Abiraterone Acetate Tablets

Type of Posting          Revision Bulletin
Posting Date            4-May-2022
Official Date           5-May-2022
Expert Committee        Small Molecules 3

In accordance with the Rules and Procedures of the Council of Experts, the Small Molecules 3 Expert Committee has revised the Abiraterone Acetate Tablets monograph. The purpose of this revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution test(s).

- *Dissolution Test 2* was validated using the Acquity UPLC CSH Fluoro-Phenyl brand of column with L43 packing. The typical retention time for abiraterone acetate is about 0.6 min.

The Abiraterone Acetate Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Robyn Fales, Senior Scientist I (240-221-2047 or mp@usp.org).
Abiraterone Acetate Tablets

DEFINITION
Abiraterone Acetate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of abiraterone acetate (C\textsubscript{28}H\textsubscript{33}NO\textsubscript{3}).

IDENTIFICATION
• A. The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.
• B. The UV spectrum of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

ASSAY

• PROCEDURE
   Solution A: 10 mM of ammonium acetate in water
   Mobile phase: See Table 1.

Table 1

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Acetonitrile (%)</th>
<th>Ethanol (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>50</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>40</td>
<td>15</td>
<td>55</td>
<td>30</td>
</tr>
<tr>
<td>47</td>
<td>0</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>58</td>
<td>0</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>60</td>
<td>50</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>70</td>
<td>50</td>
<td>20</td>
<td>30</td>
</tr>
</tbody>
</table>

[Note—Protect solutions from light.]
System suitability solution: 0.625 mg/mL of USP Abiraterone System Suitability Mixture RS in acetonitrile.
[Note—See Table 2 for relative retention times of the main components of the mixture.]

Table 2

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-Ketoabiraterone acetate</td>
<td>0.42</td>
</tr>
<tr>
<td>α-Epoxyabiraterone acetate</td>
<td>0.62</td>
</tr>
<tr>
<td>β-Epoxyabiraterone acetate</td>
<td>0.66</td>
</tr>
<tr>
<td>Name</td>
<td>Relative Retention Time</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>0.69</td>
</tr>
<tr>
<td>3-Deoxy-3-acetyl abiraterone-3-ene</td>
<td>0.85</td>
</tr>
<tr>
<td>Abiraterone acetate</td>
<td>1.0</td>
</tr>
<tr>
<td>Abiraterone ethyl ether</td>
<td>1.18</td>
</tr>
<tr>
<td>Abiraterone isopropyl ether</td>
<td>1.26</td>
</tr>
<tr>
<td>Anhydro abiraterone</td>
<td>1.29</td>
</tr>
<tr>
<td>3-Deoxy 3-chloroabiraterone</td>
<td>1.31</td>
</tr>
<tr>
<td>O-Chlorobutylabiraterone</td>
<td>1.33</td>
</tr>
</tbody>
</table>

**Standard solution:** 0.625 mg/mL of USP Abiraterone Acetate RS in acetonitrile

**Sample solution:** Nominally equivalent to 0.625 mg/mL of abiraterone acetate in acetonitrile, prepared from NLT 20 powdered Tablets as follows. Transfer the powder to a suitable volumetric flask. Add 50% of the flask volume of acetonitrile, shake by mechanical means for 30 min, and dilute with acetonitrile to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size, and use the clear solution for analysis.

**Chromatographic system**
(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 254 nm or diode array. [Note—Use a diode array detector to perform Identification B.]

**Column:** 3-mm × 15-cm; 3-µm packing L1

**Column temperature:** 15°

**Flow rate:** 0.45 mL/min

**Injection volume:** 10 µL

**System suitability**

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

**Suitability requirements**

- **Resolution:** NLT 1.0 between anhydro abiraterone and 3-deoxy 3-chloroabiraterone peaks, System suitability solution

- **Relative standard deviation:** NMT 2.0%, Standard solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of abiraterone acetate (C₂₆H₃₃NO₂) in the portion of Tablets taken:

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

- \( r_U \) = peak response from the Sample solution
- \( r_S \) = peak response from the Standard solution
- \( C_S \) = concentration of USP Abiraterone Acetate RS in the Standard solution (mg/mL)
- \( C_U \) = nominal concentration of abiraterone acetate in the Sample solution (mg/mL)
Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution (711).**

Test 1

[Note—Protect solutions from light.]

**Buffer:** 56.5 mM of *monobasic sodium phosphate* in *water*. Adjust with 5 N *sodium hydroxide* or *phosphoric acid* to a pH of 4.5.

**Medium:** 0.25% of *sodium lauryl sulfate* in *Buffer*; 900 mL

**Apparatus 2:** 50 rpm

**Time:** 45 min

**Standard solution:** 0.3 mg/mL of **USP Abiraterone Acetate RS** in *Medium* prepared as follows. Transfer **USP Abiraterone Acetate RS** into a suitable volumetric flask. Add 4% of the flask volume of *acetonitrile* to dissolve, and dilute with *Medium* to volume.

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 10-µm pore size. Use the filtrate.

**Mobile phase:** *Acetonitrile, formic acid*, and *water* (55: 0.05: 45)

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 252 nm

**Column:** 4.6-mm × 3-cm; 5-µm packing **L1**

**Flow rate:** 1 mL/min

**Injection volume:** 10 µL

**System suitability**

**Sample:** **Standard solution**

**Suitability requirements**

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 2.0%

**Analysis**

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

Calculate the percentage of the labeled amount of abiraterone acetate (C₂₆H₃₃NO₂) dissolved:

\[
\frac{r_U}{r_S} \times \frac{C_S}{L} \times V \times 100
\]

\[r_U\] = peak response from the **Sample solution**

\[r_S\] = peak response from the **Standard solution**

\[C_S\] = concentration of the **Standard solution** (mg/mL)

\[L\] = label claim (mg/Tablet)

\[V\] = volume of *Medium*, 900 mL

**Tolerances:** NLT 85% (**Q**) of the labeled amount of abiraterone acetate (C₂₆H₃₃NO₂) is dissolved.

**Test 2:** If the product complies with this test, the labeling indicates that it meets USP **Dissolution Test 2.** [Note—Protect solutions from light.]

**Buffer:** 56.5 mM of *monobasic sodium phosphate* in *water*. Adjust with 5 N *sodium hydroxide* or *phosphoric acid* to a pH of 4.5.

**Medium:** 0.25% of *sodium lauryl sulfate* in *Buffer*; 900 mL

**Apparatus 2:** 75 rpm
**Standard solution:** 0.28 mg/mL of USP Abiraterone Acetate RS in Medium prepared as follows. Transfer USP Abiraterone Acetate RS into a suitable volumetric flask. Add 4% of the flask volume of acetonitrile to dissolve, and dilute with Medium to volume.

**Sample solution:** Pass a portion of the solution under test through a suitable filter of 10-µm pore size. Use the filtrate.

**Mobile phase:** Acetonitrile and water (90:10)

**Chromatographic system**

(See Chromatography (621), System Suitability.)

**Mode:** LC

**Detector:** UV 254 nm

**Column:** 2.1-mm × 7.5-cm; 1.7-µm packing L43

**Column temperature:** 35°

**Flow rate:** 0.5 mL/min

**Injection volume:** 0.5 µL

**Run time:** NLT 1.7 times the retention time of abiraterone acetate

**System suitability**

**Sample:** Standard solution

**Suitability requirements**

- **Tailing factor:** NMT 2.0
- **Relative standard deviation:** NMT 2.0%

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of the labeled amount of abiraterone acetate \((C_{26}H_{33}NO_2)\) dissolved:

\[
\text{Result} = \left( \frac{r_U}{r_S} \right) \times C_S \times V \times \frac{1}{L} \times 100
\]

- \(r_U\) = peak response of abiraterone acetate from the Sample solution
- \(r_S\) = peak response of USP Abiraterone Acetate RS from the Standard solution
- \(C_S\) = concentration of the Standard solution (mg/mL)
- \(V\) = volume of Medium, 900 mL
- \(L\) = label claim (mg/Tablet)

**Tolerances:** NLT 80% (Q) of the labeled amount of abiraterone acetate \((C_{26}H_{33}NO_2)\) is dissolved. ▲ (RB 5-May-2022)

**Test 3:** If the product complies with this test, the labeling indicates that it meets USP Dissolution Test 3.

[Notice—Protect solutions from light.]

**Buffer:** 56.5 mM of sodium phosphate monobasic in water

**Medium:** 0.25% of sodium lauryl sulfate in Buffer, adjusted with 5 N sodium hydroxide or phosphoric acid to a pH of 4.5; 900 mL

**Apparatus 2:** 50 rpm

**Time:** 45 min

**Standard solution:** 0.3 mg/mL of USP Abiraterone Acetate RS in Medium prepared as follows. Transfer USP Abiraterone Acetate RS into a suitable volumetric flask. Add 4% of the flask volume of acetonitrile to dissolve, and dilute with Medium to volume.

**Sample solution:** Pass a portion of the solution under test through a suitable filter.

**Mobile phase:** Acetonitrile, formic acid, and water (55: 0.05: 45)

**Chromatographic system**

(See Chromatography (621), System Suitability.)
**Mode:** LC  
**Detector:** UV 252 nm  
**Column:** 4.6-mm × 3-cm; 5-µm packing L1  
**Column temperature:** 30°  
**Flow rate:** 1.0 mL/min  
**Injection volume:** 10 µL  

**System suitability**  
**Sample:** Standard solution  
**Suitability requirements**  
**Tailing factor:** NMT 2.0  
**Relative standard deviation:** NMT 2.0%  

**Analysis**  
**Samples:** Standard solution and Sample solution  
Calculate the percentage of the labeled amount of abiraterone acetate (C_{26}H_{33}NO_{2}) dissolved:  

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

- \( r_U \) = peak response of abiraterone acetate from the Sample solution  
- \( r_S \) = peak response of abiraterone acetate from the Standard solution  
- \( C_S \) = concentration of USP Abiraterone Acetate RS in the Standard solution (mg/mL)  
- \( L \) = label claim of abiraterone acetate (mg/Tablet)  
- \( V \) = volume of Medium, 900 mL  

**Tolerances:** NLT 80% (Q) of the labeled amount of abiraterone acetate (C_{26}H_{33}NO_{2}) is dissolved.  

- **Uniformity of Dosage Units (905):** Meet the requirements  

**IMPURITIES**  
- **Organic Impurities**  
  [Note—Protect solutions from light.]  
  **Solution A, Mobile phase, System suitability solution, Standard solution, Sample solution,** and **Chromatographic system:** Proceed as directed in the Assay.  
  **Sensitivity solution:** 0.3 µg/mL of USP Abiraterone Acetate RS in acetonitrile from Standard solution  

**System suitability**  
**Samples:** System suitability solution, Standard solution, and Sensitivity solution  
**Suitability requirements**  
**Resolution:** NLT 1.0 between anhydro abiraterone and 3-deoxy 3-chloroabiraterone peaks, System suitability solution  
**Signal-to-noise ratio:** NLT 10, Sensitivity solution  
**Relative standard deviation:** NMT 2.0%, Standard solution  

**Analysis**  
**Samples:** Standard solution and Sample solution  
Calculate the percentage of each impurity in the portion of Tablets taken:  

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

- \( r_U \) = peak area of each impurity from the Sample solution  
- \( r_S \) = peak area of abiraterone acetate from the Standard solution  
- \( C_S \) = concentration of USP Abiraterone Acetate RS in the Standard solution (mg/mL)  
- \( C_U \) = nominal concentration of abiraterone acetate in the Sample solution (mg/mL)  
- \( F \) = relative response factor for each individual impurity (see Table 3)
Acceptance criteria: See Table 3. Disregard any peak less than 0.05%.

### Table 3

<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>7-Ketoabiraterone acetate</td>
<td>0.42</td>
<td>1.4</td>
<td>0.50</td>
</tr>
<tr>
<td>α-Epoxyabiraterone acetate</td>
<td>0.62</td>
<td>0.26</td>
<td>0.80</td>
</tr>
<tr>
<td>β-Epoxyabiraterone acetate</td>
<td>0.66</td>
<td>0.26</td>
<td>2.0</td>
</tr>
<tr>
<td>Abiraterone</td>
<td>0.69</td>
<td>1.0</td>
<td>0.40</td>
</tr>
<tr>
<td>Abiraterone acetate</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Abiraterone ethyl ether            1a</td>
<td>1.18</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Abiraterone isopropyl ether</td>
<td>1.26</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Unspecified impurity</td>
<td>—</td>
<td>1.0</td>
<td>0.20</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>—</td>
<td>3.2</td>
</tr>
</tbody>
</table>

 1a This is a process impurity and is controlled in the drug substance monograph. It is included in the table for identification only, and it is not to be reported in the total impurities.

### ADDITIONAL REQUIREMENTS

- **Packaging and Storage**: Preserve in tight containers, and store at controlled room temperature.
- **Labeling**: When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used.
- **USP Reference Standards (11)**
  - USP Abiraterone Acetate RS
  - USP Abiraterone System Suitability Mixture RS

It contains Abiraterone Acetate and small amounts of the following:

- **Abiraterone**
  - 17-(Pyridin-3-yl)androsta-5,16-dien-3β-ol.
    - C_{24}H_{31}NO 349.52

- **Abiraterone ethyl ether**
  - 3β-Ethoxy-17-(pyridin-3-yl)androsta-5,16-diene.
    - C_{28}H_{35}NO 377.57

- **Abiraterone isopropyl ether**
  - 3β-Isopropoxy-17-(pyridin-3-yl)androsta-5,16-diene.
    - C_{27}H_{37}NO 391.60

- **Anhydro abiraterone**
  - 17-(Pyridin-3-yl)androsta-3,5,16-triene.
    - C_{24}H_{29}N 331.50

- **O-Chlorobutylabiraterone**
3β-(4-Chlorobutoxy)-17-(pyridin-3-yl)androsta-5,16-diene.
\[ C_{28}H_{38}ClNO \] 440.07

3-Deoxy-3-acetyl abiraterone-3-ene
1-[17-(Pyridin-3-yl)androsta-3,5,16-trien-3-yl]ethanone.
\[ C_{26}H_{31}NO \] 373.53

3-Deoxy 3-chloroabiraterone
3β-Chloro-17-(pyridin-3-yl)androsta-5,16-diene.
\[ C_{24}H_{30}ClN \] 367.96

α-Epoxyabiraterone acetate
17-(Pyridin-3-yl)-16α,17α-epoxyandrost-5-en-3β-yl acetate.
\[ C_{26}H_{33}NO_3 \] 407.55

β-Epoxyabiraterone acetate
17-(Pyridin-3-yl)-16β,17β-epoxyandrost-5-en-3β-yl acetate.
\[ C_{26}H_{33}NO_3 \] 407.55

7-Ketoabiraterone acetate
7-Oxo-17-(pyridin-3-yl)androsta-5,16-dien-3β-yl acetate.
\[ C_{26}H_{31}NO_3 \]