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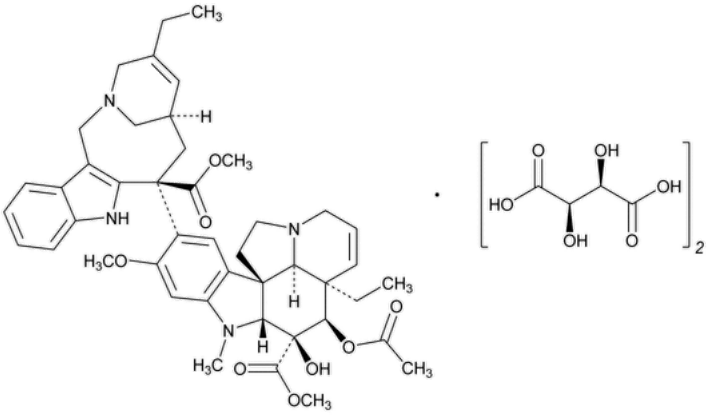
Vinorelbine Tartrate



$C_{45}H_{54}N_4O_8 \cdot 2C_4H_6O_6$ 1079.11

8'-Norvincaleukoblastine,3',4'-didehydro-4'-deoxy-,[*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:2) (salt);

3',4'-Didehydro-4'-deoxy-8'-norvincaleukoblastine L-(+)-tartrate (1:2) (salt) CAS RN®: 125317-39-7; UNII: 253GQW851Q.

DEFINITION

Vinorelbine Tartrate contains NLT 98.0% and NMT 102.0% of $C_{45}H_{54}N_4O_8 \cdot 2C_4H_6O_6$, calculated on the anhydrous basis.

[**Caution—**Vinorelbine Tartrate is cytotoxic. Great care should be taken to prevent inhaling particles and exposing the skin to it.]

IDENTIFICATION

Change to read:

- **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

  Sample: Dissolve 10 mg in 5 mL of water, add 0.5 mL of 5 N sodium hydroxide, and extract with 5 mL of methylene chloride. Filter the organic extract through anhydrous sodium sulfate, and evaporate the organic extract to a volume of about 0.5 mL.

  Acceptance criteria: Meets the requirements

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

- **C.**

  Sample solution: Equivalent to 15 mg/mL of tartaric acid in water

  Analysis: To 0.1 mL of the *Sample solution* add 0.1 mL of 100 mg/mL of potassium bromide, 0.1 mL of 20 mg/mL of resorcinol, and 3 mL of sulfuric acid. Heat on a hot water bath for 5–10 min until a dark blue color develops. Allow to cool, and pour the solution into water.

  Acceptance criteria: The color changes to red (presence of tartrate).

ASSAY

- **Procedure**

  Buffer: Dissolve 6.9 g of monobasic sodium phosphate in 900 mL of water. Adjust with phosphoric acid to a pH of 4.2, and dilute with water to 1000 mL.

  Mobile phase: Dissolve 1.22 g of sodium 1-decanesulfonate in 620 mL of methanol, and add 380 mL of *Buffer*.

  System suitability solution: Prepare a solution containing 1.4 mg/mL of USP Vinorelbine Tartrate RS and 0.01 mg/mL of USP Vinorelbine Related Compound A RS in water. Expose a portion of this solution in a suitable xenon lamp apparatus capable of supplying a dose of 1600 KJ/m^2 between 310 and 800 nm at a power of 500 W/m^2 for 1 h to generate an additional photodegradation product, 3,6-epoxy vinorelbine.

  Standard solution: 1.4 mg/mL of USP Vinorelbine Tartrate RS in *Mobile phase*

  Sample solution: 1.4 mg/mL of Vinorelbine Tartrate in *Mobile phase*

  Chromatographic system

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

  Mode: LC

  Detector: UV 267 nm

  Column: 3.9-mm × 15-cm; 5-µm packing L1

  Column temperature: 40°

  Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between vinorelbine and vinorelbine related compound A, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of vinorelbine tartrate ($C_{45}H_{54}N_4O_8 \cdot 2C_4H_6O_6$) in the portion of Vinorelbine Tartrate taken:

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

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

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

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

C_U = concentration of Vinorelbine Tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Buffer, Mobile phase, System suitability solution, Sample solution, and **System suitability:** Proceed as directed in the *Assay*.

Standard stock solution: Use the *Standard solution* as prepared in the *Assay*.

Standard solution: 0.28 µg/mL of vinorelbine tartrate in *Mobile phase*, from *Standard stock solution*

Chromatographic system: Proceed as directed in the *Assay*, except use a run time of NLT three times the retention time of vinorelbine.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Vinorelbine Tartrate taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity from the *Sample solution*

r_T = sum of the responses of all the peaks from the *Sample solution*

Acceptance criteria: See *Table 1*.

[Note—Disregard any peaks with an area less than or equal to one-half of the area of the peak for vinorelbine in the *Standard solution*.]

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
3,6-Epoxy vinorelbine[a]	0.8	0.3
Vinorelbine	1.0	—
Vinorelbine related compound A[b]	1.2	0.2
Any unspecified impurity[c]	—	0.2
Total Impurities[d]	—	0.7

[a] 3',4',7,8-Tetradehydro-3,4'-dideoxy-3,6-epoxy-6,7-dihydro-8'-norvincaleukoblastine.

[b] 4-*O*-Deacetylvinorelbine.

[c] Any individual impurity or coeluted impurities comprising an individual peak.

[d] Excluding 3,6-epoxy vinorelbine.

SPECIFIC TESTS

- **Clarity of Solution**

  Sample solution: Equivalent to 10 mg/mL of anhydrous vinorelbine in water from Vinorelbine Tartrate

  Acceptance criteria: The solution is clear.

- **Color of Solution**

  Sample solution: Equivalent to 10 mg/mL of anhydrous vinorelbine in water from Vinorelbine Tartrate

  Analysis: Determine the absorbance of the *Sample solution* in a 1-cm cell at 420 nm in a suitable spectrophotometer, using water as the blank.

  Acceptance criteria: NMT 0.03

- **pH** ⟨791⟩**:** 3.3–3.8, in a 10-mg/mL solution
- **Water Determination,** *Method Ia*⟨921⟩**:** NMT 4.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store in a freezer.
- **USP Reference Standards** ⟨11⟩

  USP Vinorelbine Related Compound A RS

  4-*O*-Deacetylvinorelbine tartrate.

  $C_{43}H_{52}N_4O_7 \cdot 2C_4H_6O_6$ 1037.07

  USP Vinorelbine Tartrate RS

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

Topic/Question	Contact	Expert Committee
VINORELBINE TARTRATE	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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