

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 rnp@usp.org).

Abiraterone Acetate Tablets

DEFINITION

Abiraterone Acetate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of abiraterone acetate ($C_{26}H_{33}NO_2$).

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

Name	Relative Retention Time
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- μ m 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 \times 15-cm; 3- μ m packing [L1](#)

Column temperature: 15°

Flow rate: 0.45 mL/min

Injection volume: 10 μ L

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

[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- μ m 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 \times 3-cm; 5- μ m packing [L1](#)

Flow rate: 1 mL/min

Injection volume: 10 μ L

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 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

Time: 30 min

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- μ m 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 \times 7.5-cm; 1.7- μ m packing [L43](#)

Column temperature: 35°

Flow rate: 0.5 mL/min

Injection volume: 0.5 μ L

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:

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

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*.

[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 (C₂₆H₃₃NO₂) dissolved:

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

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 (C₂₆H₃₃NO₂) 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:

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

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	2.0
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	—	—	3.2

^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.
- **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-3 β -ol.

$C_{24}H_{31}NO$ 349.52

Abiraterone ethyl ether

3 β -Ethoxy-17-(pyridin-3-yl)androsta-5,16-diene.

$C_{26}H_{35}NO$ 377.57

Abiraterone isopropyl ether

3 β -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.

$C_{26}H_{31}NO_3$

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