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Etomidate

$C_{14}H_{16}N_2O_2$ 244.29

1*H*-Imidazole-5-carboxylic acid, 1-(1-phenylethyl)-, ethyl ester, (+)-;

(+)-Ethyl 1-(α-methylbenzyl)imidazole-5-carboxylate CAS RN®: 33125-97-2; UNII: Z22628B598.

DEFINITION

Etomidate contains NLT 98.0% and NMT 102.0% of etomidate ($C_{14}H_{16}N_2O_2$), calculated on the dried 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**

Buffer: 0.7 g/L of monobasic sodium phosphate in water

Mobile phase: Acetonitrile and *Buffer* (40:60)

Standard solution: 0.16 mg/mL of USP Etomidate RS in acetonitrile

Sample solution: 0.16 mg/mL of Etomidate in acetonitrile

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 2.3 mL/min

Injection volume: 20 µL

Run time: NLT 3 times the retention time of etomidate

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of etomidate ($C_{14}H_{16}N_2O_2$) in the portion of Etomidate taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A: Dissolve 6 g of sodium citrate dihydrate and 4 g of anhydrous citric acid in 1 L of water.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	95	5
20	30	70
21	95	5
30	95	5

Diluent: Weigh 6 g of sodium citrate dihydrate and 4 g of anhydrous citric acid into a 1000-mL volumetric flask. Add 500 mL of water, and shake to dissolve. Add 110 mL of acetonitrile and 50 mL of methanol, and dilute with water to volume.

System suitability solution: 0.02 mg/mL each of USP Etomidate RS and USP Metomidate Hydrochloride RS in *Diluent*

Standard solution: 0.004 mg/mL of USP Metomidate Hydrochloride RS in *Diluent*

Sensitivity solution: 0.8 µg/mL of USP Metomidate Hydrochloride RS from the *Standard solution* in *Diluent*

Sample solution: 0.8 mg/mL of Etomidate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing L1

Flow rate: 2.0 mL/min

Injection volume: 50 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between etomidate and metomidate, *System suitability solution*

Relative standard deviation: NMT 3.0%, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

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

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

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

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

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

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

M_{r1} = molecular weight of metomidate free base, 230.26

M_{r2} = molecular weight of metomidate hydrochloride, 266.72

Acceptance criteria: See *Table 2*. [Note—Disregard any impurity peaks less than 0.05%.]

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Etomidate acid[a]	0.34	0.1
Metomidate[b]	0.90	0.1
Etomidate	1.0	—
Any unspecified impurity	—	0.1
Total impurities	—	1.0

[a] 1-(1-Phenylethyl)-1*H*-imidazole-5-carboxylic acid.

[b] Methyl 1-(1-phenylethyl)-1*H*-imidazole-5-carboxylate.

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

  Sample: 1 g of Etomidate

  Analysis: Dry the *Sample* over phosphorus pentoxide for 16 h.

  Acceptance criteria: NMT 0.5%

- **Optical Rotation ⟨781S⟩, *Procedures, Specific Rotation***

  Sample solution: 10 mg/mL of Etomidate in dehydrated alcohol

  Acceptance criteria: 67.0°–70.0° (*t* = 20°), calculated on the dried basis

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well closed, light-resistant containers, and store at room temperature.
- **USP Reference Standards ⟨11⟩**

  USP Etomidate RS

  USP Metomidate Hydrochloride RS

  Methyl 1-(1-phenylethyl)-1*H*-imidazole-5-carboxylate hydrochloride.

  $C_{13}H_{14}N_2O_2 \cdot HCl$ 266.72

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

Topic/Question	Contact	Expert Committee
ETOMIDATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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