

Status: Currently Official on 14-Feb-2025
 Official Date: Official as of 01-Apr-2019
 Document Type: USP Monographs
 DocId: GUID-4F498A17-41F8-4445-8CDC-5EFEE47FC296_4_en-US
 DOI: https://doi.org/10.31003/USPNF_M28570_04_01
 DOI Ref: 80kee

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Drospirenone and Ethinyl Estradiol Tablets

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<https://www.uspnf.com/rb-drospirenone-ethinyl-estradiol-tabs-20190401>

DEFINITION

Drospirenone and Ethinyl Estradiol Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of drospirenone ($C_{24}H_{30}O_3$) and NLT 90.0% and NMT 110.0% of the labeled amount of ethinyl estradiol ($C_{20}H_{24}O_2$).

IDENTIFICATION

- **A.** The retention times of the drospirenone and ethinyl estradiol peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the Assay.

ASSAY

• PROCEDURE

Solution A: Dissolve 132 g of [dibasic ammonium phosphate](#) in 0.8 L of water, adjust with [phosphoric acid](#) to a pH of 6.8, and dilute to 1 L.

Solution B: *Solution A* and water (1:24)

Mobile phase: [Acetonitrile](#) and *Solution B* (1:1). Adjust with [phosphoric acid](#) to a pH of 6.8.

Standard solution: ($L/25$) mg/mL of [USP Drospirenone RS](#) and [USP Ethinyl Estradiol RS](#) in *Mobile phase*, where L is the Tablet label claim, in mg/Tablet, of each compound

Sample solution: Transfer 10 Tablets to a 250-mL volumetric flask, add 230 mL of *Mobile phase*, and sonicate with intermittent shaking for NLT 10 min, or until the Tablets are completely dispersed. Equilibrate to room temperature. Dilute with *Mobile phase* to volume, and centrifuge the sample until a clear supernatant is obtained. Use the supernatant.

Chromatographic system

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

Mode: LC

Detector 1: UV 270 nm for drospirenone

Detector 2: Fluorescence, excitation wavelength at 285 nm, emission wavelength at 315 nm for ethinyl estradiol. [NOTE—*Detector 1* and *Detector 2* are connected in series.]

Column: 4.0-mm × 12.5-cm; 3-μm packing [L1](#)

Column temperature: 25 ± 3°

Flow rate: 1.2 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: Between 0.8 and 1.8 for both drospirenone and ethinyl estradiol

Relative standard deviation: NMT 2.0% for both drospirenone and ethinyl estradiol

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of drospirenone ($C_{24}H_{30}O_3$) in the portion of Tablets taken:

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

r_U = peak response of drospirenone from the *Sample solution*

r_S = peak response of drospirenone from the *Standard solution*

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

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

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ethinyl estradiol ($C_{20}H_{24}O_2$) in the portion of Tablets taken:

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

r_U = peak response of ethinyl estradiol from the *Sample solution*

r_S = peak response of ethinyl estradiol from the *Standard solution*

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

C_U = nominal concentration of ethinyl estradiol in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% of ethinyl estradiol; 90.0%–110.0% of drospirenone

PERFORMANCE TESTS

• [DISSOLUTION \(711\)](#)

Test 1: For drug products labeled to contain 3 mg of drospirenone and 0.03 mg of ethinyl estradiol, or 3 mg of drospirenone and 0.02 mg of ethinyl estradiol

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: ($L/900$) mg/mL of [USP Drospirenone RS](#) and [USP Ethinyl Estradiol RS](#) in *Medium*, where L is the Tablet label claim of each compound. A volume of [methanol](#) not exceeding 2% of the final total volume of solution may be used to aid in dissolving these compounds.

Sample solution: Pass a portion of the solution under test through a suitable cellulose filter of 0.45- μ m pore size, discarding the first 10 mL.

Mobile phase: [Acetonitrile](#) and water (40:60)

Chromatographic system

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

Mode: LC

Detector: UV 270 nm (for drospirenone), in series with a fluorescence detector (for ethinyl estradiol), with excitation at 210 nm and detection at 315 nm, or with excitation at 281 nm and detection at 305 nm

Column: 4.6-mm $\times$ 6-cm; 3- μ m packing [L1](#)

Column temperature: 22°

Flow rate: 1 mL/min

Injection volume: 100 μ L

System suitability

Sample: *Standard solution*

Suitability requirements

Column efficiency: NLT 2000 for both drospirenone and ethinyl estradiol

Tailing factor: Between 0.8 and 1.5 for both drospirenone and ethinyl estradiol

Relative standard deviation: NMT 3% for both drospirenone and ethinyl estradiol

Samples: *Standard solution* and *Sample solution*

[NOTE—In *Medium*, drospirenone is partially converted into 17-epidrospirenone, which has a relative retention time of approximately 1.2 relative to drospirenone. The amount of drospirenone dissolved is calculated from the sum of drospirenone and 17-epidrospirenone.]

Calculate the percentage of the labeled amounts of drospirenone ($C_{24}H_{30}O_3$) and ethinyl estradiol ($C_{20}H_{24}O_2$) 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 85% (Q) of the labeled amount of drospirenone and NLT 75% (Q) of the labeled amount of ethinyl estradiol is dissolved.

Test 2: For drug products labeled to contain 3 mg of drospirenone and 0.02 mg of ethinyl estradiol. If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Standard solution: ($L/900$) mg/mL of [USP Drospirenone RS](#) and [USP Ethinyl Estradiol RS](#) in *Medium*, where L is the Tablet label claim of each compound

Sample solution: Centrifuge a portion of the solution under test at 3500 rpm for 15 min, and use the supernatant.

Mobile phase: [Acetonitrile](#), [methanol](#), and water (40:5:55)

Chromatographic system

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

Mode: LC

Detector: UV 260 nm (for drospirenone), in series with a fluorescence detector (for ethinyl estradiol), with excitation at 280 nm and detection at 310 nm

Column: 4.6-mm × 10-cm; 3-μm packing [L1](#)

Temperatures

Column: 30°

Autosampler: 5°

Flow rate: 1 mL/min

Injection volume: 200 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2 for both drospirenone and ethinyl estradiol

Relative standard deviation: NMT 3% for both drospirenone and ethinyl estradiol

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of drospirenone ($C_{24}H_{30}O_3$) and ethinyl estradiol ($C_{20}H_{24}O_2$) 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 drospirenone and NLT 85% (Q) of the labeled amount of ethinyl estradiol is dissolved.

Test 3: For drug products labeled to contain 3 mg of drospirenone and 0.03 mg of ethinyl estradiol, or 3 mg of drospirenone and 0.02 mg of ethinyl estradiol. If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 30 min

Mobile phase: [Acetonitrile](#) and water (50:50)

Standard stock solution A: 2.8 μg/mL of [USP Ethinyl Estradiol RS](#) in [acetonitrile](#). Sonicate as needed.

Standard stock solution B: 168 μg/mL of [USP Drospirenone RS](#) in [acetonitrile](#). Sonicate as needed.

Standard solution: ($L/900$) mg/mL of [USP Drospirenone RS](#) and [USP Ethinyl Estradiol RS](#) in *Medium* from *Standard stock solution A* and *Standard stock solution B*, where L is the Tablet label claim of each compound.

Sample solution: Pass a portion of the solution under test through a suitable glass filter of 1-μm pore size, discarding the first 5 mL.

Chromatographic system

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

Mode: LC

Detector: UV 265 nm (for drospirenone), in series with a fluorescence detector (for ethinyl estradiol), with excitation at 285 nm and detection at 310 nm

Column: 4.6-mm × 15-cm; 5-μm packing [L11](#)

Temperatures

Column: 30°

Autosampler: 10°

Flow rate: 1 mL/min

Injection volume: 50 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both drospirenone and ethinyl estradiol

Relative standard deviation: NMT 2.0% for both drospirenone and ethinyl estradiol

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amounts of drospirenone ($C_{24}H_{30}O_3$) and ethinyl estradiol ($C_{20}H_{24}O_2$) dissolved