Abiraterone Acetate Tablets

Type of Posting Revision Bulletin
Posting Date 18–Nov–2019
Official Date 19–Nov–2019
Expert Committee Chemical Medicines Monographs 3
Reason for Revision Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 3 Expert Committee has revised the Abiraterone Acetate Tablets monograph. The purpose for the revision is to add *Dissolution Test 3* to accommodate FDA-approved drug products with different dissolution conditions and/or tolerances than the existing dissolution tests.

- *Dissolution Test 3* was validated using a Phenomenex Luna C18 (2) brand of column with L1 packing. The typical retention time for abiraterone acetate is about 4 min.

The *Abiraterone Acetate Tablets Revision Bulletin* supersedes the currently official monograph.¹

Should you have any questions, please contact Jane Li, Associate Scientific Liaison (301-230-6345 or Jane.Li@usp.org).

¹ Note: Addition of *Dissolution Test 2* to the Abiraterone Acetate Tablets monograph is currently being proposed under the pending monograph process.
Abiraterone Acetate Tablets

DEFINITION
Abiraterone Acetate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of abiraterone acetate (C_{10}H_{13}NO_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>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min)</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>47</td>
</tr>
<tr>
<td>58</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>70</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>
<thead>
<tr>
<th>Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>7-Ketoabiraterone acetate</td>
</tr>
<tr>
<td>α-Epoxyabiraterone acetate</td>
</tr>
<tr>
<td>β-Epoxyabiraterone acetate</td>
</tr>
<tr>
<td>Abiraterone</td>
</tr>
<tr>
<td>3-Deoxy-3-acetyl abiraterone-3-ene</td>
</tr>
<tr>
<td>Abiraterone acetate</td>
</tr>
<tr>
<td>Abiraterone ethyl ether</td>
</tr>
<tr>
<td>Abiraterone isopropyl ether</td>
</tr>
<tr>
<td>Anhydro abiraterone</td>
</tr>
<tr>
<td>3-Deoxy 3-chloroabiraterone</td>
</tr>
<tr>
<td>O-Chlorobutylabiraterone</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°C
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 (C_{10}H_{13}NO_3) in the portion of Tablets taken:

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

\( r_U \) = 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)

Change Test 1 (88:19:Nov:2019)
[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
Samples: Standard solution
Suitability requirements
Tailing factor: NMT 2.0
**2 Abiraterone**

**IMPURITIES**

- **ORGANIC IMPURITIES**
  
  **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:

  \[
  \text{Result} = \left( \frac{r_t}{r_i} \right) \times \left( \frac{C_s}{C_i} \right) \times \left( 1 / F \right) \times 100
  \]

  \( r_t \) = peak area of each impurity from the Sample solution

  \( r_i \) = peak area of abiraterone acetate from the Standard solution

  \( C_s \) = concentration of USP Abiraterone Acetate RS in the Standard solution (mg/mL)

  \( C_i \) = 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>
<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>0.80</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*</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>2.0</td>
</tr>
</tbody>
</table>

*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.

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**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**
  - C_{24}H_{31}NO_3 349.52
- **Abiraterone ethyl ether**
  - C_{25}H_{35}NO 377.57
- **Abiraterone isopropyl ether**
  - C_{26}H_{37}NO 391.60
- **Anhydro abiraterone**
  - C_{24}H_{29}N 331.50
- **O-Chlorobutylabiraterone**
  - C_{28}H_{38}ClNO 440.07
- **3-Deoxy-3-acetyl abiraterone-3-ene**
  - C_{26}H_{31}NO 373.53
- **3-Deoxy 3-chloroabiraterone**
  - C_{24}H_{30}ClN 367.96
- **α-Epoxyabiraterone acetate**
  - C_{26}H_{33}NO_3 407.55
- **β-Epoxyabiraterone acetate**
  - C_{26}H_{33}NO_3 407.55
- **7-Ketoabiraterone acetate**
  - C_{26}H_{31}NO_3 407.55
- **7-Oxo-17-(pyridin-3-yl)androsta-5,16-dien-3β-yl acetate.**
  - C_{26}H_{31}NO_3 407.55