Anastrozole Tablets

DEFINITION

Anastrozole Tablets contain NLT 90% and NMT 110% of the labeled amount of anastrozole ($C_{17}H_{19}N_5$).

IDENTIFICATION

Change to read:

- **A. INFRARED ABSORPTION ⟨197K⟩**

  Sample: Transfer the finely ground Tablet powder containing 8 mg of anastrozole into a suitable container. Add 10 mL of diethyl ether and sonicate for 5 min. Aspirate the supernatant and pass ● (IRA 1-Mar-2017) through a nylon filter of 0.45-µm pore size into another suitable container containing 400 mg of ● (IRA 1-Mar-2017) potassium bromide. Evaporate the mixture to dryness under nitrogen. Further dry it under vacuum at 50° for 1 h. ●Add an additional 400 mg of potassium bromide for preparation of pellet and analysis.● (IRA 1-Mar-2017)

  Acceptance criteria: ●The spectrum obtained from the *Sample* shows bands at approximately 2235, 1606, 1500, 1359, 1205, 1137, 1013, and 875 cm^{-1}, similar to the spectrum from the Reference Standard similarly obtained.● (IRA 1-Mar-2017)

- **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**

  Mobile phase: Acetonitrile and water (40:60)
  Diluent: Acetonitrile and water (50:50)
  Standard solution: 40 µg/mL of USP Anastrozole RS in *Diluent*. Sonication may be used to aid dissolution.
  Sample solution: Nominally equivalent to 40 µg/mL of anastrozole in *Diluent*, prepared as follows. Transfer NLT 10 Tablets to a suitable volumetric flask. Add 40% of the flask volume of water, and shake on a rotary shaker for 10 min to disintegrate the Tablets. Add 40% of the flask volume of acetonitrile, and sonicate for 15 min with intermittent shaking, maintaining the sonicator temperature at 25°. Dilute with *Diluent* to volume. Centrifuge a portion of the solution at 3500 rpm for 10 min, and use the clear solution for analysis.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 215 nm
  Column: 4.6-mm × 15-cm; 5-µm packing L1
  Flow rate: 1 mL/min
  Injection volume: 20 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 anastrozole ($C_{17}H_{19}N_5$) 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 Anastrozole RS in the *Standard solution* (mg/mL)
  C_U = nominal concentration of anastrozole in the *Sample solution* (mg/mL)
  Acceptance criteria: 90%–110%

PERFORMANCE TESTS

- **DISSOLUTION ⟨711⟩**

  Test 1
  Medium: Water; 900 mL, deaerated
  Apparatus 2: 50 rpm
  Time: 15 min
  Mobile phase: Acetonitrile and water (40:60)
  Diluent: Acetonitrile and water (50:50)
  Standard stock solution: 0.2 mg/mL of USP Anastrozole RS in *Diluent*
  Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (*L*/1000) mg/mL, where *L* is the label claim in mg/Tablet.
  Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few mL of the filtrate.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 215 nm
  Column: 4.6-mm × 15-cm; 5-µm packing L1
  Flow rate: 1 mL/min
  Injection volume: 50 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 anastrozole ($C_{17}H_{19}N_5$) dissolved:

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

  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 80% (*Q*) of the labeled amount of anastrozole ($C_{17}H_{19}N_5$) is dissolved.

  Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.
  Medium: Water; 1000 mL, deaerated
  Apparatus 2: 50 rpm
  Time: 15 min
  Mobile phase: Acetonitrile, trifluoroacetic acid, and water (300:1:700)
  Standard stock solution: 0.2 mg/mL of USP Anastrozole RS prepared as follows. Transfer USP Anastrozole RS into a suitable volumetric flask and add acetonitrile equivalent to 8% of the final volume. Sonicate to dissolve and dilute with water to volume.
  Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain a final concentration of (*L*/1000) mg/mL, where *L* is the label claim in mg/Tablet.
  Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size. Discard the first few mL of the filtrate.
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC
Detector: UV 215 nm
Column: 3.2-mm × 10-cm; 5-µm packing L42
Flow rate: 0.75 mL/min
Injection volume: 100 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: 0.9–1.4
Relative standard deviation: NMT 1.5%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of anastrozole ($C_{17}H_{19}N_5$) dissolved:

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

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*, 1000 mL

Tolerances: NLT 80% (*Q*) of the labeled amount of anastrozole ($C_{17}H_{19}N_5$) is dissolved.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

- **Organic Impurities**

Solution A: Methanol, acetonitrile, trifluoroacetic acid, and water (200: 100: 0.7: 700)
Solution B: Methanol, acetonitrile, trifluoroacetic acid, and water (500: 250: 0.7: 250)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
25	100	0
25.1	0	100
30	0	100
31	100	0
40	100	0

Diluent: Acetonitrile, trifluoroacetic acid, and water (200: 0.8: 800)
System suitability stock solution: 0.5 mg/mL of USP Anastrozole RS and 0.3 mg/mL of ethyl 4-hydroxybenzoate in *Diluent* prepared as follows. Transfer USP Anastrozole RS and ethyl 4-hydroxybenzoate into a suitable volumetric flask and add *Diluent* equivalent to 50% of the final volume. Sonicate to dissolve and dilute with *Diluent* to volume.
System suitability solution: 10 µg/mL of USP Anastrozole RS and 6 µg/mL of ethyl 4-hydroxybenzoate in *Diluent* from the *System suitability stock solution*
Standard stock solution: 0.5 mg/mL of USP Anastrozole RS in *Diluent* prepared as follows. Transfer USP Anastrozole RS into a suitable volumetric flask and add *Diluent* equivalent to 50% of the final volume. Sonicate to dissolve and dilute with *Diluent* to volume.
Standard solution: 10 µg/mL of USP Anastrozole RS in *Diluent* from the *Standard stock solution*
Sample solution: Nominally equivalent to 1.0 mg/mL of anastrozole from NLT 25 finely powdered Tablets, prepared as follows. Transfer a weighed quantity of powdered Tablets, equivalent to 10 mg of anastrozole, to a suitable container and add 10.0 mL of *Diluent*. Sonicate for 30 min and allow to cool to room temperature. Pass through a suitable filter of 0.45-µm pore size, and discard the first few mL of the filtrate. If the filtrate is not clear, pass again through a suitable filter of 0.2-µm pore size, and discard the first few mL of the filtrate.
Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)
Mode: LC
Detector: UV 215 nm
Column: 3.2-mm × 10-cm; 5-µm packing L42
Flow rate: 1.0 mL/min
Injection volume: 10 µL
Analysis time: 25 min
System suitability
Sample: *System suitability solution*
[NOTE—The relative retention times for ethyl 4-hydroxybenzoate and anastrozole are 0.7 and 1.0, respectively.]
Suitability requirements
Resolution: Greater than 4 between the ethyl 4-hydroxybenzoate and anastrozole peaks
Tailing factor: 0.9–1.3 for the anastrozole peak
Relative standard deviation: NMT 5% for the anastrozole peak
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of each impurity in the portion of Tablets taken:

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

r_U = peak response of each individual impurity from the *Sample solution*
r_S = peak response of anastrozole from the *Standard solution*
C_S = concentration of USP Anastrozole RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of anastrozole in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. Disregard any impurity peak less than 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Anastrozole diamide[a]	0.11	0.5
Anastrozole monoacid monoamide[b]	0.26	0.5
Anastrozole monoamide mononitrile[c]	0.30	0.5
Desmethyl anastrozole[d]	0.51	—
Anastrozole diacid[e]	0.71	0.5
Anastrozole monoacid mononitrile[f]	0.87	0.5

[a] 2,2′-{5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-1,3-phenylene}bis(2-methylpropanamide).
[b] 2-{3-[(1*H*-1,2,4-Triazol-1-yl)methyl]-5-(1-amino-2-methyl-1-oxopropan-2-yl)phenyl}-2-methylpropanoic acid.
[c] 2-{3-[(1*H*-1,2,4-Triazol-1-yl)methyl]-5-(2-cyanopropan-2-yl)phenyl}-2-methylpropanamide.
[d] 2-(3-(1-Cyanoethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropanenitrile. This process impurity 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.
[e] 2,2′-{5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-1,3-phenylene}bis(2-methylpropanoic acid).
[f] 2-{3-[(1*H*-1,2,4-Triazol-1-yl)methyl]-5-(2-cyanopropan-2-yl)phenyl}-2-methylpropanoic acid.

Table 2 *(Continued)*

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Anastrozole	1.00	—
Any individual unspecified impurity	—	0.5
Total impurities	—	1.0

[a] 2,2′-{5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-1,3-phenylene}bis(2-methylpropanamide).

[b] 2-{3-[(1*H*-1,2,4-Triazol-1-yl)methyl]-5-(1-amino-2-methyl-1-oxopropan-2-yl)phenyl}-2-methylpropanoic acid.

[c] 2-{3-[(1*H*-1,2,4-Triazol-1-yl)methyl]-5-(2-cyanopropan-2-yl)phenyl}-2-methylpropanamide.

[d] 2-(3-(1-Cyanoethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropanenitrile. This process impurity 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.

[e] 2,2′-{5-[(1*H*-1,2,4-Triazol-1-yl)methyl]-1,3-phenylene}bis(2-methylpropanoic acid).

[f] 2-{3-[(1*H*-1,2,4-Triazol-1-yl)methyl]-5-(2-cyanopropan-2-yl)phenyl}-2-methylpropanoic acid.

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 Anastrozole RS