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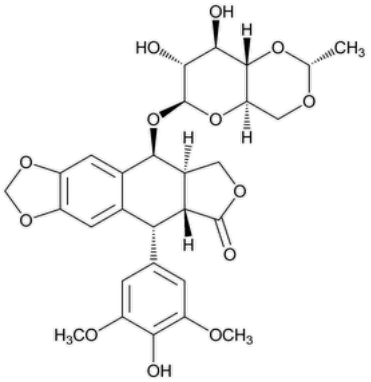
Etoposide



$C_{29}H_{32}O_{13}$ 588.56

Furo[3',4':6,7]naphtho[2,3-*d*]-1,3-dioxol-6(5a*H*)-one-, 9-[(4,6-*O*-ethylidene-β-D-glucopyranosyl)oxy]5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl), [5*R*-[5α,5aβ,8aα,9β(*R**)]]-;

4'-Demethylepipodophyllotoxin 9-[4,6-*O*-(*R*)-ethylidene-β-D-glucopyranoside] CAS RN®: 33419-42-0; UNII: 6PLQ3CP4P3.

DEFINITION

Etoposide contains NLT 95.0% and NMT 105.0% of etoposide ($C_{29}H_{32}O_{13}$), calculated on the anhydrous basis.

[CAUTION—Etoposide is potentially 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)

• **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: 2.0 mg/mL of Etoposide in acetonitrile

Sample solution: 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 etoposide ($C_{29}H_{32}O_{13}$) in the portion of Etoposide 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 = concentration of Etoposide in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0% on the anhydrous basis

IMPURITIES

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

[Note—Run time is 15 min in 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 Etoposide 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 = concentration of Etoposide in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Lignan P	0.20	0.5
Etoposide	1.0	—
Picroetoposide	1.43	1.0
Any unspecified impurity	—	—
Total impurities	—	2.0

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩
  Sample solution: 5 mg/mL in chloroform and methanol (9:1)
  Acceptance criteria: −110° to −118° (*t* = 20°)
- **Water Determination,** *Method I* ⟨921⟩**:** NMT 6.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **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.

Topic/Question	Contact	Expert Committee
ETOPOSIDE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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