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Etoposide Capsules

DEFINITION
Etoposide Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of etoposide ($C_{29}H_{32}O_{13}$).

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

IDENTIFICATION

Change to read:

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

Sample: Transfer a suitable quantity of the contents of Capsules, equivalent to 100 mg of etoposide, to a separator containing 100 mL of water. Extract twice with 20-mL portions of chloroform, separate and combine the organic layers, dry over anhydrous sodium sulfate, and filter. Transfer the dried filtrate to a second separator, extract with 30 mL of water, and allow the layers to separate. Drain the chloroform layer through a bed of anhydrous sodium sulfate contained in a filter funnel into a round-bottom flask, and evaporate the chloroform at a temperature of 30 ± 5° using a rotary evaporator. Dissolve the oily residue obtained in 5 mL of water, shake gently, and allow to stand for 30 min. Filter, collecting the precipitate formed on a glass filter funnel, wash the precipitate with three 20-mL portions of water, and allow the precipitate to dry on the filter for about 90 min in a vacuum oven at 40°. Prepare a dispersion of the precipitate in potassium bromide at a ratio of 1 in 100.

Acceptance criteria: Meet 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.*

ASSAY

• **Procedure**

Buffer: 2.72 g/L of sodium acetate in water. Adjust with glacial acetic acid to a pH of 4.0.

Mobile phase: Acetonitrile and *Buffer* (26:74)

System suitability solution: 0.3 mg/mL of USP Etoposide Resolution Mixture RS in *Mobile phase*

Standard stock solution: 2.0 mg/mL of USP Etoposide RS in acetonitrile

Standard solution: 0.2 mg/mL of USP Etoposide RS in *Mobile phase* from the *Standard stock solution*

Sample stock solution: Transfer a sufficient number of Capsules, equivalent to 500 mg of etoposide, to a 500-mL volumetric flask, add about 400 mL of *Mobile phase*, and stir using a magnetic bar for about 15 min, followed by sonication for about 1 h with occasional shaking. Cool, dilute with *Mobile phase* to volume, stir for an additional 5 min, and filter.

Sample solution: Equivalent to 0.2 mg/mL of Etoposide in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L11

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 1.5 times the retention time of etoposide

System suitability

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

Suitability requirements

Resolution: NLT 1.35 between the etoposide and α-etoposide peaks, *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 etoposide ($C_{29}H_{32}O_{13}$) in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: pH 4.5 acetate buffer; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Buffer: 2.72 g/L of sodium acetate in water. Adjust with acetic acid to a pH of 4.0.

Mobile phase: Acetonitrile and *Buffer* (26:74)

Standard solution: 55 µg/mL of USP Etoposide RS prepared as follows. Transfer a quantity of USP Etoposide RS to a suitable volumetric flask, and dissolve with sonication in methanol equivalent to 2% of the final volume. Dilute with *Medium* to volume.

Sample solution: Withdraw a 10-mL aliquot from the dissolution vessel.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 3.9-mm × 30-cm; packing L11

Flow rate: 2 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of etoposide ($C_{29}H_{32}O_{13}$) dissolved.

Tolerances: NLT 80% (*Q*) of the labeled amount of etoposide ($C_{29}H_{32}O_{13}$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Organic Impurities**

Buffer: Prepare as directed in the *Assay*.

Solution A: Acetonitrile and *Buffer* (20:80)

Solution B: Acetonitrile and *Buffer* (60:40)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
15	100	0
30	40	60
40	40	60
42	0	100
45	0	100
47	100	0
50	100	0

Diluent: Acetonitrile and 0.02 M sodium acetate previously adjusted with acetic acid to a pH of 4.0 (30:70)

Standard stock solution: 2.0 mg/mL of USP Etoposide RS in *Diluent*

System suitability stock solution: 0.2 mg/mL of *n*-propylparaben in *Diluent*

System suitability solution: Transfer 5.0 mL of the *System suitability stock solution* and 5.0 mL of the *Standard stock solution* to a 50-mL volumetric flask, and dilute with *Diluent* to volume. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, and dilute with *Diluent* to volume.

Standard solution: 10 µg/mL of USP Etoposide RS from the *Standard stock solution* in *Diluent*

Sample solution: Nominally equivalent to 2.0 mg/mL of etoposide in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 15-cm; less than 5-µm packing L11

Flow rate: 1.5 mL/min

Injection volume: 25 µL

Run time: NLT 40 min

System suitability

Run time is 15 min under isocratic conditions.

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 1.1 between propylparaben and etoposide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Capsules taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Etoposide	1.0	—
Picroetoposide	1.43	2.0
Any unspecified impurity	—	—
Total impurities	—	3.0

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers in a cold place. Do not freeze.
- **USP Reference Standards ⟨11⟩**
  USP Etoposide RS
  USP Etoposide Resolution Mixture RS

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

We apologize for the inconvenience. The exact auxiliary information for this Documentary Standard is currently unavailable. Please contact Documentary Standards Support (stdsmonographs@usp.org) for assistance during this time.

Chromatographic Database Information: Chromatographic Database

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