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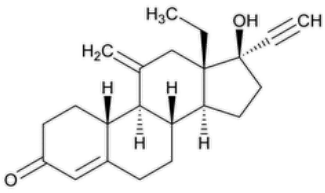
Add the following:

▲Etonogestrel



$C_{22}H_{28}O_2$ 324.46

18,19-Dinor-17α-pregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy-11-methylene-;

13-Ethyl-17-hydroxy-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-3-one CAS RN®: 54048-10-1; UNII: 304GTH6RNH.

DEFINITION

Etonogestrel contains NLT 97.5% and NMT 101.5% of etonogestrel ($C_{22}H_{28}O_2$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197A or 197K

• **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: Methanol and water (67.5: 32.5)

System suitability solution: 2 µg/mL each of USP Etonogestrel RS and USP Etonogestrel Related Compound A RS in methanol

Standard solution: 200 µg/mL of USP Etonogestrel RS in methanol

Sample solution: 200 µg/mL of Etonogestrel in methanol

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 244 nm

Column: 4-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of etonogestrel

System suitability

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

[Note—See *Table 1* for the relative retention times for etonogestrel related compound A and etonogestrel. These relative retention times are provided as information that could aid in peak assignment.]

Suitability requirements

Resolution: NLT 1.5 between etonogestrel related compound A and etonogestrel, *System suitability solution*

Tailing factor: 0.9–2.0 for etonogestrel, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of etonogestrel ($C_{22}H_{28}O_2$) in the portion of Etonogestrel taken:

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

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

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

C_S = concentration of USP Etonogestrel RS in the *Standard solution* (µg/mL)

C_U = concentration of Etonogestrel in the *Sample solution* (µg/mL)

Acceptance criteria: 97.5%–101.5% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

• **Organic Impurities**

Mobile phase, System suitability solution, and **Sample solution:** Prepare as directed in the *Assay*.

Standard solution 1: 2 µg/mL of USP Etonogestrel RS in methanol

Standard solution A: 2 µg/mL of USP Etonogestrel Related Compound A RS in methanol

Standard solution B: 2 µg/mL of USP Etonogestrel Related Compound B RS in methanol

Standard solution C: 2 µg/mL of USP Etonogestrel Related Compound C RS in methanol

Standard solution D: 2 µg/mL of USP Etonogestrel Related Compound D RS in methanol

Standard solution E: 4 µg/mL of USP Etonogestrel Related Compound E RS in methanol

Sensitivity solution: 0.1 µg/mL of USP Etonogestrel RS and 0.2 µg/mL of USP Etonogestrel Related Compound E RS in methanol

Blank solution: Methanol

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 244 nm. For etonogestrel related compound E, use UV 205 nm.

Column: 4.0-mm × 25-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 3 times the retention time of etonogestrel

System suitability

Samples: *System suitability solution*, *Standard solution 1*, and *Sensitivity solution*. [Note—The relative retention times in *Table 1* are provided as information that could aid in peak assignment.]

Table 1

Name	Relative Retention Time
Etonogestrel related compound B	0.36
Etonogestrel related compound C	0.49
Etonogestrel related compound D	0.72
Etonogestrel related compound A	0.92
Etonogestrel	1.0
Etonogestrel related compound E	1.29

Suitability requirements

Resolution: NLT 1.5 between etonogestrel related compound A and etonogestrel, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution 1*

Signal-to-noise ratio: NLT 10 for etonogestrel; NLT 3 for etonogestrel related compound E, *Sensitivity solution*

Analysis

Samples: *Sample solution*, *Standard solution 1*, *Standard solution A*, *Standard solution B*, *Standard solution C*, *Standard solution D*, *Standard solution E*, and *Blank solution*

[NOTE—Correct the peak areas of the *Sample solution*, *Standard solution A*, *Standard solution B*, *Standard solution C*, *Standard solution D*, and *Standard solution E* for the blank peak area observed in the *Blank solution* if necessary.]

Calculate the percentage of etonogestrel related compound A, etonogestrel related compound B, etonogestrel related compound C, etonogestrel related compound D, and etonogestrel related compound E in the portion of Etonogestrel taken:

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

r_U = peak area of etonogestrel related compound A, etonogestrel related compound B, etonogestrel related compound C, etonogestrel related compound D, or etonogestrel related compound E from the *Sample solution*

r_S = peak area of etonogestrel related compound A, etonogestrel related compound B, etonogestrel related compound C, etonogestrel related compound D, or etonogestrel related compound E from *Standard solution A*, *Standard solution B*, *Standard solution C*, *Standard solution D*, or *Standard solution E*

C_S = concentration of USP Etonogestrel Related Compound A RS, USP Etonogestrel Related Compound B RS, USP Etonogestrel Related Compound C RS, USP Etonogestrel Related Compound D RS, or USP Etonogestrel Related Compound E RS in *Standard solution A*, *Standard solution B*, *Standard solution C*, *Standard solution D*, or *Standard solution E* (µg/mL)

C_U = concentration of Etonogestrel in the *Sample solution* (µg/mL)

Calculate the percentage of any unspecified impurity in the portion of Etonogestrel taken:

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

r_U = peak area of any unspecified impurity from the *Sample solution*

r_S = peak area of etonogestrel from *Standard solution 1*

C_S = concentration of USP Etonogestrel RS in *Standard solution 1* (µg/mL)

C_U = concentration of Etonogestrel in the *Sample solution* (µg/mL)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.1% for etonogestrel related compound E and 0.05% for other impurities.

Table 2

Name	Acceptance Criteria, NMT (%)
Etonogestrel related compound B	0.5
Etonogestrel related compound C	0.1
Etonogestrel related compound D	0.4
Etonogestrel related compound A	0.1
Etonogestrel related compound E	0.5
Any unspecified impurity	0.10
Total impurities	1.5

SPECIFIC TESTS

- **OPTICAL ROTATION** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 10 mg/mL of Etonogestrel in absolute alcohol

Acceptance criteria: +84° to +91°, at 25° on the dried basis

- **LOSS ON DRYING** ⟨731⟩

Analysis: Dry under vacuum over silica gel desiccant at 40° to a constant weight.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Etonogestrel RS

USP Etonogestrel Related Compound A RS

13-Ethyl-11-methylenegon-4-ene-3,17-dione.

$C_{20}H_{26}O_2$ 298.43

USP Etonogestrel Related Compound B RS

13-Ethyl-6β,17β-dihydroxy-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-3-one.

$C_{22}H_{28}O_3$ 340.46

USP Etonogestrel Related Compound C RS

13-Ethyl-17β-hydroxy-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-3,6-dione.

$C_{22}H_{26}O_3$ 338.45

USP Etonogestrel Related Compound D RS

17β-Hydroxy-11-methylene-19-nor-17α-pregn-4-en-20-yn-3-one.

$C_{21}H_{26}O_2$ 310.44

USP Etonogestrel Related Compound E RS

13-Ethyl-17β-hydroxy-11-methylene-18,19-dinor-17α-pregn-5-en-20-yn-3-one.

$C_{22}H_{28}O_2$ 324.46▲ (USP 1-Aug-2024)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
ETONOGESTREL	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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