**Docetaxel**

**Change to read:**

- Anhydrous: \([114977-28-5]\).  
- Trihydrate: \([148408-66-6]\).

**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. \(\text{CAUTION}—\text{Docetaxel is cytotoxic. Great care should be taken to prevent inhaling particles of Docetaxel and exposing the skin to it.}\)

**IDENTIFICATION**
- **A. INFRARED ABSORPTION** (197)
  - [NOTE—Methods described in Infrared Absorption (197K), (197M), or (197S) may be used. Use a solution containing 60 mg/mL of Docetaxel in methylene chloride for (197S).]
  - \(\text{B. the retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.}\)

**ASSAY**
- **PROCEDURE**
  - Solution A: Water
  - Solution B: Acetonitrile
  - Mobile phase: See Table 1.

<table>
<thead>
<tr>
<th>Time (\text{(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>72</td>
<td>28</td>
</tr>
<tr>
<td>39.0</td>
<td>28</td>
<td>72</td>
</tr>
<tr>
<td>39.1</td>
<td>72</td>
<td>28</td>
</tr>
<tr>
<td>50</td>
<td>72</td>
<td>28</td>
</tr>
</tbody>
</table>

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

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

**Standard solution**: 1.0 mg/mL made by transferring a quantity of USP Docetaxel RS to a suitable volumetric flask, dissolving in alcohol, equivalent to about 5% of the final volume, and diluting with Diluent to volume

**Sample solution**: 1.0 mg/mL made by transferring a quantity of Docetaxel to a suitable volumetric flask, dissolving in alcohol, equivalent to about 5% of the final volume, and diluting 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**
  - Refrigerated 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 4 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:

\[
\text{Result} = \frac{r_U}{r_S} \times \frac{C_S}{C_U} \times 100
\]

- \(r_U\) = peak response from the Sample solution
- \(r_S\) = peak response from the Standard solution
- \(C_S\) = concentration of docetaxel in the Standard solution \((\text{mg/mL})\)
- \(C_U\) = concentration of Docetaxel in the Sample solution \((\text{mg/mL})\)

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

**IMPURITIES**
- **Residue on Ignition (281)**: NMT 0.1%

**Delete the following:**
- **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

**Add the following:**
- **Heavy Metals**
  - **Lead nitrate stock solution**: Prepare as directed in Heavy Metals (231), Special Reagents.
  - **pH 3.5 acetate buffer**: Prepare as directed in Heavy Metals (231), Method I.
  - **Diluent**: Dimethylformamide and water (17:3)
  - **Standard lead solution**: 1 µg/mL of lead in Diluent from the Lead nitrate stock solution, prepared on the day of use.
Test stock preparation: Dissolve 1 g of Docetaxel in 20 mL of Diluent.

Test preparation: Place 12 mL of the Test stock preparation in a color-comparison tube, add 2 mL of pH 3.5 acetate buffer and 1.2 mL of thioacetamide–glycerin base TS, and mix.

Monitoring preparation: Place 10 mL of the Standard lead solution in a color-comparison tube, add 2 mL of the Test stock preparation, and mix. Add 2 mL of pH 3.5 acetate buffer and 1.2 mL of thioacetamide–glycerin base TS, and mix.

Blank preparation: Place 10 mL of Diluent in a color-comparison tube, add 2 mL of the Test stock preparation, and mix. Add 2 mL of pH 3.5 acetate buffer and 1.2 mL of thioacetamide–glycerin base TS, and mix.

Blank test preparation: Place 10 mL of the Blank preparation in a color-comparison tube, add 2 mL of the Blank preparation, and mix. Add 2 mL of pH 3.5 acetate buffer and 1.2 mL of thioacetamide–glycerin base TS, and mix.

Acceptance criteria: Compared to the Blank preparation, the Monitor preparation shows a slight brown color. Any brown color in the Test preparation is not more intense than in the Monitor preparation (NMT 20 ppm).

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-debenzoyl 2-pentenoyl docetaxel are specified impurities. Procedure 2 is recommended if O-BOC N-pyruvyl docetaxel is a specified impurity.]

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 4 between 2-debenzoyl 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:

\[ \text{Result} = \left( \frac{r_u}{r_T} \right) \times \left( \frac{1}{F} \right) \times 100 \]

- \( r_u \) = 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 Table 2)

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

### 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 (if present)†</td>
<td>0.25</td>
<td>1.5</td>
<td>0.15 (RB 1-May-2012)</td>
</tr>
<tr>
<td>2-Debenzoxyl 2-pentenoyl docetaxel†</td>
<td>0.97</td>
<td>0.63</td>
<td>0.5</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>1.00</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6-Oxodocetaxel</td>
<td>1.08</td>
<td>1.0</td>
<td>0.3</td>
</tr>
<tr>
<td>4-Epidocetaxel</td>
<td>1.13</td>
<td>1.0</td>
<td>0.3</td>
</tr>
<tr>
<td>4-Epi-6-oxodocetaxel</td>
<td>1.18</td>
<td>1.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Any unspecified impurity: — 1.0 0.10

Total impurities: — 1.0

### Table 3

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>25</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>35</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>45</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>45.1</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>53</td>
<td>65</td>
<td>35</td>
</tr>
</tbody>
</table>

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

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.]

Sample solution: 1.0 mg/mL of Docetaxel in acetonitrile

Chromatographic system

(See Chromatography (621), System Suitability.)
**SPECIFIC TESTS**

- **BACTERIAL ENDOTOXINS TEST** (85): It contains NMT 0.4 USP Endotoxin Units/mg.

**ADDENDA**

- **LABELING**: Where it is an anhydrous form, the label so indicates. If a test for Organic Impurities other than Procedure 7 is used, the labeling states the test with which the article complies.

**ADDITIONAL REQUIREMENTS**

**Change to read:**

- **USP REFERENCE STANDARDS** (11)

**Add the following:**

- **USP Reference Standard**: USP Docetaxel RS

**Packaging and Storage**: Preserve in well-closed, light-resistant containers, and store at room temperature.

**Change to read:**

- **USP Reference Standard**: USP Docetaxel RS

USP Docetaxel Identification RS

It contains docetaxel and small amounts of the following:

- 2-Debenzoyl 2-pentenoyl docetaxel: (2aR,4S,4aS,5R,9S,11S,12S,12aR,12bS)-1,2,3,4,5-pentahydroxy-2,3,4,5-tetramethyl-7,11-phenylisoserine.

**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.
4-Epi-6-oxodocetaxel: (2aR,4R,4aS,9S,11S,12aR,12bS)-
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-5H-cyclodeca[3,4][benz][1,2-b]oxet-5,6-
dione 12b-acetate, 12-benzoate, 9-ester with (2R,3S)-
N-tert-butoxycarbonyl-3-phenylisoserine.
C₄₃H₅₁NO₁₄  805.86

• USP Docetaxel System Suitability RS
  Contains docetaxel and small amount of 6-
  oxodocetaxel, O-BOC N-pyruvyl docetaxel, 4-
  epidocetaxel, and 4-epi-6-oxodocetaxel. (RB 1-May-2012)

USP Endotoxin RS