Abiraterone Acetate Tablets

Type of Posting	Revision Bulletin
Posting Date	18–Nov–2019
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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 ($C_{26}H_{33}NO_2$).

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

Time (min)	Solution A (%)	Acetonitrile (%)	Ethanol (%)
0	50	20	30
40	15	55	30
47	0	20	80
58	0	20	80
60	50	20	30
70	50	20	30

[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

Name	Relative Retention Time
7-Ketoabiraterone acetate	0.42
α-Epoxyabiraterone acetate	0.62
β-Epoxyabiraterone acetate	0.66
Abiraterone	0.69
3-Deoxy-3-acetyl abiraterone-3-ene	0.85
Abiraterone acetate	1.0
Abiraterone ethyl ether	1.18
Abiraterone isopropyl ether	1.26
Anhydro abiraterone	1.29
3-Deoxy 3-chloroabiraterone	1.31
O-Chlorobutylabiraterone	1.33

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 ($C_{26}H_{33}NO_2$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of 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▲ (RB 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
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:

$$(r_U/r_S) \times (C_S/L) \times V \times 100$$

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 ($C_{26}H_{33}NO_2$) is dissolved.

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

[NOTE—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:

$$\text{Result} = (r_U/r_S) \times (C_S/L) \times V \times 100$$

r_U = peak response of abiratrone acetate from the *Sample solution*
r_S = peak response of abiratrone 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.▲ (RB 19-Nov-2019)

• **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:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
7-Ketoabiraterone acetate	0.42	1.4	0.50
α-Epoxyabiraterone acetate	0.62	0.26	0.80
β-Epoxyabiraterone acetate	0.66	0.26	0.80
Abiraterone	0.69	1.0	0.40
Abiraterone acetate	1.0	—	—
Abiraterone ethyl ether[a]	1.18	—	—
Abiraterone isopropyl ether[a]	1.26	—	—
Unspecified impurity	—	1.0	0.20
Total impurities	—	—	2.0

[a] 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.

Add the following:

▲• **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (RB 19-Nov-2019)

• **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.
$C_{26}H_{35}NO$ 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.
$C_{26}H_{31}NO_3$