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 Chromatographic 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
  Chromatographic system
  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 volume: 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

Change to read:

- **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: See *Table 2*. 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	●1.0● (RB 1-May-2012)
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 ●5*β*,20-epoxy-1,7*β*,10*β*-trihydroxy-9-oxotax-11-ene-2α,4,13α-triyl 4-acetate 13-[(2*R*,3*S*)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropanoate] 2-[(2*E*)-2-methylbut-2-enoate]. It is a process impurity and is listed in *Table 2* for identification only. It is controlled in the drug substance. It is not reported for the drug product and should not be included in the *Total impurities*.● (RB 1-May-2012)

[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 ●5*β*,20-epoxy-1,7*β*-dihydroxy-9,10-dioxotax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-[(2*R*,3*S*)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropanoate].● (RB 1-May-2012)

[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 ●5*β*,20-epoxy-1,7α,10*β*-trihydroxy-9-oxotax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-[(2*R*,3*S*)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropanoate].● (RB 1-May-2012)

[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 ●5*β*,20-epoxy-1,7α-dihydroxy-9,10-dioxotax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-[(2*R*,3*S*)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropanoate].● (RB 1-May-2012)

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 Type 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*