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Felbamate Oral Suspension

DEFINITION

Felbamate Oral Suspension is a viscous liquid containing NLT 90.0% and NMT 110.0% of the labeled amount of felbamate ($C_{11}H_{14}N_2O_4$). The product may contain suitable preservatives.

IDENTIFICATION

Change to read:

• **A.** The retention time of the major peak ▲of▲ (USP 1-Dec-2020) the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• **B.** The UV spectrum of the felbamate peak in the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2020)

ASSAY

Change to read:

• **Procedure**

Buffer: 28.5 g/L of tribasic sodium phosphate▲▲ (USP 1-Dec-2020) in water

Mobile phase: Acetonitrile and *Buffer* (23:77). Adjust with phosphoric acid to a pH of 9.9.

Diluent A: Methanol and water ▲(50:50)▲ (USP 1-Dec-2020)

Diluent B: Acetonitrile and water (23:77)

System suitability solution: ▲160 µg/mL▲ (USP 1-Dec-2020) of USP Felbamate RS and ▲20 µg/mL▲ (USP 1-Dec-2020) of USP Felbamate Related Compound A RS in *Diluent B* and methanol prepared as follows. ▲Transfer suitable amounts of USP Felbamate RS and USP Felbamate Related Compound A RS to an appropriate volumetric flask. Dissolve in 8% of the flask volume of methanol.▲ (USP 1-Dec-2020) Dilute with *Diluent B* to volume.

Standard solution: ▲160 µg/mL▲ (USP 1-Dec-2020) of USP Felbamate RS prepared as follows. ▲Transfer a suitable amount of USP Felbamate RS to▲ (USP 1-Dec-2020) a suitable volumetric flask containing 16% of the flask volume of *Diluent A*. Add 50% of the flask volume of *Diluent B*. Sonication may be used to aid dissolution. Dilute with *Diluent B* to volume.

Sample stock solution: Nominally 1 mg/mL of felbamate in *Diluent A* prepared as follows. Transfer an amount of the Oral Suspension to a suitable volumetric flask. Add 60% of the flask volume of *Diluent A*, and sonicate for 15 min. Shake mechanically for 30 min, and dilute with *Diluent A* to volume.

Sample solution: Nominally ▲160 µg/mL▲ (USP 1-Dec-2020) of felbamate from *Sample stock solution* in *Diluent B*. Pass through a filter ▲with a pore size of 0.45-µm.▲ (USP 1-Dec-2020)

Chromatographic system

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

Mode: LC

Detector: UV 210 nm. ▲For *Identification B*, use a diode array detector in the range of 190–400 nm.▲ (USP 1-Dec-2020)

Column: 4.1-mm × 15-cm; 5-µm packing L21

Column temperature: 40°

Flow rate: 1 mL/min

Injection ▲volume:▲ (USP 1-Dec-2020) 20 µL

▲Run time: NLT 2 times the retention time of felbamate▲ (USP 1-Dec-2020)

System suitability

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

Suitability requirements

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

Tailing factor: NMT ▲1.5,▲ (USP 1-Dec-2020) *Standard solution*

Relative standard deviation: NMT ▲1.0%,▲ (USP 1-Dec-2020) *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of felbamate ($C_{11}H_{14}N_2O_4$) in the portion of Oral Suspension taken:

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

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

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

C_S = concentration of USP Felbamate RS in the *Standard solution*▲(µg/mL)▲ (USP 1-Dec-2020)

C_U = nominal concentration of felbamate in the *Sample solution*▲(µg/mL)▲ (USP 1-Dec-2020)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 15 min

Mobile phase: Acetonitrile and water (35:65)

▲**System suitability stock solution:** 0.1 mg/mL of USP Methylparaben RS in methanol

System suitability solution: 0.1 mg/mL of USP Methylparaben RS from *System suitability stock solution* and 0.4 mg/mL of USP Felbamate RS prepared as follows. Transfer 40 mg of USP Felbamate RS to a 100-mL volumetric flask. Add 10 mL of *System suitability stock solution* and sonicate for 5 min. Dilute with *Medium* to volume.▲ (USP 1-Dec-2020)

Standard solution: (*L*/1000) mg/mL of USP Felbamate RS in *Medium*, where *L* is the ▲▲ (USP 1-Dec-2020) label claim in mg/mL. An amount of methanol, not exceeding 10% of the final volume, can be used to help in solubilizing felbamate.

Sample solution: Using a syringe, accurately weigh by difference approximately 5 mL of the well-mixed Oral Suspension. Introduce the sample into the dissolution vessel with the paddles rotating, and avoid getting the sample on the paddle or shaft. At the time specified, withdraw an aliquot of the solution under test, and pass through a suitable filter.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 10-µm packing L7

Flow rate: 2 mL/min

Injection ▲volume

System suitability: 25 µL

Analysis: 15 µL

Run time: NLT 3.5 times the retention time of felbamate▲ (USP 1-Dec-2020)

System suitability

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

[Note—The relative retention times for felbamate and methylparaben are about 1.0 and 1.5, respectively.]

Suitability requirements

Resolution: NLT 2.0 between methylparaben and felbamate, *System suitability solution*

Tailing factor: NMT 2, *Standard solution*

Relative standard deviation: NMT 2%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of felbamate ($C_{11}H_{14}N_2O_4$) dissolved:

$$\text{▲Result} = (r_U/r_S) \times C_S \times V \times (d/W) \times (1/L) \times 100\text{▲ (USP 1-Dec-2020)}$$

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

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

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

V = volume of *Medium*, 900 mL

$▲d_{▲ (USP 1-Dec-2020)}$ = density of the Oral Suspension (g/mL)

W = weight of the Oral Suspension taken (g)

L = label claim of the Oral Suspension (mg/mL)

Tolerances: NLT 80% (Q) of the labeled amount of felbamate ($C_{11}H_{14}N_2O_4$) is dissolved.

IMPURITIES

Change to read:

• **Organic Impurities**

Mobile phase, Diluent A, Diluent B, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: ▲200 µg/mL▲ (USP 1-Dec-2020) of USP Felbamate RS and ▲20 µg/mL▲ (USP 1-Dec-2020) of USP Felbamate Related Compound A RS in *Diluent B* prepared as follows. Transfer suitable quantities of USP Felbamate RS and USP Felbamate Related Compound A RS into a suitable volumetric flask. Dissolve in 8% of the flask volume of methanol. Dilute with *Diluent B* to volume.

Standard stock solution: ▲200 µg/mL▲ (USP 1-Dec-2020) of USP Felbamate RS in *Diluent A*

Standard solution: 0.2 µg/mL of USP Felbamate RS from *Standard stock solution* in *Diluent B* prepared as follows. Transfer a suitable volume of *Standard stock solution* to a suitable volumetric flask containing 0.8% of the flask volume of methanol, and dilute with *Diluent B* to volume.

System suitability

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

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

Suitability requirements

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

Tailing factor: NMT 2.0 for the felbamate peak, *Standard solution*

Relative standard deviation: NMT 10% for the felbamate peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Oral Suspension 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 felbamate from the *Standard solution*

C_S = concentration of USP Felbamate RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of felbamate in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Phenylpropanediol[a]	0.63	2.6	0.2
Felbamate related compound A▲▲ (USP 1-Dec-2020)	0.78	1.8	0.2
Felbamate	1.0	—	—
▲Any▲ (USP 1-Dec-2020) individual unspecified degradation product	—	1.0	0.2
Total impurities	—	—	0.75

[a] 2-Phenylpropane-1,3-diol.

SPECIFIC TESTS

Change to read:

• **pH** ⟨791⟩

▲**Sample solution:** Use a portion of well-stirred Oral Suspension.

Acceptance criteria: 4.5–6.0▲ (USP 1-Dec-2020)

• **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** The total aerobic microbial count is NMT 10^2 cfu/mL. The total yeasts and molds count is NMT 10^1 cfu/mL. It meets the requirements of the test for absence of *Escherichia coli*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Felbamate RS

USP Felbamate Related Compound A RS

3-Hydroxy-2-phenylpropyl carbamate.

$C_{10}H_{13}NO_3$ 195.22

USP Methylparaben RS

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

Topic/Question	Contact	Expert Committee
FELBAMATE ORAL SUSPENSION	Documentary Standards Support	SM42020 Small Molecules 4

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