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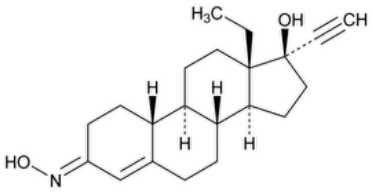
Norelgestromin



$C_{21}H_{29}NO_2$ 327.46

18,19-Dinorpregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy-, oxime, (17α)-;

13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one oxime CAS RN®: 53016-31-2; UNII: R0TAY3X631.

DEFINITION

Norelgestromin is a mixture of (*E*)- and (*Z*)-isomers having a ratio of (*E*)- to (*Z*)-isomer between 1.3 and 1.6, and the sum of both isomers is NLT 98.0% and NMT 102.0% of norelgestromin ($C_{21}H_{29}NO_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

• **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: Cyclohexane and *absolute alcohol* (100:2)

Diluent: Cyclohexane and *absolute alcohol* (90:10)

System suitability solution: 1.5 mg/mL of USP Norelgestromin RS and 8 µg/mL of USP Norelgestromin Related Compound A RS in *Diluent*

Standard solution: 1.5 mg/mL of USP Norelgestromin RS in *Diluent*

Sample solution: 1.5 mg/mL of Norelgestromin in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing L20

Column temperature: 50°

Flow rate: 1.2 mL/min

Injection volume: 25 µL

Run time: NLT 1.6 times the retention time of (*Z*)-norelgestromin

System suitability

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

[Note—The relative retention times for the (*Z*)-isomer of norelgestromin related compound A, (*E*)-norelgestromin, and (*Z*)-norelgestromin are about 0.77, 0.85, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.4 between the (*Z*)-isomer of norelgestromin related compound A and (*E*)-norelgestromin, *System suitability solution*

Tailing factor: 0.8–1.2 for both (*E*)- and (*Z*)-norelgestromin, *Standard solution*

Relative standard deviation: NMT 0.73% for both (*E*)- and (*Z*)-norelgestromin, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of norelgestromin ($C_{21}H_{29}NO_2$) in the portion of Norelgestromin taken:

$$\text{Result} = \{[(r_{UE} \times F) + r_{UZ}]/[(r_{SE} \times F) + r_{SZ}]\} \times (C_S/C_U) \times 100$$

r_{UE} = peak response of (*E*)-norelgestromin from the *Sample solution*

F = response factor for (*E*)-norelgestromin, 1.04

r_{UZ} = peak response of (*Z*)-norelgestromin from the *Sample solution*

r_{SE} = peak response of (*E*)-norelgestromin from the *Standard solution*

r_{SZ} = peak response of (*Z*)-norelgestromin from the *Standard solution*

C_S = concentration of USP Norelgestromin RS in the *Standard solution* (mg/mL)

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

Calculate the ratio of (*E*)- to (*Z*)-norelgestromin:

$$\text{Result} = (r_{UE} \times F)/r_{UZ}$$

r_{UE} = peak response of (*E*)-norelgestromin from the *Sample solution*

F = response factor for (*E*)-norelgestromin, 1.04

r_{UZ} = peak response of (*Z*)-norelgestromin from the *Sample solution*

Acceptance criteria

Both isomers: 98.0%–102.0% on the anhydrous basis

Ratio of (*E*)- to (*Z*)-isomer: 1.3–1.6

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Mobile phase, Diluent, System suitability solution, Standard solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 1.5 µg/mL of USP Norelgestromin RS in *Diluent* from the *Standard solution*

System suitability

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

Suitability requirements

Resolution: NLT 1.4 between the (*Z*)-isomer of norelgestromin related compound A and (*E*)-norelgestromin, *System suitability solution*

Tailing factor: 0.8–1.2 for both (*E*)- and (*Z*)-norelgestromin, *Standard solution*

Relative standard deviation: NMT 0.73% for both (*E*)- and (*Z*)-norelgestromin, *Standard solution*

Signal-to-noise ratio: NLT 3 for both (*E*)- and (*Z*)-norelgestromin, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Norelgestromin taken:

$$\text{Result} = \{r_U/[(r_{SE} \times F) + r_{SZ}]\} \times (C_S/C_U) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_{SE} = peak response of (*E*)-norelgestromin from the *Standard solution*

F = response factor for (*E*)-norelgestromin, 1.04

r_{SZ} = peak response of (*Z*)-norelgestromin from the *Standard solution*

C_S = concentration of USP Norelgestromin RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: See *Table 1*. Disregard peaks that are less than 0.05% of the total peak areas of (*E*)- and (*Z*)-norelgestromin.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Norgestrel[a]	0.37	0.5
(*E*)- and (*Z*)-Norgestimate[b]	0.43[c], 0.47[d]	0.5[e]
Norelgestromin 5(10)-ene[f,g]	0.68	—
Norelgestromin related compound A[g]	0.73[h], 0.77[i]	—
(*E*)-Norelgestromin	0.85	—
(*Z*)-Norelgestromin	1.0	—
Any other individual impurity	—	0.10
Total impurities	—	1.0

[a] (±)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one.

[b] 18,19-Dinor-17-pregn-4-en-20-yn-3-one, 17-(acetyloxy)-13-ethyl-,oxime, (17α)-(+)-; (+)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one oxime acetate (ester).

[c] (*E*)-Norgestimate.

[d] (*Z*)-Norgestimate.

[e] The combined limits for (*E*)- and (*Z*)-norgestimate are NMT 0.5%.

[f] 13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-5(10)-en-20-yn-3-one oxime.

[g] This is not a specified impurity and is included in this table for identification only. It is not to be reported or included in the total impurities.

[h] (*E*)-Isomer of norelgestromin related compound A.

[i] (*Z*)-Isomer of norelgestromin related compound A.

SPECIFIC TESTS

- **Optical Rotation ⟨781S⟩, *Procedures, Specific Rotation***
  Sample solution: 5 mg/mL in alcohol and water (75:25)
  Acceptance criteria: +35° to +41°
- **Water Determination ⟨921⟩, *Method I, Method Ic*:** NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers, and store at controlled room temperature.
- **USP Reference Standards ⟨11⟩**
  USP Norelgestromin RS
  USP Norelgestromin Related Compound A RS
  Mixture of (*E*)- and (*Z*)-isomers.
  13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-5(6)-en-20-yn-3-one oxime.
  $C_{21}H_{29}NO_2$ 327.46

Topic/Question	Contact	Expert Committee
NORELGESTROMIN	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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