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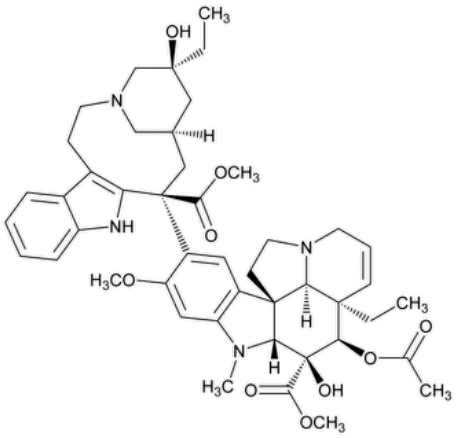
Vinblastine Sulfate



• H_2SO_4

$C_{46}H_{58}N_4O_9 \cdot H_2SO_4$ 909.06

Vincaleukoblastine, sulfate (1:1) (salt);

Vincaleukoblastine sulfate (1:1) (salt) CAS RN®: 143-67-9; UNII: N00W22YO2B.

DEFINITION

Vinblastine Sulfate contains NLT 96.0% and NMT 102.0% of vinblastine sulfate ($C_{46}H_{58}N_4O_9 \cdot H_2SO_4$), corrections being applied for loss in weight.

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

IDENTIFICATION

Change to read:

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

Analysis: The sample specimen and Reference Standard are previously dried under vacuum at 60° for 16 h.

Acceptance criteria: Meets the requirements ▲of 197K or 197A▲ (USP 1-Dec-2020)

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

Sample: 10 mg/mL in water

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 (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 of USP Vincristine Sulfate RS in *Standard solution*.▲ (USP 1-Dec-2020) [Note—No loss on drying determination is needed for USP Vincristine Sulfate RS.]

Sample solution: 0.4 mg/mL of Vinblastine Sulfate in water. Equilibrate a portion of Vinblastine 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 262 nm

Columns

Precolumn: Packed with porous silica gel; installed between the pump and the injector

Analytical: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 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 0.73%, *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 taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of vinblastine from the *Sample solution*

r_S = peak response of vinblastine from the *Standard solution*

C_S = concentration of USP Vinblastine Sulfate RS in the *Standard solution* (mg/mL)

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

IMPURITIES

• **Organic Impurities**

Mobile phase, Standard solution, System suitability solution, and **System suitability:** Proceed 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

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

Mode: LC

Detector: UV 262 nm

Columns

Precolumn: Packed with porous silica gel; installed between the pump and the injector

Analytical: 4.6-mm × 15-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection volume: 200 µL (20 µL for *System suitability*)

Analysis

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

Calculate the percentage of each individual impurity in the portion of Vinblastine Sulfate taken:

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

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

r_{UB} = peak response of vinblastine from *Sample solution B*

Calculate the percentage of total impurities:

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

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

r_{UB} = peak response of vinblastine from *Sample solution B*

Acceptance criteria

Individual impurities: NMT 1.0%

Total impurities: NMT 3.0%

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°/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 (about 160°).

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, and store 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 Vinblastine Sulfate RS

USP Vincristine Sulfate RS

[Note—No loss on drying determination is needed ▲for 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
VINBLASTINE 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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