Status: Currently Official on 16-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-DC7CA84F-9E31-4B0F-B102-C09178DD4D38_1_en-US
DOI: https://doi.org/10.31003/USPNF_M57680_01_01
DOI Ref: 8s6jk

Norgestimate and Ethinyl Estradiol Tablets

DEFINITION

Norgestimate and Ethinyl Estradiol Tablets contain NLT 90.0% and NMT 110.0% of the labeled amounts of norgestimate ($C_{23}H_{31}NO_3$) and ethinyl estradiol ($C_{20}H_{24}O_2$).

IDENTIFICATION

• **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay.*

ASSAY

• **Procedure**

Mobile phase: Tetrahydrofuran, methanol, and water (5:2:13)

Internal standard solution: 0.05 mg/mL of dibutyl phthalate in methanol

Standard solution: Dissolve appropriate quantities of USP Ethinyl Estradiol RS and USP Norgestimate RS in a volume of *Internal standard solution* equivalent to 80% of the final volume. Add a volume of water equivalent to 20% of the final volume, and mix to obtain a solution having a known concentration of about 7 µg/mL of ethinyl estradiol and a known concentration of norgestimate similar to that expected in the *Sample solution*. Pass through a suitable filter of 0.45-µm pore size.

Sample solution: Add a number of Tablets, equivalent to 0.35 mg of ethinyl estradiol, to a suitable glass container. Add 10 mL of water, and mix with a vortex mixer until the Tablets are completely disintegrated. Add 40 mL of *Internal standard solution,* and mix with a vortex mixer for at least 23 min. Sonicate the sample for at least 5 min, pass an aliquot through a suitable filter of 0.45-µm pore size, and use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 5-cm; 5-µm packing L1

Flow rate: 2.1 mL/min

Injection size: 25 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for ethinyl estradiol, (*Z*)-norgestimate, (*E*)-norgestimate, and dibutyl phthalate are about 0.5, 1.0, 1.2, and 1.5, respectively.]

Suitability requirements

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

Relative standard deviation: NMT 2.0% for the peak response ratio of ethinyl estradiol, (*Z*)-norgestimate, and (*E*)-norgestimate to dibutyl phthalate

Analysis

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:

$$\text{Result} = (R_{UE}/R_{SE}) \times (C_{SE}/C_{UE}) \times 100$$

R_{UE} = ratio of the peak responses of ethinyl estradiol to dibutyl phthalate from the *Sample solution*

R_{SE} = ratio of the peak responses of ethinyl estradiol to dibutyl phthalate from the *Standard solution*

C_{SE} = concentration of USP Ethinyl Estradiol RS in the *Standard solution* (mg/mL)

C_{UE} = nominal concentration of ethinyl estradiol in the *Sample solution* (mg/mL)

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

$$\text{Result} = (C_{SN}/C_{UN}) \times [P_A(R_{UA}/R_{SA}) + P_S(R_{US}/R_{SS})] \times 100$$

C_{SN} = concentration of USP Norgestimate RS in the *Standard solution* (mg/mL)

C_{UN} = nominal concentration of norgestimate in the *Sample solution* (mg/mL)

P_A = fraction of (*E*)-norgestimate in USP Norgestimate RS

R_{UA} = ratio of the peak responses of (*E*)-norgestimate to dibutyl phthalate from the *Sample solution*

R_{SA} = ratio of the peak responses of (*E*)-norgestimate to dibutyl phthalate from the *Standard solution*

P_S = fraction of (*Z*)-norgestimate in the USP Norgestimate RS

R_{US} = ratio of the peak responses of (*Z*)-norgestimate to dibutyl phthalate from the *Sample solution*

R_{SS} = ratio of the peak responses of (*Z*)-norgestimate to dibutyl phthalate from the *Standard solution*

Calculate the ratio of the content of (*Z*)-norgestimate to ethinyl estradiol in the portion of Tablets taken, for use in the test for *Organic Impurities*:

$$C_Z/C_E = [(C_{SN} \times P_S) \times (R_{US}/R_{SS})]/[C_{SE}(R_{UE}/R_{SE})]$$

The terms are as defined above.

Acceptance criteria: 90.0%–110.0% each of ethinyl estradiol and norgestimate

PERFORMANCE TESTS

- **Disintegration ⟨701⟩:** 15 min
- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

- **Organic Impurities**

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

Chromatographic system

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

Mode: LC

Detector: 254 nm

Column: 4.6-mm × 5-cm; 5-µm packing L1

Flow rate: 2 mL/min

Injection size: 50 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times for ethinyl estradiol, (*Z*)-norgestimate, and (*E*)-norgestimate are about 0.5, 1.0, and 1.2, respectively.]

Suitability requirements

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

Relative standard deviation: NMT 2.0% for the (*Z*)-norgestimate and (*E*)-norgestimate peaks

Analysis

Sample: *Sample solution*

Calculate the percentage of any impurity having a relative retention time of about 0.2 or 0.4, relative to the (*Z*)-norgestimate peak, and detected at 254 nm in the portion of Tablets taken:

$$\text{Result} = (r_U/r_Z) \times (C_Z/C_E) \times F \times 100$$

r_U = peak response for each impurity

r_Z = peak response for (*Z*)-norgestimate

C_Z/C_E = ratio of (*Z*)-norgestimate to ethinyl estradiol, as defined in the *Assay*

F = relative response factor of these impurities, 1.54

Acceptance criteria: The sum of the impurities having relative retention times of about 0.2 and 0.4 is NMT 4.0%.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩
  USP Ethinyl Estradiol RS
  USP Norgestimate RS

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

Topic/Question	Contact	Expert Committee
NORGESTIMATE AND ETHINYL ESTRADIOL TABLETS	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 44(6)

Current DocID: GUID-DC7CA84F-9E31-4B0F-B102-C09178DD4D38_1_en-US
DOI: https://doi.org/10.31003/USPNF_M57680_01_01
DOI ref: 8s6jk