vincristine Sulfate RS▲▲ (USP 1-Dec-2020) in water

System suitability solution: 1 mg/mL of USP Vinblastine Sulfate RS in the *Standard solution*. [Note—No loss on drying determination is needed for USP Vinblastine Sulfate RS.]

Sample solution: 1.2 mg/mL 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.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 297 nm

Columns

Precolumn: Porous silica gel packing

Guard: 2- to 5-cm; packing L1

Analytical: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solution* and *System suitability solution*

Suitability requirements

Resolution: NLT 4.0 between the vincristine sulfate and vinblastine sulfate peaks, *System suitability solution*▲▲ (USP 1-Dec-2020)

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 of vincristine sulfate from the *Sample solution*

r_S = peak response of vincristine sulfate from the *Standard solution*

C_S = concentration of USP Vincristine Sulfate RS▲▲ (USP 1-Dec-2020) in the *Standard solution* (mg/mL)

C_U = concentration of Vincristine Sulfate in 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

Sample solution A: Prepare as directed for the *Sample solution* in the *Assay*.

Sample solution B: 0.04 mg/mL of Vincristine Sulfate in water, from *Sample solution A*

Chromatographic system: Proceed as directed in the *Assay*, except for the *Flow rate* and *Injection volume*.

Flow rate: 2 mL/min

Injection volume: 200 µL

Analysis

Samples: *Sample solution A* and *Sample solution B*

Calculate the percentage of each impurity in the portion of Vincristine Sulfate taken:

$$\text{Result} = [r_{UA}/(\Sigma r_{UA} + 30r_{UB})] \times 100$$

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*

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

$$\text{Result} = [\Sigma r_{UA}/(\Sigma r_{UA} + 30 r_{UB})] \times 100$$

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: NMT 12.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. 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 1-Dec-2020)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
VINCRISTINE SULFATE	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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