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Add the following:

## ^Etoposide Phosphate for Injection

### DEFINITION

Etoposide Phosphate for Injection is sterile, lyophilized powder of Etoposide Phosphate and suitable added substances. It contains NLT 90% and NMT 105% of the labeled amount of etoposide phosphate ( $C_{29}H_{33}O_{16}P$ ).

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

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

### ASSAY

#### • PROCEDURE

**Solution A:** 2.3 g/L of [ammonium phosphate, monobasic](#) in [water](#)

**Mobile phase:** [Acetonitrile](#) and *Solution A* (15:85). Adjust with [phosphoric acid](#) to a pH of 2.5.

**Standard solution:** 0.24 mg/mL of [USP Etoposide Phosphate RS](#) in *Mobile phase*. Sonicate to assist with dissolution.

**Sample solution:** Nominally equivalent to 0.24 mg/mL of etoposide phosphate in *Mobile phase* from Etoposide Phosphate for Injection. Sonicate to assist with dissolution.

#### Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

**Mode:** LC

**Detector:** UV 230 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.

**Column:** 4.6-mm × 15-cm; 5-μm packing [L11](#)

**Flow rate:** 1.5 mL/min

**Injection volume:** 25 μL

#### System suitability

**Sample:** *Standard solution*

#### Suitability requirements

**Tailing factor:** NMT 1.5

**Relative standard deviation:** NMT 1.0%

#### Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of etoposide phosphate ( $C_{29}H_{33}O_{16}P$ ) in the portion of Etoposide Phosphate for Injection taken:

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

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

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

$C_S$  = concentration of [USP Etoposide Phosphate RS](#) in the *Standard solution* (mg/mL)

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

**Acceptance criteria:** 90%–105%

**PERFORMANCE TESTS**

- **UNIFORMITY OF DOSAGE UNITS (905):** Meets the requirements

**IMPURITIES**

• **ORGANIC IMPURITIES**

**Mobile phase, Sample solution, and Chromatographic system:** Proceed as directed in the Assay.

**Standard stock solution A:** Use the *Standard solution* in the Assay.

**Standard solution A:** 2.4 µg/mL of [USP Etoposide Phosphate RS](#) in *Mobile phase*, from *Standard stock solution A*

**Standard stock solution B:** 0.024 mg/mL of [USP Etoposide RS](#) in [acetonitrile](#)

**Standard solution B:** 4.8 µg/mL of [USP Etoposide RS](#) in *Mobile phase*

**Sensitivity solution:** 0.24 µg/mL of [USP Etoposide Phosphate RS](#) in *Mobile phase*, from *Standard solution A*

**System suitability**

**Samples:** *Standard solution A, Standard solution B, and Sensitivity solution*

**Suitability requirements**

**Relative standard deviation:** NMT 10% for etoposide phosphate and etoposide, *Standard solution A* and *Standard solution B*

**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*

**Analysis**

**Samples:** *Sample solution, Standard solution A, and Standard solution B*

Calculate the percentage of etoposide in the portion of Etoposide Phosphate for Injection taken:

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

$r_U$  = peak area of etoposide from the *Sample solution*

$r_S$  = peak area of etoposide from *Standard solution B*

$C_S$  = concentration of [USP Etoposide RS](#) in *Standard solution B* (mg/mL)

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

Calculate the percentage of lignan P phosphate and each individual unspecified impurity in the portion of Etoposide Phosphate for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

$r_U$  = peak area of lignan P phosphate and each individual unspecified impurity from the *Sample solution*

$r_S$  = peak area of etoposide phosphate from *Standard solution A*

$C_S$  = concentration of [USP Etoposide Phosphate RS](#) in *Standard solution A* (mg/mL)

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

$F$  = relative response factor (see [Table 1](#))

**Acceptance criteria:** See [Table 1](#).

**Table 1**

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Lignan P phosphate <sup>a</sup>	0.6	0.94	2.5
Etoposide phosphate	1.0	—	—
Etoposide	3.9	—	3.0

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Any individual unspecified impurity	—	1.0	0.3
Total impurities	—	—	6

<sup>a</sup> (5*R*,5*aR*,8*aR*,9*S*)-9-[β-*D*-Glucopyranosyloxy]-5,8,8*a*,9-tetrahydro-5-[3,5-dimethoxy-4-(phosphonooxy)phenyl]furo[3',4':6,7]naphtho[2,3-*d*]-1,3-dioxol-6(5*aH*)-one.

#### SPECIFIC TESTS

- **BACTERIAL ENDOTOXINS TEST** (85): Meets the requirements
- **STERILITY TESTS** (71): Meets the requirements
- **PARTICULATE MATTER IN INJECTIONS** (788): Meets the requirements for small-volume injections
- **pH** (791):  
**Sample solution:** A constituted solution prepared as directed in the labeling  
**Acceptance criteria:** 4.0–5.0
- **OTHER REQUIREMENTS:** Meets the requirements in *Injections and Implanted Drug Products* (1).

#### ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve as directed in *Packaging and Storage Requirements* (659), *Injection Packaging, Packaging for Constitution*. Store at 2°–8° and protect from light.

- **USP REFERENCE STANDARDS** (11).

[USP Etoposide RS](#)

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

C<sub>29</sub>H<sub>32</sub>O<sub>13</sub> 588.56

[USP Etoposide Phosphate RS](#)▲ (USP 1-Dec-2021)

**Auxiliary Information** - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
ETOPOSIDE PHOSPHATE FOR INJECTION	<a href="#">Documentary Standards Support</a>	SM32020 Small Molecules 3

**Chromatographic Database Information:** [Chromatographic Database](#)

#### Most Recently Appeared In:

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