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Vincristine Sulfate for Injection

Change to read:

DEFINITION

Vincristine Sulfate for Injection is a sterile mixture of Vincristine Sulfate with suitable diluents. It contains NLT 90.0% and NMT 110.0% of the labeled amount of vincristine sulfate ($C_{46}H_{56}N_4O_{10} \cdot H_2SO_4$).

[**Caution—**Handle ▲vincristine sulfate▲ (USP 1-Aug-2022) with great care because it is a potent cytotoxic agent.]

IDENTIFICATION

• **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

Standard solution: 10 mg/mL of USP Vincristine Sulfate RS in methylene chloride and methanol (3:1)

Sample stock solution: 25 mg/mL of vincristine sulfate in water, from Vincristine Sulfate for Injection

Sample solution: 10 mg/mL of vincristine sulfate in methanol, from *Sample stock solution*

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 20 µL

Developing solvent system: Fresh ether, methanol, and methylamine solution (2 in 5) (19:2:1)

Spray reagent: Dissolve 2.0 g of ceric ammonium sulfate in 100 mL of water with heating and stirring, and slowly add 100 mL of phosphoric acid. Filter if necessary.

Analysis

Samples: *Standard solution* and *Sample solution*

Develop the chromatographic plate in a methanol prewash tank; for maximum sensitivity, dry NMT 2 h before use. Score the plate about 15 cm above the points of application. Apply the *Standard solution* and the *Sample solution* at points about 2.5 cm from the lower edge of the plate, and dry thoroughly (a current of cool air may be used to help dry the spots). Place the plate in the nonequilibrated developing chamber that contains a paper liner around the back and sides and *Developing solvent system* to a depth of about 2 cm. Remove the plate when the solvent moves to the scored line (about 80 min), and discard the solvent system. Dry the plate in a fume hood at room temperature, heat on a metal plate on a steam bath for about 15 min, and spray the plate while still hot with *Spray reagent*. Continue heating the plate for 15 min to stabilize the spots.

Acceptance criteria: The R_F value and the color of the principal spot from the *Sample solution* correspond to those from the *Standard solution*.

• **B.** 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**

▲Buffer▲ (USP 1-Aug-2022) : Diethylamine and water (1:59). Adjust with phosphoric acid to a pH of 7.5.

Mobile phase: Methanol and ▲*Buffer▲ (USP 1-Aug-2022)* (70:30)

Standard solution: 1.2 mg/mL of USP Vincristine Sulfate RS 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: Nominally 1.2 mg/mL of vincristine sulfate in water, from Vincristine Sulfate for Injection

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 vincristine▲ (USP 1-Aug-2022) and vinblastine▲ (USP 1-Aug-2022), *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of vincristine sulfate ($C_{46}H_{56}N_4O_{10} \cdot H_2SO_4$) in the portion of Vincristine Sulfate for Injection taken:

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

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

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

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

C_U = nominal concentration of vincristine sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Uniformity of Dosage Units ⟨905⟩:** ▲Meets the requirements▲ (USP 1-Aug-2022)

IMPURITIES

Change to read:

• **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: Nominally 1 mg/mL of vincristine sulfate in water, from Vincristine Sulfate for Injection

Sample solution B: Nominally 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 ▲individual▲ (USP 1-Aug-2022) impurity in the portion of Vincristine Sulfate for Injection taken:

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

r_{UA} = peak response of each ▲individual▲ (USP 1-Aug-2022) 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 for Injection taken:

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

r_{UA} = peak response of each ▲individual▲ (USP 1-Aug-2022) 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 2.0%

Total impurities: NMT 5.0%

SPECIFIC TESTS

Change to read:

• **Bacterial Endotoxins Test ⟨85⟩:** ▲Meets the requirements▲ (USP 1-Aug-2022)

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **Constituted Solution:** At the time of use, it meets the requirements for *Injections and Implanted Drug Products ⟨1⟩, Product Quality Tests Common to Parenteral Dosage Forms, Specific Tests, Completeness and clarity of solutions*.

• **Other Requirements:** It meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*, and store in a refrigerator.

Change to read:

• **Labeling:** ▲Label to indicate:▲ (USP 1-Aug-2022) "For Intravenous Use Only—Fatal If Given By Other Routes."

Where labeled as containing more than 2 mg, it must also be labeled as a Pharmacy Bulk Package (see *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*). ▲▲ (USP 1-Aug-2022) When packaged in a Pharmacy Bulk Package, it is exempt from the requirement in ▲*Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for Constitution*▲ (USP 1-Aug-2022) that the closure be penetrated only one time after constitution with a suitable sterile transfer device or dispensing set, when it contains a suitable substance or mixture of substances to prevent the growth of microorganisms.

When dispensed, the container ▲▲ (USP 1-Aug-2022) (holding the individual dose prepared for administration to the patient) must ▲bear▲ (USP 1-Aug-2022) the statement▲: ▲ (USP 1-Aug-2022) "For Intravenous Use Only—Fatal If Given By Other Routes."

• **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

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

Topic/Question	Contact	Expert Committee
VINCRISTINE SULFATE FOR INJECTION	Documentary Standards Support	SM32020 Small Molecules 3

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

Chromatographic Database Information: Chromatographic Database

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