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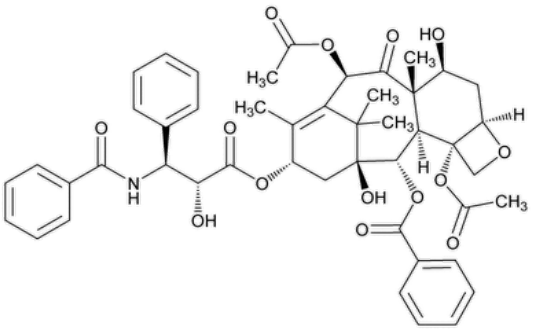
Paclitaxel



$C_{47}H_{51}NO_{14}$ 853.92

Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, 6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-9-yl ester, [2a*R*-[2aα,4β,4aβ,6β,9α(α*R**,β*S**),11α,12α,12aα,12bα]];
(2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-1,2a,3,4,4a,6,9,10,11,12,12a,12b-Dodecahydro-4,6,9,11,12,12b-hexahydroxy-4a,8,13,13-tetramethyl-7,11-methano-5*H*-cyclodeca[3,4]-benz[1,2-*b*]oxet-5-one 6,12b-diacetate, 12-benzoate, 9-ester with (2*R*,3*S*)-*N*-benzoyl-3-phenylisoserine;
(2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-12-(benzoyloxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate CAS RN®: 33069-62-4; UNII: P88XT4IS4D.

DEFINITION

Paclitaxel contains NLT 97.0% and NMT 102.0% of paclitaxel ($C_{47}H_{51}NO_{14}$), calculated on the anhydrous and solvent-free basis.

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

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K
- **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**

Diluent: Methanol and acetic acid (200:1)

Mobile phase: Acetonitrile and water (45:55)

Standard solution: 1 mg/mL of USP Paclitaxel RS in *Diluent*. Sonicate to dissolve if necessary.

Sample solution: 1 mg/mL of Paclitaxel in *Diluent*. Sonicate to dissolve if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 25-cm; 5-µm packing L43

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: 0.7–1.3

Relative standard deviation: NMT 1.5%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of paclitaxel ($C_{47}H_{51}NO_{14}$) in the portion of Paclitaxel taken:

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

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

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

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

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

Acceptance criteria: 97.0%–102.0%, on the anhydrous and solvent-free basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.2%

Change to read:

• **Organic Impurities**

Test 1 (for material labeled as isolated from natural sources)**:** If the material complies with this test, the labeling indicates that it meets the requirements of USP *Organic Impurities Test 1*.

Solution A: Acetonitrile

Solution B: Water

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	35	65
35	35	65
60	80	20
70	35	65
80	35	65

Diluent: Methanol and acetic acid (200:1)

System suitability stock solution: 10 µg/mL each of USP Paclitaxel Related Compound A RS and USP Paclitaxel Related Compound B RS in methanol

System suitability solution: 1 µg/mL each of USP Paclitaxel Related Compound A RS and USP Paclitaxel Related Compound B RS from *System suitability stock solution* in *Diluent*

Standard solution: 5 µg/mL of USP Paclitaxel RS in *Diluent*. Sonicate to dissolve if necessary.

Sample solution: 1 mg/mL of Paclitaxel in *Diluent*. Sonicate to dissolve if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 25-cm; 5-µm packing L43

Column temperature: 30°

Flow rate: 2.6 mL/min

Injection volume: 15 µL

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.0 between paclitaxel related compound A and paclitaxel related compound B, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each specified and unspecified impurity in the portion of Paclitaxel taken:

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

r_U = peak response of each individual impurity

r_S = peak response of paclitaxel

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Baccatin III[a]	0.24	0.78	0.2
10-Deacetylpaclitaxel[b]	0.53	1.00	0.5
7-Xylosylpaclitaxel[c]	0.57	1.00	0.2
Paclitaxel related compound A	0.78	0.79	a_1[d]
Paclitaxel *sec*-Butyl analog[e]	0.78	0.79	a_2[d]
Paclitaxel related compound B	0.86	1.00	0.5
Paclitaxel	1.00	—	—
Paclitaxel benzyl analog[f]	1.10	1.00	b_1[g]
3",4"-Dehydro paclitaxel C[h]	1.10	1.00	b_2[g]
7-Epicephalomannine[i]	1.40	1.00	0.3
7-Epipaclitaxel[j]	1.85	1.00	0.5
Any unspecified impurity	—	1.00	0.1
Total impurities	—	—	2.0

[a] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,9,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[b] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12b-Acetoxy-9-{[(2*R*,3*S*)-3-benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate.

[c] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-12-(benzoyloxy)-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-(D-xylopyranosyloxy)-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-

b]oxete-6,12b(2a*H*)-diyl diacetate.

[d] Resolution may be incomplete for these peaks depending upon the relative amounts present; the sum of a_1 and a_2 is NMT 0.5%.

[e] 2",3"-Dihydrocephalomannine; (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-{[(2*R*,3*S*)-2-hydroxy-3-(2-methylbutanamido)-3-phenylpropanoyl]oxy}-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[f] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-{[(2*R*,3*S*)-2-hydroxy-3-phenyl-3-(2-phenylacetamido)propanoyl]oxy}-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[g] Resolution may be incomplete for these peaks depending upon the relative amounts present; the sum of b_1 and b_2 is NMT 0.5%.

[h] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-9-({(2*R*,3*S*)-3-[(*Z*)-hex-3-enamido]-2-hydroxy-3-phenylpropanoyl}oxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[i] (2a*R*,4*R*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-({(2*R*,3*S*)-2-hydroxy-3-[(*E*)-2-methylbut-2-enamido]-3-phenylpropanoyl}oxy)-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[j] (2a*R*,4*R*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-12-(benzoyloxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

Test 2 (for material labeled as produced by a semisynthetic process)**:** If the material complies with this test, the labeling indicates that it meets the requirements of USP *Organic Impurities Test 2*.

Solution A: Acetonitrile and water (40:60)

Solution B: Acetonitrile

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	100	0
20	100	0
60	10	90
62	100	0
70	100	0

System suitability solution: 0.96 mg/mL of USP Paclitaxel RS and 0.008 mg/mL of USP Paclitaxel Related Compound B RS in *Solution B*. Sonicate to dissolve if necessary.

Sample solution: 1 mg/mL of Paclitaxel in *Solution B*. Sonicate to dissolve if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 35°

Flow rate: 1.2 mL/min

Injection volume: 15 µL

System suitability

Sample: *System suitability solution*

[Note—See *Table 4* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.2 between paclitaxel related compound B and paclitaxel

Relative standard deviation: NMT 2.0% for paclitaxel

Analysis

Sample: *Sample solution*

Calculate the percentage of each specified and unspecified impurity in the portion of Paclitaxel taken:

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

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

r_T = sum of all the peak responses from the *Sample solution*

F = relative response factor for each impurity (see *Table 4*)

Acceptance criteria: See *Table 4*.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
10-Deacetylbaccatin III[a]	0.11	0.81	0.1
Baccatin III[b]	0.20	0.78	0.2
Paclitaxel photodegradant[c]	0.42	0.72	0.1
10-Deacetylpaclitaxel[d]	0.47	1.00	0.5
2-Debenzoylpaclitaxel-2-pentenoate[e]	0.80	1.00	0.7
Oxetane ring opened, acetyl and benzoyl migrated[f]	0.92[g]	1.00	x_1[g]
10-Acetoacetylpaclitaxel[h]	0.92[g]	1.00	x_2[g]
Paclitaxel related compound B	0.94[g]	1.00	x_3[g]
Paclitaxel	1.00	—	—
7-Epipaclitaxel[i]	1.37	1.00	0.4
10,13-Bissidechainpaclitaxel[j]	1.45	1.00	0.5
7-Acetylpaclitaxel[k]	1.54	1.00	0.6
13-O-(Triethylsilyl)baccatin III[l]	1.80	0.57	0.1
7-O-(Triethylsilyl)paclitaxel[m]	2.14	1.00	0.3
Any unspecified impurity	—	1.00	0.1
Total impurities	—	—	2.0

[a] ▲(2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12b-(Acetyloxy)-12-(benzoyloxy)-1,2a,3,4,4a,6,9,10,11,12,12a,12b-dodecahydro-4,6,9,11-tetrahydroxy-4a,8,13,13-tetramethyl-7,11-methano-5*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-5-one.▲ (ERR 1-Oct-2024)

[b] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,9,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[c] (1*S*,2*S*,4*S*,5*S*,5a*R*,6*R*,7a*S*,8*S*,9a*R*,11a*S*,11b*S*)-4-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-1-(benzoyloxy)-2,8-dihydroxy-5,7a,12,12-tetramethyl-7-oxodecahydro-1*H*-2,5a-methanocyclohepta[3,3a]indeno[5,4-*b*]oxete-6,11a(11*H*)-diyl diacetate.

[d] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12b-Acetoxy-9-{[(2*R*,3*S*)-3-benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate.

[e] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-4,11-dihydroxy-4a,8,13,13-tetramethyl-12-{[(*E*)-2-methylbut-2-enoyl]oxy}-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[f] (1*S*,3*S*,4*S*,4a*R*,5*S*,6*S*,8*S*,11*R*,12a*S*)-8-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-4-[(benzoyloxy)methyl]-1,4,5,6-tetrahydroxy-9,12a,13,13-tetramethyl-12-oxo-1,2,3,4,4a,5,6,7,8,11,12,12a-dodecahydro-6,10-methanobenzocyclodecen-3,11-diyl diacetate.

[g] Resolution may be incomplete for these peaks depending upon the relative amounts present; the sum of x_1, x_2, and x_3 is NMT 0.4%.

[h] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-6-Acetoxy-9-{[(2*R*,3*S*)-3-benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-12b-[(3-oxobutanoyl)oxy]-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate.

[i] (2a*R*,4*R*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-12-(benzoyloxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[j] (2a*R*,4*S*,4a*S*,6*S*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12b-Acetoxy-12-(benzoyloxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,9-diyl (2*R*,2'*R*,3*S*,3'*S*)-bis(3-benzamido-2-hydroxy-3-phenylpropanoate).

[k] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-12-(benzoyloxy)-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-4-(acetyloxy)-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[l] 13-Tes-baccatin III; (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-6,12b-(Diacetyloxy)-12-(benzoyloxy)-9-(triethylsilyloxy)-1,2a,3,4,4a,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-7,11-methano-5*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-5-one.

[m] 7-Tes-paclitaxel; (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-12-(benzoyloxy)-4-(triethylsilyloxy)-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

Test 3 (for material labeled as produced by a plant cell fermentation process)**:** If the material complies with this test, the labeling indicates that it meets the requirements of USP *Organic Impurities Test 3*.

Solution A: Acetonitrile and water (40:60)

Solution B: Acetonitrile

Mobile phase: See *Table 5*.

Table 5

Time (min)	Solution A (%)	Solution B (%)
0	100	0
28	100	0
33	98	2
58	10	90
60	10	90

Time (min)	Solution A (%)	Solution B (%)
63	100	0
70	100	0

System suitability solution: 1 mg/mL of USP Paclitaxel Impurity Mixture RS in *Solution B*. Sonicate to dissolve if necessary.

Standard solution: 1 mg/mL of USP Paclitaxel RS in *Solution B*. Sonicate to dissolve if necessary.

Sample solution: 1 mg/mL of Paclitaxel in *Solution B*. Sonicate to dissolve if necessary.

Chromatographic system

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

Mode: LC

Detector: UV 227 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Flow rate: 1.2 mL/min

Injection volume: 12 µL

System suitability

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

[NOTE—See *Table 6* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.8 between paclitaxel and paclitaxel benzyl analog, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Sample: *Sample solution*

Calculate the percentage of each specified and unspecified impurity in the portion of Paclitaxel taken:

$$\text{Result} = (r_U/r_T) \times 100$$

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

r_T = sum of all the peak responses from the *Sample solution*

Acceptance criteria: See *Table 6*.

Table 6

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Paclitaxel propyl analog[a]	0.54	0.2
Paclitaxel related compound A	0.76	0.5
Paclitaxel *sec*-Butyl analog[b]	0.81	0.2
Paclitaxel *n*-Butyl analog[c]	0.89	0.1
Paclitaxel	1.00	—
Paclitaxel benzyl analog[d]	1.10	0.4
Baccatin VI[e]	1.23	0.2
Paclitaxel pentyl analog[f]	1.31	0.2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
7-Epipaclitaxel[g]	1.51	0.4
Any unspecified impurity	—	0.1
Total impurities	—	2.0

[a] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-9-{[(2*R*,3*S*)-3-butyramido-2-hydroxy-3-phenylpropanoyl)oxy}-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[b] 2″,3″-Dihydrocephalomannine; (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-{[(2*R*,3*S*)-2-hydroxy-3-(2-methylbutanamido)-3-phenylpropanoyl]oxy}-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[c] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-{[(2*R*,3*S*)-2-hydroxy-3-pentanamido-3-phenylpropanoyl]oxy}-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[d] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-{[(2*R*,3*S*)-2-hydroxy-3-phenyl-3-(2-phenylacetamido)propanoyl]oxy}-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[e] (2a*R*,4*S*,4a*S*,5*R*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-11-hydroxy-4a,8,13,13-tetramethyl-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-4,5,6,9,12b(2a*H*)-pentayl pentaacetate.

[f] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-9-{[(2*R*,3*S*)-3-hexanamido-2-hydroxy-3-phenylpropanoyl]oxy}-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

[g] (2a*R*,4*R*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-9-{[(2*R*,3*S*)-3-Benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-12-(benzoyloxy)-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^2 cfu/g. It meets the requirements of the tests for absence of *Salmonella* species, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*.

• **Optical Rotation ⟨781S⟩,** *Procedures, Specific Rotation*

Sample solution: 10 mg/mL of paclitaxel in methanol

Acceptance criteria: −49.0° to −55.0° at 20°, calculated on the anhydrous, solvent-free basis

• **Water Determination ⟨921⟩,** *Method I, Method Ic*: NMT 4.0%

• **Bacterial Endotoxins Test ⟨85⟩:** Where the label states Paclitaxel must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins are such that the requirement under the relevant dosage form monograph(s) in which Paclitaxel is used can be met.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.

• **Labeling:** Label it to indicate the type of process used to produce the material and the *Organic Impurities* test with which the material complies. Where Paclitaxel is intended for use in preparing injectable or other sterile dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable or other sterile dosage forms to ensure acceptable levels of bacterial endotoxins.

• **USP Reference Standards ⟨11⟩**

USP Paclitaxel RS

USP Paclitaxel Related Compound A RS

Cephalomannine; (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-({(2*R*,3*S*)-2-hydroxy-3-[(*E*)-2-methylbut-2-enamido]-3-phenylpropanoyl}oxy)-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

$C_{45}H_{53}NO_{14}$ 831.91

USP Paclitaxel Related Compound B RS

10-Deacetyl-7-epipaclitaxel; (2a*R*,4*R*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12b-Acetoxy-9-{[(2*R*,3*S*)-3-benzamido-2-hydroxy-3-phenylpropanoyl]oxy}-4,6,11-trihydroxy-4a,8,13,13-tetramethyl-5-oxo-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxet-12-yl benzoate.

$C_{45}H_{49}NO_{13}$ 811.88

USP Paclitaxel Impurity Mixture RS

It contains a mixture of the following two compounds:

Paclitaxel;

Paclitaxel benzyl analog: (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-12-(Benzoyloxy)-4,11-dihydroxy-9-{[(2*R*,3*S*)-2-hydroxy-3-phenyl-3-(2-phenylacetamido)propanoyl]oxy}-4a,8,13,13-tetramethyl-5-oxo-3,4,4a,5,6,9,10,11,12,12a-decahydro-1*H*-7,11-methanocyclodeca[3,4]benzo[1,2-*b*]oxete-6,12b(2a*H*)-diyl diacetate.

$C_{48}H_{53}NO_{14}$ 867.95

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

Topic/Question	Contact	Expert Committee
PACLITAXEL	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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