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

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **HEAVY METALS,** *Method I* ⟨**231**⟩
  Sample solution: Dissolve 1 g in 20 mL of a mixture of dimethylformamide and water (17:3). To 12 mL of this solution, add 2 mL of *pH 3.5 Acetate Buffer* and mix. Add 1.2 mL of thioacetamide–glycerin base TS and mix.
  Acceptance criteria: NMT 20 ppm

Organic Impurities

- **PROCEDURE**
  Standard solution, System suitability 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 4 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 the responses of all peaks from the *Sample solution*
F = relative response factor for each individual impurity (see *Impurity Table 1*)

  Acceptance criteria
  Individual impurities: See *Impurity Table 1*. [NOTE—Disregard any impurity peaks less than 0.05%.]
  Total impurities: NMT 1.0%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
2-Debenzoxyl 2-pentenoyl docetaxel[a]	0.97	0.63	0.5
Docetaxel	1.00	—	—
6-Oxodocetaxel[b]	1.08	1.0	0.3
4-Epidocetaxel[c]	1.13	1.0	0.3
4-Epi-6-oxodocetaxel[d]	1.18	1.0	0.2
Any unspecified impurity	—	1.0	0.10

[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-[(*E*)-2-methylbut-2-enoate], 9-ester with (2 *R*,3*S*)-*N*-*tert*-butoxycarbonyl-3-phenylisoserine.
[b] (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] (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.
[d] (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.

SPECIFIC TESTS

- **MICROBIAL ENUMERATION TESTS ⟨61⟩** and **TESTS FOR SPECIFIED MICROORGANISMS ⟨62⟩:** The total aerobic microbial limit does not exceed 100 cfu/g. The total yeast and mold count does not exceed 10 cfu/g.
- **BACTERIAL ENDOTOXINS TEST ⟨85⟩:** It contains NMT 0.3 USP Endotoxin Units/mg.
- **WATER DETERMINATION,** *Method Ic* ⟨**921**⟩**:** 5.0%–7.0%
- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩**:** −39° to −41° (t=20°), calculated on the anhydrous and solvent-free basis.
  Sample solution: 10 mg/mL in methanol

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well closed, light-resistant containers, and store at room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Docetaxel RS
  USP Docetaxel Identification RS
  Contains docetaxel and small amount of 2-debenzoxyl 2-pentenoyl docetaxel, 6-oxodocetaxel, 4-epidocetaxel, and 4-epi-6-oxodocetaxel.
  USP Endotoxin RS

Add the following:

▲Docetaxel Injection

DEFINITION

Docetaxel Injection is a sterile solution of Docetaxel. It contains NLT 90.0% and NMT 110.0% of the labeled amount of docetaxel (anhydrous) ($C_{43}H_{53}NO_{14}$). It contains polysorbate 80 and/or other suitable solubilizing agents in the infusion vehicle. It may also contain dehydrated alcohol.

IDENTIFICATION

- **A. THIN-LAYER CHROMOTOGRAPHIC IDENTIFICATION TEST ⟨201⟩**
  Standard solution: 0.4 mg/mL of USP Docetaxel RS in methylene chloride containing 1% (v/v) of polysorbate 80
  Sample solution: 0.4 mg/mL of docetaxel (anhydrous) in methylene chloride, from Injection
  Adsorbent: 0.25-mm layer of chromatographic silica gel mixture containing a fluorescent indicator

Developing solvent system: Methylene chloride and methanol (23:2)
TLC tank: Lined with filter paper
Analysis: After removing the plate from the tank, allow to dry in a fume hood, and view under UV light at 254 nm.
Acceptance criteria: Meets the requirements

- **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	0	100
49.0	0	100
49.1	72	28
60	72	28

Diluent: Acetonitrile, acetic acid, and water (100: 0.1: 100)
System suitability solution: 1 mg/mL of USP Docetaxel Identification RS in *Diluent*
Standard solution: 0.2 mg/mL of USP Docetaxel RS. Transfer USP Docetaxel RS into a suitable volumetric flask, and dissolve in alcohol equivalent to 5% of the final volume. Dilute with *Diluent* to volume.
Sample solution (for the Injection labeled as one-vial formulation)**:** Dilute a portion of the Injection with *Diluent* to obtain a solution containing 0.2 mg/mL of docetaxel (anhydrous).
Sample solution (for the Injection labeled as two-vial formulation)**:** Transfer the content of the vial containing the Injection concentrate to a suitable volumetric flask. Dissolve in an amount of alcohol equivalent to 5% of the final volume, and dilute with *Diluent* to volume to obtain a solution having a concentration of 0.2 mg/mL of docetaxel (anhydrous).
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 232 nm
Refrigerated autosampler temperature: 10°
Column: 4.6-mm × 15-cm; 3.5-µm packing L1
Column temperature: 45°
Flow rate: 1.2 mL/min
Injection size: 20 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 the labeled amount of docetaxel ($C_{43}H_{53}NO_{14}$) in the portion of Injection taken:

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

r_U = peak area from the *Sample solution*
r_S = peak area from the *Standard solution*
C_S = concentration of USP Docetaxel RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of docetaxel (anhydrous) in the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0%

IMPURITIES

- **ORGANIC IMPURITIES**

Mobile phase, Diluent, System suitability solution, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.
Sensitivity solution: 0.2 µg/mL of USP Docetaxel RS in *Diluent*, from the *Standard solution*
System suitability
Samples: *System suitability solution*, *Standard 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*
Relative standard deviation: NMT 1.0%, *Standard solution*
Analysis
Sample: *Sample solution*
Calculate the percentage of each impurity in the portion of Injection taken:

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

r_U = peak area of each individual impurity from the *Sample solution*
r_T = sum of all of the peak areas from the *Sample solution*
F = relative response factor for each individual impurity (see *Table 2*)
Acceptance criteria
Individual impurities: See *Table 2*. [NOTE—Disregard any impurity peak less than 0.1% and any peak with a relative retention time less than 0.2 or greater than 1.3.]

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
10-Deacetyl baccatin[a]	0.27	1.5	0.30
2-Debenzoxyl 2-pentenoyl docetaxel[b]	0.97	—	—
Docetaxel	1.00	—	—
Crotonaldehyde analog[c]	1.05	1.0	1.3
6-Oxodocetaxel[d]	1.08	1.0	1.5
4-Epidocetaxel[e]	1.13	1.0	0.5
4-Epi-6-oxodocetaxel[f]	1.18	1.0	0.5
Any unspecified impurity	—	1.0	0.2
Total impurities	—	—	3.5

[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] (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. The alternative chemical name is (2b,5b,7b,10b,13a)-4-acetoxy-13-(((2*R*,3*S*)- 3-[(*tert*-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoyl)oxy)-1,7,10-trihydroxy-9-oxo-5,20-epoxytax-11-en-2-yl (2*E*)-2- methylbut-2-enoate.

[c] (1*S*,2*S*,3*R*,9*S*,*E*)-3-[(*S*,*E*)-2-Acetoxy-1-hydroxy-5-oxopent-3-en-2-yl]-1,5,9-trihydroxy-4,8,11,11-tetramethyl-6-oxobicyclo[5.3.1]undeca-4,7-dien-2-yl benzoate, 9-ester with (2*R*,3*S*)-*N*-*tert*-butoxycarbonyl-3-phenylisoserine.

[d] (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. The alternative chemical name is (2b,5b,7a,10b,13a)-4-acetoxy-13-(((2*R*,3*S*)- 3-[(*tert*-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoyl)oxy)-1,7,10-trihydroxy-9-oxo-5,20-epoxytax-11-en-2-yl benzoate.

[e] (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. The alternative chemical name is (2b,5b,7a,10b,13a)-4-acetoxy-13-(((2*R*,3*S*)-3-[(*tert*-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoyl)oxy)-1,7,10-trihydroxy-9-oxo-5,20-epoxytax-11-en-2-yl benzoate.

[f] (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. The alternative chemical name is (2b,5b,7a,13a)- 4-acetoxy-13-(((2*R*,3*S*)-3-[(*tert*-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoyl)oxy)-1,7-dihydroxy-9,10-dioxo-5,20-epoxytax-11-en-2-yl benzoate.

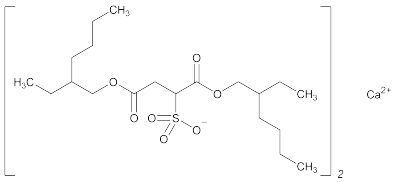
SPECIFIC TESTS

- **BACTERIAL ENDOTOXINS TEST** ⟨**85**⟩**:** It contains NMT 1.94 USP Endotoxin Units/mg of docetaxel (anhydrous).
- **STERILITY TESTS** ⟨**71**⟩**:** It meets the requirements when tested as directed in the *Test for Sterility of the Product to Be Examined, Membrane Filtration*.
- **PARTICULATE MATTER IN INJECTIONS** ⟨**788**⟩**:** Meets the requirements for small-volume injections
- **OTHER REQUIREMENTS:** Meets the requirements in *Injections* ⟨1⟩

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in single-dose or multiple-dose containers, preferably of T ype I glass. Store at controlled room temperature.
- **LABELING:** Label it to indicate whether it is a one-vial formulation or two-vial formulation (Injection concentrate and diluent), and also label it to indicate that it is to be diluted with a suitable parenteral vehicle before intravenous infusion.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Docetaxel RS
  USP Docetaxel Identification RS
  [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.]
  USP Endotoxin RS ▲*USP35*

Docusate Calcium



$C_{40}H_{74}CaO_{14}S_2$ 883.22
Butanedioic acid, sulfo-, 1,4-bis(2-ethylhexyl) ester, calcium salt.
1,4-Bis(2-ethylhexyl) sulfosuccinate, calcium salt [128-49-4].

» Docusate Calcium contains not less than 91.0 percent and not more than 100.5 per cent of $C_{40}H_{74}CaO_{14}S_2$, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Docusate Calcium RS
USP Bis(2-ethylhexyl) Maleate RS
$C_{20}H_{36}O_4$ 340.51

Clarity of solution—Dissolve 25 g in 94 mL of alcohol: the solution does not develop a haze within 24 hours when maintained at a temperature of 25 ± 1°.

Identification—

A: Place a small piece of it on a salt plate, add 1 drop of acetone, and promptly cover with another salt plate. Rub the plates together to dissolve the specimen, slide the plates apart, and allow the acetone to evaporate: the IR absorption spectrum of the film so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Docusate Calcium RS.

B: Dissolve 25 mg in 2 mL of acetone. Add 2 mL of water, mix, and add 2 drops of sulfuric acid: a white precipitate is formed.

C: Prepare a solution of it in isopropyl alcohol containing 10 mg per mL, and mix. Apply, with the aid of a stream of nitrogen, 10 µL of this solution and 10 µL of an isopropyl alcohol solution of USP Docusate Calcium RS containing 10 mg per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel. Allow the spots to dr y, and develop the chromatogram in a solvent system consisting of a mixture of ethyl acetate, ammonium hydroxide, and alcohol (5:2:2) until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Expose the plate to iodine vapors in a closed chamber for about 30 minutes, and locate the spots: the R_F value of the spot obtained from the test