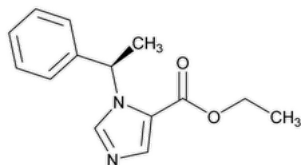


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Etomidate



$C_{14}H_{16}N_2O_2$ 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 μ L

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