

BRIEFING

Anastrozole. This proposal, based on the specification in the Drug Master File cited in an FDA tentatively approved ANDA, was published on the USP website as a Draft 1 USP Pending Monograph revision on April 24, 2009 for public comment. No comments were received. Therefore, the revision was approved by the MD-ODD Expert Committee as an Authorized USP Pending Monograph revision. Currently, there is an official *USP–NF* monograph for this drug substance, which differs in the *Definition*, the limit for *Total impurities in Organic Impurities*, and the test for water content. These changes may later be adopted into the *USP–NF*, once the regulatory submission is fully approved by the FDA.

(MD-ODD: F. Mao.) RTS—C73259

Anastrozole

v. 1 Authorized November 1, 2009

DEFINITION

Anastrozole contains NLT 98.0% and NMT 102.0% of C₁₇H₁₉N₅, calculated on the dried basis.

IMPURITIES

Organic Impurities

• **PROCEDURE**

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

Peak identification stock solution: 0.5 mg/mL each of USP Anastrozole RS and USP Anastrozole Related Compound A RS. Dissolve first in acetonitrile using 40% of the final volume, and dilute with *Solution A* to volume.

Peak identification solution: 10 µg/mL each of USP Anastrozole RS and USP Anastrozole Related Compound A RS in *Solution A*, from *Peak identification stock solution*

Standard solution: Dissolve USP Anastrozole RS in acetonitrile, and dilute with *Solution A* to obtain a solution having a known concentration of 0.02 mg/mL.

Blank solution: Dilute 10 mL of acetonitrile with *Solution A* to 25 mL.

Sample solution: 50 mg of Anastrozole to a 25-mL volumetric flask, and add 10 mL of acetonitrile. Dissolve in and dilute with *Solution A* to volume.

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: Between 0.9 and 1.4

Relative standard deviation: NMT 5%

Analysis

Samples: *Peak identification solution, Standard solution, Blank solution, and Sample solution*

[NOTE—Adjust the peak areas for any interference from the *Blank solution*.]

Calculate the percentage of each anastrozole related compound in the portion of Anastrozole taken:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$

r_u = response of anastrozole related compound from the *Sample solution*

r_s = response of anastrozole related compound from the *Standard solution*

C_s = concentration of USP Anastrozole RS in the *Standard solution* (mg/mL)

C_u = concentration of Anastrozole in the *Sample solution* (mg/mL)

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.0%

[NOTE—Any impurity of less than 0.05% is disregarded.]

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Anastrozole related compound B ^a	0.6	0.2
Anastrozole	1.0	—
Anastrozole related compound C ^b	2.0	0.2
Anastrozole related compound A ^c	4.0	—
Anastrozole related compound D ^d	4.3	0.1
Anastrozole related compound E ^e	5.4	0.1
Individual unspecified impurity	—	0.1
Total unspecified impurities	—	0.2

^a 2-(3-(1-Cyanoethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropionitrile [C₁₆H₁₇N₅, 279.34].

^b 2,3-Bis(3-(1-cyano-1-methylethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropionitrile [C₃₀H₃₁N₉, 517.63].

^c The relative retention time of anastrozole related compound A has been included for system suitability purposes only and is not intended for quantification.

^d 2,2'-(5-(Bromomethyl)-1,3-phenylene)bis(2-methylpropionitrile) [C₁₅H₁₇BrN₂, 305.21].

^e 2,2'-(5-(Dibromomethyl)-1,3-phenylene)bis(2-methylpropionitrile) [C₁₅H₁₆Br₂N₂, 384.11].

SPECIFIC TESTS

• **LOSS ON DRYING (731):** Dry it at 60° for 3 h: it loses NMT 0.5% of its weight.