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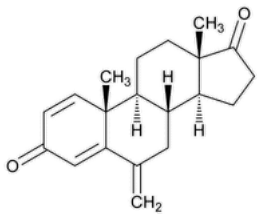
Exemestane



$C_{20}H_{24}O_2$ 296.40

Androsta-1,4-diene-3,17-dione, 6-methylene-;

6-Methyleneandrosta-1,4-diene-3,17-dione CAS RN®: 107868-30-4; UNII: NY22HMQ4BX.

DEFINITION

Exemestane contains NLT 97.0% and NMT 102.0% of exemestane ($C_{20}H_{24}O_2$), calculated on the anhydrous and solvent-free 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**

Solution A: Water

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
15	60	40
18	10	90
28	10	90
30	60	40
35	60	40

Diluent: Acetonitrile and water (1:1)

Standard solution: 0.1 mg/mL of USP Exemestane RS in *Diluent*

Sample solution: 0.1 mg/mL of Exemestane in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 247 nm

Column: 4.6-mm × 15-cm; 3-µm packing L1

Column temperature: 45°

Flow rate: 1.0 mL/min

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Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of exemestane ($C_{20}H_{24}O_2$) in the portion of Exemestane taken:

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

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

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

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

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

Acceptance criteria: 97.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

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

Solution A: Water

Solution B: Acetonitrile

Mobile phase: See *Table 2*. Return to original conditions and re-equilibrate the system.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	75	25
30	55	45
40	5	95
45	5	95

Diluent: Acetonitrile and water (3:1)

System suitability solution: 1 mg/mL of USP Exemestane RS, 0.01 mg/mL of USP Exemestane Related Compound B RS, and 0.01 mg/mL of USP Exemestane Related Compound C RS in *Diluent*

Sensitivity solution: 0.5 µg/mL each of USP Exemestane RS, USP Exemestane Related Compound B RS, and USP Exemestane Related Compound C RS in *Diluent*

Standard solution: 5 µg/mL of USP Exemestane RS in *Diluent*

Sample solution: 1 mg/mL of Exemestane in *Diluent*. The concentration is calculated on the anhydrous and solvent-free basis.

Chromatographic system

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

Mode: LC

Detector: UV 247 nm

Column: 4.6-mm × 25-cm; 3.5-µm packing L1

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between exemestane related compound B and exemestane related compound C; NLT 2.0 between exemestane related compound C and exemestane, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Signal-to-noise ratio: NLT 10 for the exemestane, exemestane related compound B, and exemestane related compound C peaks, *Sensitivity solution*

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Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

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

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

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

C_U = concentration of Exemestane in the *Sample solution* (mg/mL) (the concentration is calculated on the anhydrous and solvent-free basis)

F = relative response factor for each individual impurity (see *Table 3*)

Acceptance criteria: See *Table 3*. Disregard any impurity peaks less than 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Exemestane related compound B	0.34	0.95	0.15
Exemestane related compound C	0.77	1.1	1.0
Exemestane	1.0	—	—
Any unspecified impurity	—	1.0	0.1

- **Limit of Exemestane Related Compound D**

Mobile phase: Hexane, isopropyl alcohol, and diethylamine (90:10:0.1)

System suitability solution: 8 mg/mL of USP Exemestane System Suitability Mixture RS in anhydrous alcohol

Standard solution: 0.04 mg/mL of USP Exemestane RS in anhydrous alcohol

Sensitivity solution: 4 µg/mL of USP Exemestane RS in anhydrous alcohol, from the *Standard solution*

Sample solution: 8 mg/mL of Exemestane in anhydrous alcohol. The concentration is calculated on the anhydrous and solvent-free basis.

Chromatographic system

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

Mode: LC

Detector: UV 247 nm

Column: 4.6-mm × 25-cm; 10-µm packing L80

Column temperature: 30°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

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

Suitability requirements

Resolution: NLT than 2.0 between exemestane and exemestane related compound D, *System suitability solution*

Relative standard deviation: NMT 5%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of exemestane related compound D in the portion of Exemestane taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of exemestane related compound D from the *Sample solution*

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

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

C_U = concentration of Exemestane in the *Sample solution* (mg/mL) (the concentration is calculated on the anhydrous and solvent-free basis)

F = relative response factor for exemestane related compound D (see *Table 4*)

Acceptance criteria: See *Table 4*.

Table 4

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Exemestane	1.0	1.0	—
Exemestane related compound D	1.55	1.1	0.10

Total impurities: NMT 2.5%. Total impurities include the impurities in *Table 3* and *Table 4*.

SPECIFIC TESTS

- **Water Determination** ⟨921⟩, *Method I*: NMT 0.3%
- **Optical Rotation** ⟨781S⟩, *Specific Rotation*

  Sample solution: 10 mg/mL in methanol

  Acceptance criteria: +290° to +300° on the anhydrous basis

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

USP Exemestane RS

USP Exemestane Related Compound B RS

6-Hydroxymethylandrosta-1,4-diene-3,17-dione.

$C_{20}H_{26}O_3$ 314.42

USP Exemestane Related Compound C RS

Androsta-1,4-diene-3,17-dione.

$C_{19}H_{24}O_2$ 284.39

USP Exemestane System Suitability Mixture RS

Exemestane containing a small amount of exemestane related compound D (16-Methyleneandrosta-1,4-diene-3,17-dione).

$C_{20}H_{24}O_2$ 296.40

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

Topic/Question	Contact	Expert Committee
EXEMESTANE	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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