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Ethosuximide Capsules

DEFINITION

Ethosuximide Capsules contain NLT 93.0% and NMT 107.0% of the labeled amount of ethosuximide ($C_7H_{11}NO_2$), present in the form of a solution of Ethosuximide in Polyethylene Glycol 400 or other suitable solvent.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197S**▲ (CN 1-May-2020)

Standard solution: ▲66.7 mg/mL▲ (USP 1-May-2019) of USP Ethosuximide RS in chloroform

Sample solution: Nominally 60 mg/mL of ethosuximide in chloroform prepared as follows. Transfer the equivalent of about 300 mg of ethosuximide from Capsules to a separator containing 50 mL of ethyl ether. Shake with three 10-mL portions of water, discarding the aqueous extracts. Add about 5 g of anhydrous sodium sulfate, swirl for 3 min, and filter through a small pledget of cotton that previously has been washed with ethyl ether into a small flask. Evaporate the ethyl ether solution at room temperature in a current of air to dryness, and dissolve the residue in 5 mL of chloroform.

Wavelength range: 3000–1650 cm^{-1}

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: Meet the requirements

Add the following:

▲• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2019)

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.

System suitability solution: 0.062 mg/mL of USP Ethosuximide RS and 0.064 mg/mL of 2-ethyl-2-methylsuccinic acid in *Mobile phase*

Standard solution: 0.062 mg/mL of USP Ethosuximide RS in *Mobile phase*

Sample solution: Nominally 0.062 mg/mL of ethosuximide from Capsules in *Mobile phase* prepared as follows. Transfer 20 Capsules into a 2-L volumetric flask, dissolve in 1800 mL of *Mobile phase*, and dilute with *Mobile phase* to volume. Transfer 5.0 mL of the resulting solution to a 200-mL volumetric flask and dilute with *Mobile phase* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 3.9-mm × 15-cm; ▲4-µm▲ (USP 1-May-2019) packing L1

Flow rate: 1 mL/min

Injection volume: 10 µL

▲Run time: NLT 2 times the retention time of ethosuximide▲ (USP 1-May-2019)

System suitability

Sample: *System suitability solution*

▲[Note—The relative retention times for ethosuximide and 2-ethyl-2-methylsuccinic acid are 1.0 and 1.3, respectively.]▲ (USP 1-May-2019)

Suitability requirements

Resolution: NLT 3.5 between ethosuximide and 2-ethyl-2-methylsuccinic acid

Tailing factor: NMT 1.5

Relative standard deviation: NMT ▲1.0%▲ (USP 1-May-2019) for ethosuximide and NMT 5.0% for 2-ethyl-2-methylsuccinic acid

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ethosuximide ($C_7H_{11}NO_2$) in the portion of Capsules 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 Ethosuximide RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

▲**Test 1:** Use *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Immediate-Release Dosage Forms, Procedure for a pooled sample for immediate-release dosage forms*.▲ (USP 1-May-2019)

Medium: pH 6.8 phosphate buffer; 900 mL

Apparatus 1: 50 rpm

Time: 30 min

Mobile phase: Acetonitrile and water (20:80)

Standard solution: USP Ethosuximide RS in *Medium*

Sample solution: Prepare as indicated in *Dissolution ⟨711⟩, Procedure, Apparatus 1 and Apparatus 2, Immediate-Release Dosage Forms, Procedure for a pooled sample for immediate-release dosage forms*. Dilute with *Medium* to a concentration that is similar to that of the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 4-mm × 30-cm; packing L1

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

▲Calculate the percentage of the labeled amount of ethosuximide ($C_7H_{11}NO_2$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

▲ (USP 1-May-2019)

Tolerances: NLT 80% (Q) of the labeled amount of ethosuximide ($C_7H_{11}NO_2$) is dissolved.

▲**Test 2:** If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: pH 6.8 phosphate buffer (prepared by adding 0.9 g sodium hydroxide per liter of 6.8-g/L monobasic potassium phosphate in water; adjust with sodium hydroxide to a pH of 6.8, if necessary; sonicate for about 15 min); 900 mL

Apparatus 2: 50 rpm

Time: 30 min

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

Standard solution: (L/900) mg/mL of USP Ethosuximide RS prepared as follows, where L is the label claim in mg/Capsule. Transfer a suitable portion of USP Ethosuximide RS to an appropriate volumetric flask. Add 80% of the total flask volume of *Medium* and sonicate

for NLT 5 min or until the solids are dissolved. Allow the resulting solution to cool to room temperature, and dilute with *Medium*.

Sample solution: Centrifuge a 10-mL aliquot of the solution under test for about 15 min. Use the supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm

Column: 3.9-mm × 15-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 50 µL

Run time: NLT 4 times the retention time of ethosuximide

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of ethosuximide ($C_7H_{11}NO_2$) dissolved:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of ethosuximide ($C_7H_{11}NO_2$) is dissolved.▲ (USP 1-May-2019)

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

• **Limit of 2-Ethyl-2-Methylsuccinic Acid**

Mobile phase, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Standard solution: 0.026 mg/mL of 2-ethyl-2-methylsuccinic acid in *Mobile phase*

Sample solution: Nominally 2.5 mg/mL of ethosuximide from Capsules in *Mobile phase* prepared as follows. Transfer 20 Capsules into a 2-L volumetric flask, dissolve in 1800 mL of *Mobile phase*, dilute with *Mobile phase* to volume, and mix.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of 2-ethyl-2-methylsuccinic acid in the portion of Capsules taken:

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

r_U = peak response of 2-ethyl-2-methylsuccinic acid from the *Sample solution*

r_S = peak response of 2-ethyl-2-methylsuccinic acid from the *Standard solution*

C_S = concentration of 2-ethyl-2-methylsuccinic acid in the *Standard solution* (mg/mL)

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

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in tight containers. ▲Store at controlled room temperature.▲ (USP 1-May-2019)

Add the following:

▲• **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.▲ (USP 1-May-2019)

• **USP Reference Standards ⟨11⟩**

USP Ethosuximide RS

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

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

Chromatographic Database Information: Chromatographic Database

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