the peaks. Calculate the per centage of each impurity in the portion of Tablets taken by the formula:

$$100V(F/W)C(r_i / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Bethanechol Chloride RS in the *Standard solution; F* is the relative response factor and is equal to 0.79 for 2-hydroxypropyltrimethyl ammonium chloride and 1.0 for any other impurity; r_i is the peak response for any impurity in the *Test solution;* r_S is the peak response of USP Bethanechol Chloride RS in the *Standard solution;* and *W* is the amount, in mg, of bethanechol chloride based on the average weight, labeled dose, and amount taken to prepare the *Test solution*. Not more than 1.0% of 2-hydroxypropyltrimethyl ammonium chloride is found; not more than 0.2% of any other impurity is found; and the sum of all the impurities is not more than 1.5%.

Assay—

Buffer solution—Transfer about 29 mg of edetic acid to a 1000-mL volumetric flask, and dissolve in 500 mL of water. Add 300 µL of nitric acid to the volumetric flask, and dilute with water to volume. Pass through a 0.45- µm nylon membrane filter.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (95:5). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Bethanechol Chloride RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessar y, with *Mobile phase* to obtain a solution having a known concentration of about 0.1 mg of USP Bethanechol Chloride RS per mL.

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to 1 T ablet, to a suitable volumetric flask so that the final solution yields a concentration of about 0.1 mg per mL of bethanechol chloride. Add an amount of *Mobile phase,* about 60% to 70% of the total volume of the flask. Sonicate for 20 minutes. Shake by mechanical means for about 15 minutes. Dilute with *Mobile phase* to volume, and mix. Allow to stand for 10 minutes, and pass the solution through a 1- µm glass filter, discarding the first 3 mL of the filtrate.

System suitability solution—Transfer about 25 mg of bethanechol chloride, accurately weighed, to a 250-mL volumetric flask. Add 10 mL of 0.1 N sodium hydroxide, and allow to stand for about 15 minutes. Add 10 mL of 0.1 N hydrochloric acid. Dissolve in and dilute with *Mobile phase* to volume, and mix.

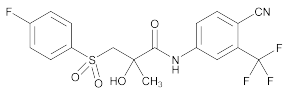
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a conductivity detector and a 3.9- × 150-mm column containing packing L55. The flow rate is about 1.0 mL per minute. The detector and column temperatures are maintained at 35 ° and 30 °, respectively. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the relative retention time is about 0.9 for 2-hydroxypropyltrimethyl ammonium chloride and 1.0 for bethanechol; and the resolution, *R,* between 2-hydroxypropyltrimethyl ammonium chloride and bethanechol is not less than 0.8. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 3.5; and the relative standard deviation for replicate injections is not more than 3.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the quantity, in mg, of bethanechol chloride ($C_7H_{17}ClN_2O_2$) in the portion of T ablets taken by the formula:

$$VC(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Bethanechol Chloride RS in the *Standard preparation; V* is the volume, in mL, of the flask used to prepare the *Assay preparation;* and r_U and r_S are the bethanechol chloride peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Bicalutamide



$C_{18}H_{14}F_4N_2O_4S$ 430.37

Propanamide, *N*-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-, (±)-;
(±)-4′-Cyano-α,α,α-trifluoro-3-[(*p*-fluorophenyl)sulfonyl]-2-methyl-*m*-lactotoluidide [90357-06-5].

DEFINITION

Bicalutamide contains NLT 98.0% and NMT 102.0% of $C_{18}H_{14}F_4N_2O_4S$, calculated on the anhydrous and solvent-free basis.

IDENTIFICATION

- **A. Infrared Absorption** ⟨197M⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 0.01% (v/v) of trifluoroacetic acid in water
Solution B: 0.01% (v/v) of trifluoroacetic acid in acetonitrile
Mobile phase: *Solution A* and *Solution B* (52:48)
Diluent: *Solution A* and *Solution B* (1:2)
System suitability solution: 5 µg/mL of USP Bicalutamide Related Compound A RS and 50 µg/mL of USP Bicalutamide RS in *Diluent*
Standard solution: 0.05 mg/mL of USP Bicalutamide RS in *Diluent*
Sample solution: 0.05 mg/mL of Bicalutamide in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 270 nm
Column: 4.0-mm × 10-cm; 3-µm packing L1
Flow rate: 1 mL/min
Injection size: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for bicalutamide related compound A isomer A and bicalutamide related compound A isomer B are 0.75 and 0.78, respectively.]
Suitability requirements
Resolution: NLT 2.0 between bicalutamide related compound A isomer B and bicalutamide, *System suitability solution*
Relative standard deviation: NMT 2%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the per centage of $C_{18}H_{14}F_4N_2O_4S$ in the portion of Bicalutamide 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 Bicalutamide RS in the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 98.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **HEAVY METALS,** *Method II* **⟨231⟩:** NMT 10 ppm

Organic Impurities

- **PROCEDURE**

Solution A, Solution B, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	67	33
16.5	67	33
26.5	40	60
32.5	5	95
32.6	67	33
35	67	33

Standard solution: 1 µg/mL of USP Bicalutamide RS in *Diluent*

Sample solution: 1 mg/mL of Bicalutamide in *Diluent*

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution 1: NLT 0.8 between bicalutamide related compound A isomer A and bicalutamide related compound A isomer B

Resolution 2: NLT 8.5 between bicalutamide related compound A isomer B and bicalutamide

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Bicalutamide 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 bicalutamide from the *Standard solution*

C_S = concentration of bicalutamide in the *Standard solution* (mg/mL)

C_U = concentration of Bicalutamide in the *Sample solution* (mg/mL)

F = relative response factor (see *Impurity Table 1*)

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 0.5%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Bicalutamide aminobenzonitrile[a]	0.30	1.4	0.1
Bicalutamide related compound A isomer A[b]	0.64	1.0	0.1
Bicalutamide related compound A isomer B[b]	0.67	1.0	0.1
Desfluoro bicalutamide[c]	0.83	1.1	0.2
2-Fluoro bicalutamide[d]	0.94	1.0	0.2
Bicalutamide	1.00	—	—
Deoxybicalutamide[e]	1.33	1.0	0.2
Bicalutamide sulfide[f]	1.56	1.0	0.1
Any unspecified impurity	—	1.0	0.1

[a] 4-Amino-2-(trifluoromethyl)benzonitrile.
[b] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfinyl]-2-hydroxy-2-methylpropanamide.
[c] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-2-hydroxy-2-methyl-3-(phenylsulfonyl)propanamide.
[d] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-(2-fluorophenylsulfonyl)-2-hydroxy-2-methylpropanamide.
[e] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-(4-fluorophenylsulfonyl)-2-methylpropanamide.
[f] *N*-[4-Cyano-3-(trifluoromethyl)phenyl]-3-(4-fluorophenylthio)-2-hydroxy-2-methylpropanamide.

SPECIFIC TESTS

- **WATER DETERMINATION,** *Method I* **⟨921⟩:** NMT 0.2%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at room temperature.
- **USP REFERENCE STANDARDS ⟨11⟩**

USP Bicalutamide RS

USP Bicalutamide Related Compound A RS

[*N*-[4-cyano-3-(trifluoromethyl)phenyl]-3-[(4-fluorophenyl)sulfinyl]-2-hydroxy-2-methylpropanamide]

($C_{18}H_{14}F_4N_2O_3S$ 414.37)

Bicalutamide Tablets

» Bicalutamide Tablets contain not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of bicalutamide ($C_{18}H_{14}F_4N_2O_4S$).

Packaging and storage—Preserve in tight containers. 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

Identification—The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Dissolution ⟨711⟩—

TEST 1—

Medium: 1.0% w/v sodium laur yl sulfate in water; 1000 mL.