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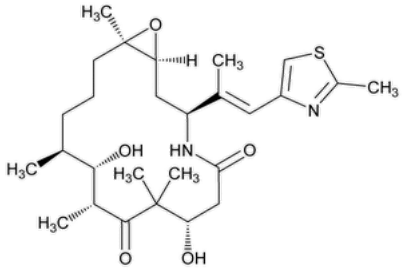
Ixabepilone



$C_{27}H_{42}N_2O_5S$ 506.70

17-Oxa-4-azabicyclo[14.1.0]heptadecane-5,9-dione, 7,11-dihydroxy-8,8,10,12,16-pentamethyl-3-[(1*E*)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (1*S*,3*S*,7*S*,10*R*,11*S*,12*S*,16*R*)-;
(1*S*,3*S*,7*S*,10*R*,11*S*,12*S*,16*R*)-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[(*E*)-1-(2-methylthiazol-4-yl)prop-1-en-2-yl]-17-oxa-4-azabicyclo[14.1.0]heptadecane-5,9-dione. CAS RN®: 219989-84-1.

DEFINITION

Ixabepilone contains NLT 97.5% and NMT 102.0% of ixabepilone ($C_{27}H_{42}N_2O_5S$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 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 stock solution: 100 mM tris(hydroxymethyl)aminomethane in water prepared as follows. Dissolve 12.1 g of tris(hydroxymethyl)aminomethane in 1 L of water and adjust to a pH of 8.5.

Buffer: 5 mM tris(hydroxymethyl)aminomethane in water, from *Buffer stock solution*

Solution A: Acetonitrile and *Buffer* (10:90)

Solution B: Acetonitrile and *Buffer* (90:10)

Mobile phase: See *Table 1*. Return to original conditions and re-equilibrate the system for 6 min.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
2.5	70	30
10	60.6	39.4
20	35	65
22	12.5	87.5
25	12.5	87.5

Standard solution: 1.0 mg/mL of USP Ixabepilone RS in acetonitrile. Sonicate to assist the dissolution.

Sample solution: 1.0 mg/mL of Ixabepilone in acetonitrile. Sonicate to assist the dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Autosampler temperature: 4°

Flow rate: 1.8 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.8–1.5

Relative standard deviation: NMT 1.0% for six injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ixabepilone ($C_{27}H_{42}N_2O_5S$) in the portion of Ixabepilone 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 Ixabepilone RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 97.5%–102.0% on the anhydrous basis

IMPURITIES

• **Organic Impurities**

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

System suitability solution: 1.0 mg/mL of USP Ixabepilone System Suitability Mixture RS in acetonitrile. Sonicate to assist the dissolution.

Sensitivity solution: 0.3 µg/mL of USP Ixabepilone RS in acetonitrile from *Standard solution*

System suitability

Samples: *System suitability solution* and *Sensitivity solution*

Suitability requirements

Resolution: NLT 1.0 between ixabepilone oxazine analog and desmethyl ixabepilone peaks, *System suitability solution*

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

Analysis

Sample: *Sample solution*

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

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

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

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

r_T = peak response of ixabepilone from the *Sample solution*

Acceptance criteria: See *Table 2*. Disregard any impurity peak less than 0.03%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Ixabepilone diol	0.47	1.0	0.15
Ixabepilone oxazine analog	0.79	1.0	0.15
Desmethyl ixabepilone	0.85	1.0	0.4
Ixabepilone	1.0	—	—

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
(*Z*)-Ixabepilone	1.19	0.83	0.15
Any individual unspecified impurity	—	1.0	0.1
Total impurities	—	—	0.8

SPECIFIC TESTS

- **Water Determination** ⟨921⟩, *Method I, Method Ic*: NMT 0.2%
- **Bacterial Endotoxins Test** ⟨85⟩: It contains NMT 0.32 USP Endotoxin Units/mg of ixabepilone.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Protect from light and store at 2°–8°.
- **USP Reference Standards** ⟨11⟩

USP Endotoxin RS
USP Ixabepilone RS
USP Ixabepilone System Suitability Mixture RS

It contains ixabepilone and small amounts of:

Ixabepilone diol;
(4*S*,7*R*,8*S*,9*S*,13*R*,14*R*,16*S*)-4,8,13,14-Tetrahydroxy-5,5,7,9,13-pentamethyl-16-[(*E*)-1-(2-methylthiazol-4-yl)prop-1-en-2-yl]azacyclohexadecane-2,6-dione.
$C_{27}H_{44}N_2O_6S$ 524.72

Ixabepilone oxazine analog;
(1*R*,2*R*,6*S*,7*S*,8*R*,11*S*,15*S*)-2,7,11-Trihydroxy-2,6,8,10,10-pentamethyl-15-[(*E*)-1-(2-methylthiazol-4-yl)prop-1-en-2-yl]-17-oxa-14-azabicyclo[11.3.1]heptadec-13-en-9-one. $C_{27}H_{42}N_2O_5S$ 506.70

Desmethyl ixabepilone;
(1*S*,3*S*,7*S*,10*R*,11*S*,12*S*,16*R*)-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[(*E*)-1-(2-methylthiazol-4-yl)prop-1-en-2-yl]-17-oxa-4-azabicyclo[14.1.0]heptadecane-5,9-dione. $C_{26}H_{40}N_2O_5S$ 492.68

(*Z*)-Ixabepilone;
(1*S*,3*S*,7*S*,10*R*,11*S*,12*S*,16*R*)-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[(*Z*)-1-(2-methylthiazol-4-yl)prop-1-en-2-yl]-17-oxa-4-azabicyclo[14.1.0]heptadecane-5,9-dione. $C_{27}H_{42}N_2O_5S$ 506.70

[Note—It may contain other impurities.]

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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