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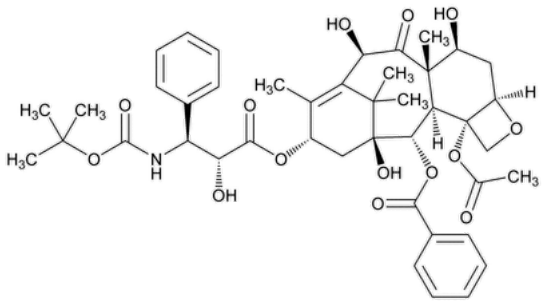
# Docetaxel



$C_{43}H_{53}NO_{14} \cdot 3H_2O$ 861.93
Anhydrous 807.88

Benzenepropanoic acid, β-[[(1,1-dimethylethoxy) carbonyl]amino]-α-hydroxy-, 12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,6,11-trihydroxy-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]]-;
(2*R*,3*S*)-*N*-Carboxy-3-phenylisoserine, *N*-*tert*-butyl ester, 13-ester with 5β,20-epoxy-1,2α,4,7β,10β,13α-hexahydroxytax-11-en-9-one 4-acetate 2-benzoate;

Trihydrate CAS RN®: 148408-66-6; UNII: 15H5577CQD.

Anhydrous CAS RN®: 114977-28-5; UNII: 699121PHCA.

## DEFINITION

Docetaxel contains NLT 97.5% and NMT 102.0% of docetaxel ($C_{43}H_{53}NO_{14}$), calculated on the anhydrous and solvent-free basis. [**Caution—**

Docetaxel is cytotoxic. Great care should be taken to prevent inhaling particles of Docetaxel and exposing the skin to it.]

## IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A, 197K, 197M, or 197S

[Note—Use a solution containing 60 mg/mL of Docetaxel in methylene chloride for ⟨197S⟩.]

• **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**

**Solution A:** Water

**Solution B:** Acetonitrile

**Mobile phase:** See *Table 1*.

**Table 1**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 72 | 28 |
| 9.0 | 72 | 28 |
| 39.0 | 28 | 72 |
| 39.1 | 72 | 28 |
| 50 | 72 | 28 |

**Diluent:** Acetonitrile, water, and glacial acetic acid (100:100:0.1)

**System suitability solution:** 1 mg/mL of USP Docetaxel Identification RS in *Diluent*. [Note—USP Docetaxel Identification RS contains docetaxel and small amounts of 2-debenzoxyl 2-pentenoyl docetaxel, 6-oxodocetaxel, 4-epidocetaxel, and 4-epi-6-oxodocetaxel. See *Table 2*.]

**Standard solution:** 1.0 mg/mL of USP Docetaxel RS prepared as follows. Transfer a quantity of USP Docetaxel RS to a suitable volumetric flask, dissolve in alcohol equivalent to about 5% of the final volume, and dilute with *Diluent* to volume.

**Sample solution:** 1.0 mg/mL of Docetaxel prepared as follows. Transfer a quantity of Docetaxel to a suitable volumetric flask, dissolve in alcohol equivalent to about 5% of the final volume, and dilute with *Diluent* to volume.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 232 nm

**Column:** 4.6-mm × 15-cm; 3.5-µm packing L1

**Temperatures**

**Autosampler:** 10°

**Column:** 45°

**Flow rate:** 1.2 mL/min

**Injection volume:** 10 µL

**System suitability**

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

**Suitability requirements**

**Resolution:** NLT 3.5 between 2-debenzoxyl 2-pentenoyl docetaxel and docetaxel, *System suitability solution*

**Relative standard deviation:** NMT 1.0%, *Standard solution*

**Analysis**

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

Calculate the percentage of docetaxel ($C_{43}H_{53}NO_{14}$) in the portion of Docetaxel 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 Docetaxel RS in the *Standard solution* (mg/mL)

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

**Acceptance criteria:** 97.5%–102.0% on the anhydrous and solvent-free basis

**IMPURITIES**

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

***Change to read:***

• **Organic Impurities, Procedure 1**

[Note—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 1* is recommended if 10-deacetyl baccatin and 2-debenzoxyl 2-pentenoyl docetaxel are specified impurities. *Procedure 2* is recommended if O-BOC *N*-pyruvyl docetaxel is a specified impurity.]

▲**Mobile phase, Diluent,**▲ (ERR 1-Jun-2024) **System suitability solution, Standard solution, Sample solution,** and **Chromatographic system:** Proceed as directed in the *Assay*.

**Sensitivity solution:** 0.5 µg/mL of USP Docetaxel RS in *Diluent* from the *Standard solution*

**System suitability**

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

**Suitability requirements**

**Resolution:** NLT 3.5 between 2-debenzoxyl 2-pentenoyl docetaxel and docetaxel, *System suitability solution*

**Signal-to-noise ratio:** NLT 10 for the docetaxel peak, *Sensitivity solution*

**Analysis**

**Sample:** *Sample solution*

Calculate the percentage of each impurity in the portion of Docetaxel 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 peak responses from the *Sample solution*

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

**Acceptance criteria:** See *Table 2*. Disregard any peaks less than 0.05%.

**Table 2**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| 10-Deacetyl baccatin (if present)[a,b] | 0.25 | 1.5 | 0.15 |
| *N*-Formyl impurity (if present)[b,c] | 0.57 | 1.1 | 0.15 |
| 2-Debenzoxyl 2-pentenoyl docetaxel | 0.97 | 0.63 | 0.5 |
| Docetaxel | 1.00 | — | — |
| 6-Oxodocetaxel | 1.08 | 1.0 | 0.3 |
| 4-Epidocetaxel | 1.13 | 1.0 | 0.3 |
| 4-Epi-6-oxodocetaxel | 1.18 | 1.0 | 0.2 |
| 6-Dichloroethoxycarbonyl docetaxel (if present)[b,d] | 1.31 | 0.82 | 0.15 |
| Any unspecified impurity | — | 1.0 | 0.10 |
| Total impurities | — | — | 1.0 |

[a] (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 12b-acetate, 12-benzoate.

[b] If possible from the manufacturing process.

[c] (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-formamido-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.

[d] (2a*R*,4*S*,4a*S*,6*R*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-6-{[(2,2-Dichloroethoxy)carbonyl]oxy}-1,2a,3,4,4a,6,9,10,11,12,12a,12b-dodecahydro-4,9,11,12,12b-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-5*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-5-one 12b-acetate, 12-benzoate, 9-ester with (2*R*,3*S*)-*N*-tert-butoxycarbonyl-3-phenylisoserine.

- **Organic Impurities, Procedure 2**

**Solution A:** Water

**Solution B:** Acetonitrile

**Mobile phase:** See *Table 3*.

**Table 3**

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 0 | 65 | 35 |
| 25 | 45 | 55 |
| 35 | 20 | 80 |
| 45 | 20 | 80 |
| 45.1 | 65 | 35 |

| Time (min) | Solution A (%) | Solution B (%) |
|---|---|---|
| 53 | 65 | 35 |

**System suitability solution:** 1 mg/mL of USP Docetaxel System Suitability Mixture RS in acetonitrile. [NOTE—USP Docetaxel System Suitability Mixture RS contains docetaxel and a small amount of 6-oxodocetaxel, O-BOC *N*-pyruvyl docetaxel, 4-epidocetaxel, and 4-epi-6-oxodocetaxel. See *Table 4*.]

**Standard solution:** 5.0 µg/mL of USP Docetaxel RS in acetonitrile

**Sample solution:** 1.0 mg/mL of Docetaxel in acetonitrile

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 230 nm

**Column:** 4.6-mm × 15-cm; 3.5-µm packing L1

**Temperatures**

**Column:** 40°

**Sample:** 4°

**Flow rate:** 1.2 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** *System suitability solution*

**Suitability requirements**

**Resolution:** NLT 2.0 between O-BOC *N*-pyruvyl docetaxel and 4-epidocetaxel

**Tailing factor:** 0.8–1.5 for the docetaxel peak

**Analysis**

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

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

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

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

$r_S$ = peak area of docetaxel from the *Standard solution*

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

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

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

**Acceptance criteria:** See *Table 4*. Disregard any peaks less than 0.05%.

**Table 4**

| Name | Relative Retention Time | Relative Response Factor | Acceptance Criteria, NMT (%) |
|---|---|---|---|
| Docetaxel | 1.0 | — | — |
| 6-Oxodocetaxel | 1.19 | 1.1 | 0.15 |
| O-BOC *N*-pyruvyl docetaxel[a] | 1.24 | 0.80 | 0.15 |
| 4-Epidocetaxel | 1.29 | 0.96 | 0.15 |
| 4-Epi-6-oxodocetaxel | 1.42 | 1.2 | 0.15 |
| Any unspecified impurity | — | 1.0 | 0.10 |
| Total impurities | — | — | 2.0 |

[a] (2a*R*,4*R*,4a*S*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-1,2a,3,4,4a,6,9,10,11,12,12a,12b-Dodecahydro-4, 9,11,12,12b-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-5*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-5,6-dione 12b-acetate, 12-benzoate, 9-ester with (2*R*,3*S*)-2-(*tert*-butoxycarbonyloxy)-3-(2-oxopropanamido)-3-phenylpropanoic acid.

**SPECIFIC TESTS**

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial limit does not exceed $10^2$ cfu/g. The total molds and yeasts count does not exceed 10 cfu/g.

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.4 USP Endotoxin Units/mg.

• **Water Determination ⟨921⟩, *Method I, Method Ic*:** 5.0%–7.0%. If labeled as an anhydrous form: NMT 1.5%.

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

**Sample solution:** 10 mg/mL in methanol

**Acceptance criteria:** −39° to −41° (*t* = 20°), calculated on the anhydrous and solvent-free basis. If labeled as an anhydrous form: −35° to −45° (*t* = 20°), calculated on the as-is basis.

**ADDITIONAL REQUIREMENTS**

• **Labeling:** Where it is an anhydrous form, the label so indicates. If a test for *Organic Impurities* other than *Procedure 1* is used, the labeling states the test with which the article complies.

• **Packaging and Storage:** Preserve in well-closed, light-resistant containers, and store at room temperature or between 2° and 8°.

• **USP Reference Standards ⟨11⟩**

USP Docetaxel RS

USP Docetaxel Identification RS

It contains docetaxel and small amounts of the following:

2-Debenzoxyl 2-pentenoyl docetaxel: (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 12b-acetate, 12-[(*E*)-2-methylbut-2-enoate], 9-ester with (2*R*,3*S*)-*N*-*tert*-butoxycarbonyl-3-phenylisoserine.

$C_{41}H_{55}NO_{14}$ 785.87

6-Oxodocetaxel: (2a*R*,4*S*,4a*S*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-1,2a,3,4,4a,6,9,10,11,12,12a,12b-Dodecahydro-4, 9,11,12,12b-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-5*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-5,6-dione 12b-acetate, 12-benzoate, 9-ester with (2*R*,3*S*)-*N*-*tert*-butoxycarbonyl-3-phenylisoserine.

$C_{43}H_{51}NO_{14}$ 805.86

4-Epidocetaxel: (2a*R*,4*R*,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 12b-acetate, 12-benzoate, 9-ester with (2*R*,3*S*)-*N*-*tert*-butoxycarbonyl-3-phenylisoserine.

$C_{43}H_{53}NO_{14}$ 807.88

4-Epi-6-oxodocetaxel: (2a*R*,4*R*,4a*S*,9*S*,11*S*,12*S*,12a*R*,12b*S*)-1,2a,3,4,4a,6,9,10,11,12,12a,12b-Dodecahydro-4, 9,11,12,12b-pentahydroxy-4a,8,13,13-tetramethyl-7,11-methano-5*H*-cyclodeca[3,4]benz[1,2-*b*]oxet-5,6-dione 12b-acetate, 12-benzoate, 9-ester with (2*R*,3*S*)-*N*-*tert*-butoxycarbonyl-3-phenylisoserine.

$C_{43}H_{51}NO_{14}$ 805.86

USP Docetaxel System Suitability Mixture RS

Contains docetaxel and a small amount of 6-oxodocetaxel, O-BOC *N*-pyruvyl docetaxel, 4-epidocetaxel, and 4-epi-6-oxodocetaxel.

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| DOCETAXEL | Documentary Standards Support | SM32020 Small Molecules 3 |

**Chromatographic Database Information:** Chromatographic Database

**Most Recently Appeared In:**
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