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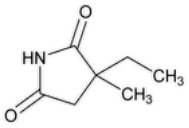
Ethosuximide



$C_7H_{11}NO_2$ 141.17

2,5-Pyrrolidinedione, 3-ethyl-3-methyl-, (±)-;

(±)-2-Ethyl-2-methylsuccinimide CAS RN®: 77-67-8; UNII: 5SEH9X1D1D.

Change to read:

DEFINITION

Ethosuximide contains NLT 98.0% and NMT ▲102.0%▲ (USP 1-Aug-2022) of ethosuximide ($C_7H_{11}NO_2$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A▲ (USP 1-Aug-2022)

• **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

Change to read:

• **Procedure**

▲**Mobile phase:** Acetonitrile and water (12.5: 87.5). To each liter, add 1.0 mL of glacial acetic acid.

Standard solution: 2.0 mg/mL of USP Ethosuximide RS in *Mobile phase*

Sample solution: 2.0 mg/mL of Ethosuximide in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 2 times the retention time of ethosuximide

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 0.73%▲ (USP 1-Aug-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ethosuximide ($C_7H_{11}NO_2$) in the portion of Ethosuximide taken:

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

r_U = peak response ▲of ethosuximide▲ (USP 1-Aug-2022) from the *Sample solution*

r_S = peak response ▲of ethosuximide▲ (USP 1-Aug-2022) from the *Standard solution*

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

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

Acceptance criteria: 98.0%–▲102.0%▲ (USP 1-Aug-2022) on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.5%

Change to read:

• **Organic Impurities**

▲**Mobile phase:** Acetonitrile and water (12.5: 87.5). To each liter, add 1.0 mL of glacial acetic acid.

System suitability solution: 50 mg/mL of USP Ethosuximide RS and 0.25 mg/mL of USP Ethosuximide Related Compound A RS in *Mobile phase*

Sensitivity solution: 0.025 mg/mL of USP Ethosuximide RS in *Mobile phase*

Standard solution: 0.05 mg/mL each of USP Ethosuximide RS and USP Ethosuximide Related Compound A RS in *Mobile phase*

Sample solution: 50 mg/mL of Ethosuximide in *Mobile phase*. Sonicate as needed.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 10 µL

Run time: NLT 5 times the retention time of ethosuximide

System suitability

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

[Note—See *Table 1* for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between ethosuximide and ethosuximide related compound A, *System suitability solution*

Relative standard deviation: NMT 5.0% for ethosuximide and ethosuximide related compound A, *Standard solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ethosuximide related compound A in the portion of Ethosuximide taken:

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

r_U = peak response of ethosuximide related compound A from the *Sample solution*

r_S = peak response of ethosuximide related compound A from the *Standard solution*

C_S = concentration of USP Ethosuximide Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of each unspecified impurity in the portion of Ethosuximide taken:

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

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

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

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

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

Acceptance criteria: See *Table 1*. The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Ethosuximide	1.0	—
Ethosuximide related compound A	1.3	0.10

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Any individual unspecified impurity	—	0.10
Total impurities	—	0.50▲ (USP 1-Aug-2022)

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NMT 0.5%

Change to read:

• **Limit of Cyanide**

Sample solution: 100 mg/mL ▲of Ethosuximide▲ (USP 1-Aug-2022) in alcohol

Analysis: To 10 mL of *Sample solution*, add 3 drops of ferrous sulfate TS, 1 mL of 1 N sodium hydroxide VS, and a few drops of ferric chloride TS. Warm gently, and acidify with 2 N sulfuric acid TS.

Acceptance criteria: No blue precipitate or blue color is formed within 15 min.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Ethosuximide RS

▲ USP Ethosuximide Related Compound A RS

2-Ethyl-2-methylsuccinic acid

$C_7H_{12}O_4$ 160.17▲ (USP 1-Aug-2022)

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

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

Chromatographic Database Information: Chromatographic Database

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