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Teniposide Injection

DEFINITION

Teniposide Injection contains NLT 90.0% and NMT 110.0% of the labeled amount of teniposide ($C_{32}H_{32}O_{13}S$). It is a sterile solution in a nonaqueous medium and may contain benzyl alcohol or other suitable preservatives.

[**Caution—**Great care should be taken in handling teniposide, because it is a cytotoxic agent.]

IDENTIFICATION

• **A.** 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**

Solution A: Acetonitrile and water (25:75)

Solution B: Acetonitrile and water (56:44)

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system for 10 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
4	100	0
16	64.5	35.5
36	64.5	35.5
60	0	100
90	0	100

Diluent: Acetonitrile and 5 µM monobasic potassium phosphate (1:1)

Standard solution: 0.4 mg/mL of USP Teniposide RS in *Diluent*, prepared as follows. Transfer a known amount of USP Teniposide RS into a suitable volumetric flask and add acetonitrile equivalent to 10% of the final volume. Dissolve with the aid of sonication and dilute with *Diluent* to volume.

Sample solution: Nominally equivalent to 0.4 mg/mL of teniposide in *Diluent,* prepared as follows. Dilute a portion of the Injection with *Diluent* to obtain a solution containing 0.4 mg/mL of teniposide.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 5-µm packing L11

Flow rate: 1.3 mL/min

Injection volume: 10 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 teniposide ($C_{32}H_{32}O_{13}S$) in the portion of Injection taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

Solution A, Solution B, Diluent, and **Sample solution:** Proceed as directed in the *Assay*.

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system for 10 min. [Note—The duration of initial isocratic hold may be adjusted from 4 min to up to 10 min to meet the resolution requirements and to achieve the retention time of the teniposide peak to about 35 min.]

Benzaldehyde stock solution: 0.15 mg/mL of USP Benzaldehyde RS in *Diluent*

Teniposide related compound A stock solution: 0.15 mg/mL of USP Teniposide Related Compound A RS, prepared as follows. Transfer USP Teniposide Related Compound A RS to a suitable volumetric flask, add acetonitrile equivalent to 20% of the final volume, and sonicate to dissolve. Dilute with *Diluent* to volume.

System suitability solution 1: 15 µg/mL each of USP Teniposide Related Compound A RS and USP Benzaldehyde RS in *Diluent* from *Teniposide related compound A stock solution* and *Benzaldehyde stock solution*

System suitability solution 2: Use the *Standard solution* in the *Assay*. [Note—USP Teniposide RS contains a small amount of *R*-3-thienylidene regioisomer.]

Chromatographic system: Proceed as directed in the *Assay*, except for the *Detectors*.

Detectors

UV 242 nm: For thiophenealdehyde

UV 220 nm: For all other impurities

System suitability

Samples: *System suitability solution 1* and *System suitability solution 2*

[Note—The relative retention times for benzaldehyde, teniposide related compound A, *R*-3-thienylidene regioisomer, and teniposide are about 0.42, 0.43, 0.97, and 1.0, respectively.]

Suitability requirements

Resolution 1: NLT 0.9 between benzaldehyde and teniposide related compound A, *System suitability solution 1*

Resolution 2: NLT 1.2 between *R*-3-thienylidene regioisomer and teniposide peaks, *System suitability solution 2*

Analysis

Sample: *Sample solution*

Calculate the percentage of each specified degradation product in the portion of Injection taken:

$$\text{Result} = r_U/\{\Sigma[r_U \times (1/F)] + r_T\} \times (1/F) \times 100$$

r_U = peak area of each specified degradation product from the *Sample solution* at 242 nm for thiophenealdehyde and 220 nm for all other impurities

F = relative response factor for each individual impurity (see *Table 2*)

r_T = peak area of teniposide from the *Sample solution* at 220 nm

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lignan P[a]	0.16	1.0	2.5
Thiophenealdehyde[b]	0.28	1.2	0.5
Teniposide	1.0	—	—
Picroteniposide[c]	1.11	1.0	0.25
Total specified degradation products	—	—	3.0

[a] 4'-Demethylepipodophyllotoxin 9-β-D-glucopyranoside.

[b] Thiophene-2-carbaldehyde. It is quantitated at 242 nm.

[c] (5*R*,5a*S*,8a*R*,9*S*)-9-[4,6-*O*-(*R*)-2-Thenylidene-β-D-glucopyranosyloxy]-5,8,8a,9-tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)furo[3',4':6,7]naphtho[2,3-*d*]-1,3-dioxol-6(5a*H*)-one.

SPECIFIC TESTS

- **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 1.5 USP Endotoxin Units/mg of teniposide.
- **Sterility Tests ⟨71⟩:** Meets the requirements
- **pH ⟨791⟩**

  Sample solution: Dilute 5 mL of Injection with 45 mL of water.

  Acceptance criteria: 4.0–6.5
- **Particulate Matter in Injections ⟨788⟩:** It meets the requirements for small-volume injections.
- **Other Requirements:** It meets the requirements in *Injections and Implanted Drug Products ⟨1⟩*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Store under refrigeration and protect from light.
- **Labeling:** Label it to indicate that the Injection is to be diluted with a suitable parenteral vehicle prior to intravenous infusion.
- **USP Reference Standards ⟨11⟩**

  USP Benzaldehyde RS

  USP Teniposide RS

  USP Teniposide Related Compound A RS

  4'-Demethylepipodophyllotoxin.

  $C_{21}H_{20}O_8$ 400.38

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

Topic/Question	Contact	Expert Committee
TENIPOSIDE INJECTION	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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