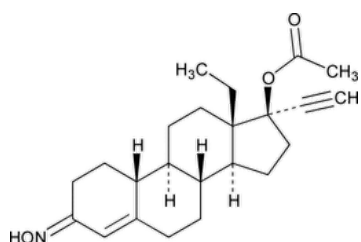


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Norgestimate

Change to read:



$C_{23}H_{31}NO_3$ ▲369.51 ▲ (IRA 1-Aug-2024)

18,19-Dinor-17-pregn-4-en-20-yn-3-one, 17-(acetyloxy)-13-ethyl-, oxime, (17 α)-(+)-;

(+)-13-Ethyl-17-hydroxy-18,19-dinor-17 α -pregn-4-en-20-yn-3-one oxime acetate (ester) CAS RN[®]: 35189-28-7; UNII: C291HFX4DY.

DEFINITION

Norgestimate is a mixture of (*E*)- and (*Z*)-isomers having a ratio of (*E*)- to (*Z*)-isomer between 1.27 and 1.78, and it contains NLT 98.0% and NMT 102.0% of norgestimate ($C_{23}H_{31}NO_3$), calculated on the dried basis.

IDENTIFICATION

Change to read:

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** ▲197A or ▲ (IRA 1-Aug-2024) 197K

▲ (IRA 1-Aug-2024)

Change to read:

- **B.** The retention ▲times of the major peaks for the (*E*)- and (*Z*)-isomers of the *Sample solution* correspond to those▲ (IRA 1-Aug-2024) of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

• PROCEDURE

Diluent: [Methanol](#) and [water](#) (80:20)

Mobile phase: [Tetrahydrofuran](#), [acetonitrile](#), and [water](#) (22:18:60)

Standard solution: 0.5 mg/mL of [USP Norgestimate RS](#) in *Diluent*

▲ (IRA 1-Aug-2024)

Sample solution: 0.5 mg/mL of Norgestimate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 244 nm

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

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 25 μ L

▲**Run time:** NLT 1.5 times the retention time of (*E*)-norgestimate▲ (IRA 1-Aug-2024)

System suitability

Sample: *Standard solution* ▲▲ (IRA 1-Aug-2024)

[NOTE— ▲ See [Table 1](#) for the relative retention times for (Z)-norgestimate and (E)-norgestimate. ▲ (IRA 1-Aug-2024)]

Suitability requirements

Resolution: NLT 1.5 between (Z)-norgestimate and (E)-norgestimate

Tailing factor: NMT 1.5 for (E)-norgestimate and (Z)-norgestimate

Relative standard deviation: NMT ▲0.73% ▲ (IRA 1-Aug-2024) for the ▲sum of the peak responses of ▲ (IRA 1-Aug-2024) (E)-norgestimate and (Z)-norgestimate

▲ (IRA 1-Aug-2024)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of norgestimate ($C_{23}H_{31}NO_3$) in the portion of Norgestimate taken:

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

r_U = sum of the peak ▲responses ▲ (IRA 1-Aug-2024) of (Z)-norgestimate and (E)-norgestimate from the *Sample solution*

r_S = sum of the peak ▲responses ▲ (IRA 1-Aug-2024) of (Z)-norgestimate and (E)-norgestimate from the *Standard solution*

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

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

Calculate the percentages of the (Z)- and (E)-isomers, U_Z and U_E , respectively, in the portion of Norgestimate taken:

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

r_U = peak response of ▲(Z)-norgestimate and (E)-norgestimate ▲ (IRA 1-Aug-2024) from the *Sample solution*

r_S = peak response of the ▲corresponding ▲ (IRA 1-Aug-2024) norgestimate isomer from the *Standard solution*

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

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

P = fraction of (E)- or (Z)-norgestimate in [USP Norgestimate RS](#)

Calculate the ratio of U_E to U_Z :

$$\text{▲Result} = (U_E/U_Z)$$

U_E = percentage of (E)-norgestimate in the *Sample solution* (%)

U_Z = percentage of (Z)-norgestimate in the *Sample solution* (%)

▲ (IRA 1-Aug-2024)

Acceptance criteria

Content: 98.0%–102.0% on the dried basis

Ratio of (E)- to (Z)-isomer: 1.27–1.78

IMPURITIES

- [RESIDUE ON IGNITION \(281\)](#): NMT 0.3%

Change to read:

- **ORGANIC IMPURITIES, PROCEDURE 1**

Diluent, Mobile phase, ▲ (IRA 1-Aug-2024) and **Sample solution:** Prepare as directed in the Assay.

System suitability solution: 0.5 mg/mL each of [USP Norgestimate RS](#), [USP Norgestimate Related Compound A RS](#), and ▲[USP Norelgestromin RS](#) ▲ (IRA 1-Aug-2024) in *Diluent*

▲Sensitivity solution: 0.4 µg/mL of [USP Norgestimate RS](#) in *Diluent*

Standard solution: 0.0008 mg/mL of [USP Norgestimate RS](#) in *Diluent* ▲ (IRA 1-Aug-2024)

Chromatographic system

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

- Mode: LC
- Detector: UV 244 nm
- Column: 4.6-mm × 10-cm; 3-µm packing [L1](#)
- Column temperature: 40°
- Flow rate: 1.2 mL/min
- Injection volume: 25 µL
- ▲Run time: NLT 1.5 times the retention time of (E)-norgestimate▲ (IRA 1-Aug-2024)

System suitability

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

Table 1▲ (IRA 1-Aug-2024)

Name	Relative Retention Time
▲(Z)-Norelgestromin▲ (IRA 1-Aug-2024)	0.50
▲(E)-Norelgestromin▲ (IRA 1-Aug-2024)	0.56
Norgestimate related compound A▲▲ (IRA 1-Aug-2024)	0.72
(Z)-Norgestimate	0.86
(E)-Norgestimate	1.0

Suitability requirements

- Resolution: NLT 1.5 between ▲(Z)-norelgestromin and (E)-norelgestromin;▲ (IRA 1-Aug-2024) NLT 1.5 between ▲(E)-norelgestromin▲ (IRA 1-Aug-2024) and norgestimate related compound A, System suitability solution
- Tailing factor: NMT 1.5 for (E)-norgestimate and (Z)-norgestimate, System suitability solution
- Relative standard deviation: ▲NMT 5.0% for (E)-norgestimate, Standard solution▲ (IRA 1-Aug-2024)
- Signal-to-noise ratio: NLT ▲10▲ (IRA 1-Aug-2024) for ▲(E)▲ (IRA 1-Aug-2024) -norgestimate, Sensitivity solution

Analysis

Samples: Standard solution and Sample solution
Calculate the percentage of ▲any▲ (IRA 1-Aug-2024) impurity in the portion of Norgestimate taken:

Result = (r_U/r_S) × (C_S/C_U) × (1/F) × P × 100

- r_U = peak ▲response▲ (IRA 1-Aug-2024) of each impurity from the Sample solution
- r_S = peak ▲response▲ (IRA 1-Aug-2024) of (E)-norgestimate from the Standard solution
- C_S = concentration of [USP Norgestimate RS](#) in the Standard solution (mg/mL)
- C_U = concentration of Norgestimate in the Sample solution (mg/mL)
- F = relative response factor for each impurity (see [Table 2](#))
- P = fraction of (E)-norgestimate in [USP Norgestimate RS](#)