Bicalutamide Tablets

Type of Posting	Revision Bulletin
Posting Date	26–Oct–2018
Official Date	01–Nov–2018
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 Bicalutamide Tablets monograph. The purpose for the revision is to add *Dissolution Test 3* to accommodate FDA-approved drug products with different conditions and tolerances than the existing dissolution tests.

The Bicalutamide Tablets Revision Bulletin supersedes the currently official monograph.

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

Bicalutamide Tablets

DEFINITION

Bicalutamide Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$).

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*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ 2S (USP41)

ASSAY

Change to read:

• **PROCEDURE**

Mobile phase: Tetrahydrofuran, acetonitrile, and water (20:15:65)

System suitability stock solution: 0.8 mg/mL of USP Bicalutamide RS and 0.4 mg/mL of USP Bicalutamide Related Compound B RS in tetrahydrofuran

System suitability solution: 0.04 mg/mL of USP Bicalutamide RS and 0.02 mg/mL of USP Bicalutamide Related Compound B RS in *Mobile phase* from the *System suitability stock solution*

Standard stock solution: 0.8 mg/mL of USP Bicalutamide RS in tetrahydrofuran

Standard solution: 0.04 mg/mL of USP Bicalutamide RS in *Mobile phase* from the *Standard stock solution*

Sample stock solution: 0.5 mg/mL of bicalutamide in tetrahydrofuran prepared as follows. Transfer an equivalent to 50 mg of bicalutamide from finely powdered Tablets (NLT 20) into a 100-mL volumetric flask. Add 50 mL of tetrahydrofuran, and sonicate for NLT 10 min to complete dissolution. Allow to cool to room temperature, and dilute with tetrahydrofuran to volume. Pass through a suitable filter of 0.45-µm pore size.

Sample solution: 0.04 mg/mL of bicalutamide in *Mobile phase* from the *Sample stock solution*

Chromatographic system

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

Mode: LC

Detector: UV 270 nm. ▲For *Identification B*, use a diode array detector in the range of 190–400 nm.▲ 2S (USP41)

Column: 5-mm × 12.5-cm; 3-µm packing L1

Column temperature: 50°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for bicalutamide and bicalutamide related compound B are 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: Greater than 1.9 between bicalutamide and bicalutamide related compound B

Tailing factor: Less than 1.3 for bicalutamide

Relative standard deviation: NMT ▲1.0%▲ 2S (USP41) for bicalutamide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$) in the portion of Tablets taken:

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

r_U = peak area from the *Sample solution*
r_S = peak area from the *Standard solution*
C_S = concentration of USP Bicalutamide RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of bicalutamide in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **DISSOLUTION** ⟨711⟩

Test 1

Medium: 1.0% w/v sodium lauryl sulfate in water; 1000 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: 0.05 mg/mL of USP Bicalutamide RS in *Medium* prepared as follows. Transfer USP Bicalutamide RS to a suitable volumetric flask, dissolve in tetrahydrofuran equivalent to 1% of the final volume, and dilute with *Medium* to volume.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV

Analytical wavelength: 270 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$) dissolved:

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

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Bicalutamide RS in the *Standard solution* (mg/mL)
V = volume of *Medium* (mL)
L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$) is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium, Apparatus 2, Time, Standard solution, Sample solution, and **Instrumental conditions:** Proceed as directed for *Test 1*.

Tolerances: NLT 75% (Q) of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$) is dissolved.

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

Medium: 1.0% (w/v) sodium lauryl sulfate in water; 1000 mL

Apparatus 2: 75 rpm

Time: 60 min

Standard solution: 0.01 mg/mL of USP Bicalutamide RS in *Medium*, sonicate to aid dissolution. Pass a portion of the solution through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few milliliters of the filtrate. Dilute with

Medium to a concentration that is similar to that of the *Standard solution*.

Instrumental conditions
(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)
Mode: UV
Analytical wavelength: 270 nm
Blank: *Medium*

Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Bicalutamide RS in the *Standard solution* (mg/mL)
D = dilution factor for the *Sample solution*
V = volume of *Medium* (mL)
L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$) is dissolved. ▲ (RB 1-Nov-2018)

• **Uniformity of Dosage Units** ⟨905⟩

Procedure for content uniformity
Diluent: 10 mg/mL of sodium lauryl sulfate in water
Standard solution: 0.05 mg/mL of USP Bicalutamide RS in *Diluent*. [Note—Dissolve USP Bicalutamide RS in a minimum volume of tetrahydrofuran before dilution with *Diluent*.]
Sample stock solution: Transfer 1 Tablet to a 100-mL volumetric flask. Add 10 mL of water, and sonicate for approximately 30 min. Add 80 mL of tetrahydrofuran, and sonicate for 30 min to complete dissolution of bicalutamide. Allow to cool to room temperature, and dilute with tetrahydrofuran to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.
Sample solution: Transfer 10.0 mL of the *Sample stock solution* into a 100-mL volumetric flask, and dilute with *Diluent* to volume.
Instrumental conditions
(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)
Mode: UV
Analytical wavelength: 270 nm
Blank: *Diluent*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$) in the Tablet taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of USP Bicalutamide RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of bicalutamide in the *Sample solution* (mg/mL)

Acceptance criteria: Meet the requirements

IMPURITIES

• **Limit of 4-Amino-2-(trifluoromethyl)benzonitrile**
Mobile phase and **System suitability solution:** Prepare as directed in the *Assay*.
Standard stock solution: 0.2 mg/mL of USP Bicalutamide RS in tetrahydrofuran
Standard solution: 0.02 mg/mL of USP Bicalutamide RS in *Mobile phase* from the *Standard stock solution*
Sample solution: Transfer the equivalent to 50 mg of bicalutamide from powdered Tablets (NLT 20) to a 25-mL volumetric flask. Add 2 mL of tetrahydrofuran, and allow to stand for 5 min. Add 20 mL of *Mobile phase*, sonicate for 10 min, and allow to cool to room temperature. Dilute with *Mobile phase* to volume, and pass through a suitable filter of 0.2-µm pore size.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 5-mm × 12.5-cm; 3-µm packing L1
Column temperature: 50°
Flow rate: 1.5 mL/min
Injection volume: 10 µL
System suitability
Sample: *System suitability solution*
[Note—The relative retention times of 4-amino-2-(trifluoromethyl)benzonitrile, bicalutamide, and bicalutamide related compound B are about 0.4, 1.0, and about 1.1, respectively.]
Suitability requirements
Resolution: Greater than 1.9 between bicalutamide and bicalutamide related compound B
Tailing factor: Less than 1.3 for bicalutamide
Relative standard deviation: NMT 2.0% for bicalutamide
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of 4-amino-2-(trifluoromethyl) benzonitrile 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 4-amino-2-(trifluoromethyl) benzonitrile from the *Sample solution*
r_S = peak area of bicalutamide from the *Standard solution*
C_S = concentration of USP Bicalutamide RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of bicalutamide in the *Sample solution* (mg/mL)
F = relative response factor for 4-amino-2-(trifluoromethyl)benzonitrile, 1.4

Acceptance criteria: NMT 0.1%

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 test used only if *Test 1* is not used.
• **USP Reference Standards** ⟨11⟩
USP Bicalutamide RS
USP Bicalutamide Related Compound B RS
(*RS*)-*N*-(4-Cyano-3-(trifluoromethyl)phenyl)-3-(3-fluorophenylsulfonyl)-2-hydroxy-2-methylpropanamide.
$C_{18}H_{14}F_4N_2O_4S$ 430.37