### 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**

  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>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>72</td>
<td>28</td>
</tr>
<tr>
<td>9.0</td>
<td>28</td>
<td>72</td>
</tr>
<tr>
<td>39.0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>49.0</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>49.1</td>
<td></td>
<td>28</td>
</tr>
<tr>
<td>60</td>
<td>72</td>
<td>28</td>
</tr>
</tbody>
</table>

**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°C.
- **Column:** 4.6-mm × 15-cm; 3.5-µm packing L1.
- **Column temperature:** 45°C.
- **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:

  \[ Result = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100 \]

  \( r_U \) = 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:

  \[ Result = \left( \frac{r_U}{r_S} \right) \times \left( \frac{1}{F} \right) \times 100 \]

  \( r_U \) = peak area of each individual impurity from the Sample solution.

  \( r_S \) = 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

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Relative Response Factor</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-Deacetyl baccatin^a</td>
<td>0.27</td>
<td>1.5</td>
<td>0.30</td>
</tr>
<tr>
<td>2-Debenzoxyl 2-pentenyl docetaxel^b</td>
<td>0.97</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>1.00</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Crotonaldehyde analog</td>
<td>1.05</td>
<td>1.0</td>
<td>1.3</td>
</tr>
<tr>
<td>6-Oxodocetaxel^d</td>
<td>1.08</td>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>4-Epidoxetaxel^e</td>
<td>1.13</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>4-Epi-6-oxodocetaxel^f</td>
<td>1.18</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Any unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>3.5</td>
</tr>
</tbody>
</table>

^a (2aR,4S,4aS,6bS,9S,11S,12S,12aR,12bS)-1,2-acetoxy-1-hydroxy-5-oxopent-3-yl-1,5,9-trihydroxy-4,8,11,11-tetramethyl-6-oxobicyclo[3.3.1]lendeca-4,7-dien-2-yl benzoate, 9-ester with (2S,3S)-N′-ter-butoxy-carbonyl-3-phenylisoserine. The alternative chemical name is \(5\beta\)-20-epoxy-1,7β,10β-trihydroxy-9-oxotax-11-ene-2,4,13-triy-4-aceate 13-[(2R,3S)-3-[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropionate 2-[2β]-2-methylbut-2-enolate. It is a process impurity and is listed in Table 2 for identification only. It is not reported for the drug product and should not be included in the total impurities. • (EB 1-May-2012)

^b (1S,2S,3R,4S,5R,6R)-1,2-acetoxy-1-hydroxy-5-oxopent-3-yl-1,5,9-trihydroxy-4,8,11,11-tetramethyl-6-oxobicyclo[3.3.1]lendeca-4,7-dien-2-yl benzoate, 9-ester with (2S,3S)-N′-ter-butoxy-carbonyl-3-phenylisoserine. The alternative chemical name is \(5\beta\)-20-epoxy-1,7β,10β-trihydroxy-9,10-dioxotax-11-ene-2,4,13-triy-4-aceate 2-benzoate 13-[(2R,3S)-3-[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropionate. • (EB 1-May-2012)

^c (2aR,4S,4aS,6bS,9S,11S,12S,12aR,12bS)-1,2-acetoxy-1-hydroxy-5-oxopent-3-yl-1,5,9-trihydroxy-4,8,11,11-tetramethyl-6-oxobicyclo[3.3.1]lendeca-4,7-dien-2-yl benzoate, 9-ester with (2S,3S)-N′-ter-butoxy-carbonyl-3-phenylisoserine. The alternative chemical name is \(5\beta\)-20-epoxy-1,7β,10β-trihydroxy-9,10-dioxotax-11-ene-2,4,13-triy-4-aceate 2-benzoate 13-[(2R,3S)-3-[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropionate. • (EB 1-May-2012)

^d (2aR,4S,4aS,6bS,9S,11S,12S,12aR,12bS)-1,2-acetoxy-1-hydroxy-5-oxopent-3-yl-1,5,9-trihydroxy-4,8,11,11-tetramethyl-6-oxobicyclo[3.3.1]lendeca-4,7-dien-2-yl benzoate, 9-ester with (2S,3S)-N′-ter-butoxy-carbonyl-3-phenylisoserine. The alternative chemical name is \(5\beta\)-20-epoxy-1,7β,10β-trihydroxy-9,10-dioxotax-11-ene-2,4,13-triy-4-aceate 2-benzoate 13-[(2R,3S)-3-[(1,1-dimethylethoxy)carbonyl]amino]-2-hydroxy-3-phenylpropionate. • (EB 1-May-2012)

### ADDITIONAL REQUIREMENTS

**PACKAGING AND STORAGE:** Preserve in single-dose or multiple-dose containers, preferably of Type 1 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-pentenyl docetaxel, 6-oxodocetaxel, 4-epidocetaxel, and 4-epi-6-oxodocetaxel.]

USP Endotoxin RS ▲ (USP35)

### 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 and Membrane Filtration.

**PARTICULATE MATTER IN INJECTIONS** (78B): Meets the requirements for small-volume injections

**OTHER REQUIREMENTS:** Meets the requirements in Injections (1)