

BRIEFING

**Anastrozole.** A USP Pending Monograph revision is proposed for Anastrozole, based on the specification in the Drug Master File cited in a FDA tentatively approved ANDA. Currently, there is an official *USP–NF* monograph for this drug substance, which differs in the *Definition*, the limit for *Total impurities in Procedure*, *Organic Impurities*, and the test for *Water content*. The proposal therefore includes only the *Definition*, *Total impurities in Procedure*, *Organic Impurities*, and *Loss on Drying*, which may later be adopted into the *USP–NF*, once the substance is fully approved by the FDA.

(MD-ODD: F. Mao.) RTS—C73259

**Anastrozole**

Draft 1

**DEFINITION**

**Change to read:**

Anastrozole contains NLT 98.0% and NMT 102.0% of C<sub>17</sub>H<sub>19</sub>N<sub>5</sub>, calculated on the dried basis. (1-Nov-2009)

**IMPURITIES**

**Change to read:**

**Organic Impurities**

• **PROCEDURE**

**Solution A, Solution B, and Chromatographic system:** Proceed as directed under *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<sub>u</sub> = response of anastrozole related compound from the *Sample solution*

r<sub>s</sub> = response of anastrozole related compound from the *Standard solution*

C<sub>s</sub> = concentration of USP Anastrozole RS in the *Standard solution* (mg/mL)

C<sub>u</sub> = concentration of Anastrozole in the *Sample solution* (mg/mL)

**Acceptance criteria**

**Individual impurities:** See *Impurity Table 1*.

**Total impurities:** NMT 1.0% (1-Nov-2009)

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

**Impurity Table 1**

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

<sup>a</sup>2-(3-(1-Cyanoethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropionitrile [C<sub>16</sub>H<sub>17</sub>N<sub>5</sub>, 279.34].

<sup>b</sup>2,3-Bis(3-(1-cyano-1-methylethyl)-5-(1*H*-1,2,4-triazol-1-ylmethyl)phenyl)-2-methylpropionitrile [C<sub>30</sub>H<sub>31</sub>N<sub>9</sub>, 517.63].

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

<sup>d</sup>2,2'-(5-(Bromomethyl)-1,3-phenylene)bis(2-methylpropionitrile) [C<sub>15</sub>H<sub>17</sub>BrN<sub>2</sub>, 305.21].

<sup>e</sup>2,2'-(5-(Dibromomethyl)-1,3-phenylene)bis(2-methylpropionitrile) [C<sub>15</sub>H<sub>16</sub>Br<sub>2</sub>N<sub>2</sub>, 384.11].

**SPECIFIC TESTS**

**Add the following:**

• **Loss on Drying (731):** Dry it at 60° for 3 h: it loses NMT 0.5% of its weight. (1-Nov-2009)