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Clomiphene Citrate Tablets

DEFINITION

Clomiphene Citrate Tablets contain NLT 93.0% and NMT 107.0% of the labeled amount of clomiphene citrate ($C_{26}H_{28}ClNO \cdot C_6H_8O_7$).

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.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Use low-actinic glassware for all solutions.

Mobile phase: [Methanol](#), [water](#), and [triethylamine](#) (55: 45: 0.3). Adjust with [phosphoric acid](#) to a pH of 2.5.

System suitability solution: 0.002 mg/mL of [USP Clomiphene Related Compound A RS](#) and 0.05 mg/mL of [USP Clomiphene Citrate RS](#) in *Mobile phase*.

Standard solution: 0.05 mg/mL of [USP Clomiphene Citrate RS](#) in *Mobile phase*

Sample stock solution: Nominally 0.5 mg/mL of clomiphene citrate prepared in *Mobile phase* as follows. Transfer an equivalent of 50 mg of clomiphene citrate from finely powdered Tablets (NLT 20) to a 100-mL volumetric flask. Add about 50 mL of *Mobile phase*, and stir using a magnetic bar for 30 min. Remove the magnetic bar from the flask, dilute with *Mobile phase* to volume, and filter.

Sample solution: Nominally 0.05 mg/mL of clomiphene citrate prepared from the *Sample stock solution* in *Mobile phase*. Filter, and discard the first 10 mL.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 233 nm. For *Identification B*, use a diode array detector in the range of 190–400 nm.

Column: 4.6-mm × 25-cm; 5-μm packing [L26](#)

Flow rate: 1.0 mL/min

Injection volume: 50 μL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for clomiphene related compound A, (Z)-isomer, and (E)-isomer are about 0.9, 1.0, and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.0 between clomiphene related compound A and (Z)-isomer; NLT 1.5 between (Z)-isomer and (E)-isomer, *System suitability solution*

Column efficiency: NLT 2000 theoretical plates for the (E)-isomer, *Standard solution*

Tailing factor: NMT 3.0 for the (E)-isomer, *Standard solution*

Relative standard deviation: NMT 2.0% for both (E)- and (Z)-isomers, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clomiphene citrate ($C_{26}H_{28}ClNO \cdot C_6H_8O_7$) in the portion of Tablets taken:

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

r_U = sum of the peak responses of the (E)- and (Z)-isomers of clomiphene from the *Sample solution*

r_S = sum of the peak responses of the (E)- and (Z)-isomers of clomiphene from the *Standard solution*

C_S = concentration of [USP Clomiphene Citrate RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of clomiphene citrate in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Medium: [Water](#); 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: [USP Clomiphene Citrate RS](#) in [0.1 N hydrochloric acid](#)

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with [0.1 N hydrochloric acid](#) to a concentration similar to the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 232 nm

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of clomiphene citrate ($C_{26}H_{28}ClNO \cdot C_6H_8O_7$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)

Tolerances: NLT 75% (Q) of the labeled amount of clomiphene citrate ($C_{26}H_{28}ClNO \cdot C_6H_8O_7$) is dissolved.

• [UNIFORMITY OF DOSAGE UNITS \(905\)](#): Meet the requirements

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

Use low-actinic glassware for all solutions.

Buffer: [Acetonitrile](#), [diethylamine](#), and [water](#) (40:0.8:60). Adjust with [phosphoric acid](#) to a pH of 6.2.

Solution A: *Buffer* and [water](#) (90:10)

Solution B: *Buffer*

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
3.0	100	0
23.0	0	100
33.0	0	100
33.5	100	



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