Bicalutamide Tablets

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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 (C₈H₁₄F₃N₂O₅S).

**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. \[\text{▲} 25\ (\text{USP}41)\]

**ASSAY**

**Change to read:**

- **PERFORMANCE TESTS**

  **CHANGE TO:**

- **DILUTION** (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:
    - Mode: UV
    - Analytical wavelength: 270 nm
    - Blank: Medium
  - Analysis:
    - Samples: Standard solution and Sample solution
    - Calculate the percentage of the labeled amount of bicalutamide (C₈H₁₄F₃N₂O₅S) dissolved:
      \[
      \text{Result} = \left(\frac{A_s}{A_r}\right) \times C_s \times V \times \left(\frac{1}{L}\right) \times 100
      \]
    - Tolerances: NLT 80% (Q) of the labeled amount of bicalutamide (C₈H₁₄F₃N₂O₅S) 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, and Instrumental conditions:
      - Proceed as directed for Test 1.
    - Tolerances: NLT 75% (Q) of the labeled amount of bicalutamide (C₈H₁₄F₃N₂O₅S) 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...
2 Bicalutamide

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 \((C_{18}H_{13}F_{4}N_{2}O_{5})\) dissolved:

\[
\text{Result} = \left( \frac{A_s}{A_f} \right) \times \left( \frac{C_s}{C_f} \right) \times D \times V \times (1/L) \times 100
\]

- **Uniformity of Dosage Units**
  (905)

Procedure for content uniformity

Diluent: 10 mg/mL of sodium lauryl sulfate in water
Standard solution: 0.03 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 \((C_{18}H_{13}F_{4}N_{2}O_{5})\) dissolved in the Tablet taken:

\[
\text{Result} = \left( \frac{A_s}{A_f} \right) \times \left( \frac{C_s}{C_f} \right) \times 100
\]

- **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 x 12.5-cm; 3-µm packing L1
Column temperature: 50°C
Flow rate: 1.5 mL/min
Injection volume: 10 µL

System suitability
Sample: System suitability solution
Calculate the percentage of 4-amino-2-(trifluoromethyl)benzonitrile in the portion of Tablets taken:

\[
\text{Result} = \left( \frac{r_s}{r_f} \right) \times \left( \frac{C_f}{C_s} \right) \times (1/f) \times 100
\]

- **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**
  - USP Bicalutamide RS
  - USP Bicalutamide Related Compound B RS (RS)-N-(4-Cyano-3-(trifluoromethyl)phenyl)-3-(3-fluorophenylsulfonyl)-2-hydroxy-2-methylpropanamide.
  - \(C_{18}H_{13}F_{4}N_{2}O_{5}\) 430.37

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