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Primidone Tablets

DEFINITION
Primidone Tablets contain NLT 95.0% and NMT 105.0% of the labeled amount of primidone ($C_{12}H_{14}N_2O_2$).

IDENTIFICATION

• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Add the following:

▲• **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-Dec-2022)

ASSAY

Change to read:

• **Procedure**

Buffer: 6.8 g/L of monobasic potassium phosphate ▲in water▲ (USP 1-Dec-2022)

Mobile phase: Methanol, tetrahydrofuran, and *Buffer* (35: 0.5: 65)

Diluent: Methanol and water (35:65)

Standard stock solution: 0.5 mg/mL of USP Primidone RS in methanol

Standard solution: 0.05 mg/mL of USP Primidone RS from the *Standard stock solution* in *Diluent*

Sample stock solution: ▲Nominally 1 mg/mL of primidone prepared as follows. Finely powder Tablets (NLT 20) and transfer a portion of the powder to an appropriate volumetric flask. Add methanol to about 50% of the flask volume, sonicate, and shake by mechanical means until all of the solid is dispersed. Allow the solution to cool to room temperature, and dilute with methanol to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size and discard the first 5 mL of the filtrate.▲ (USP 1-Dec-2022)

Sample solution: 0.05 mg/mL of primidone from the ▲*Sample*▲ *(ERR 1-Dec-2022) stock solution* in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm. ▲For *Identification B*, use a diode array detector in the range of 200–400 nm.▲ (USP 1-Dec-2022)

Column: 4.6-mm × 10-cm; 3-µm packing L1

Column temperature: 35°

Flow rate: 1.3 mL/min

Injection volume: 20 µL

▲**Run time:** NLT 2.5 times the retention time of primidone▲ (USP 1-Dec-2022)

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲ (USP 1-Dec-2022)

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of primidone ($C_{12}H_{14}N_2O_2$) in the portion of Tablets taken:

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

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

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

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

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

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution** ⟨711⟩

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 60 min

Standard solution: ▲*L*/900 (mg/mL) of▲ (USP 1-Dec-2022) USP Primidone RS in *Medium*, ▲where *L* is the label claim in mg/Tablet▲ (USP 1-Dec-2022)

Sample solution: Pass a portion of the solution under test through a suitable filter. Dilute with *Medium*, if necessary, to obtain a concentration that is similar to that of the *Standard solution*.

Instrumental conditions

Mode: UV

Analytical wavelength: 257 nm

[Note—Perform baseline corrections, if necessary, in determining the absorbance by extrapolating the baseline through the absorbance minima at 300 nm and 280 nm and beyond 257 nm.]

▲**Analysis**

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of primidone ($C_{12}H_{14}N_2O_2$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

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

D = dilution factor of the *Sample solution*, if needed

V = volume of *Medium*, 900 mL

L = label claim (mg/Tablet)▲ (USP 1-Dec-2022)

Tolerances: NLT 75% (*Q*) of the labeled amount of primidone ($C_{12}H_{14}N_2O_2$) is dissolved.

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

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer, Mobile phase, and **Diluent**▲▲ (USP 1-Dec-2022) **:** Prepare as directed in the *Assay*.

Primidone related compound A stock solution: 200 µg/mL of USP Primidone Related Compound A RS in methanol

Primidone related compound A solution: 20 µg/mL of USP Primidone Related Compound A RS from *Primidone related compound A stock solution* in *Diluent*

Standard stock solution: 0.05 mg/mL of USP Primidone RS in methanol

System suitability solution: ▲1 µg/mL of USP Primidone Related Compound A RS from the *Primidone related compound A solution* and 2 µg/mL of USP Primidone RS from the *Standard stock solution* in *Diluent*▲ (USP 1-Dec-2022)

Standard solution: 2 µg/mL of USP Primidone RS from the *Standard stock solution* in *Diluent*

▲**Sensitivity solution:** 0.5 µg/mL of USP Primidone RS from the *Standard solution* in *Diluent*▲ (USP 1-Dec-2022)

Sample solution: ▲Nominally 1000 µg/mL of primidone prepared as follows. Finely powder Tablets (NLT 20) and transfer a portion of the powder to an appropriate volumetric flask. Add methanol to about 36% of the flask volume, sonicate, and shake by mechanical means until all of the solid is dispersed. Allow the solution to cool to room temperature, and dilute with water to volume. Pass a portion of the solution through a suitable filter of 0.45-µm pore size and discard the first 5 mL of the filtrate.▲ (USP 1-Dec-2022)

Chromatographic system: Proceed as directed in the *Assay* ▲except for the *Run time*.

Run time: NLT 15 times the retention time of primidone▲ (USP 1-Dec-2022)

System suitability

Samples: *System suitability solution*, *Standard solution*, ▲and *Sensitivity solution*▲ (USP 1-Dec-2022)

[NOTE—The relative retention times for primidone related compound A and primidone are 0.5 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 4.0 between primidone related compound A and primidone, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

▲**Signal-to-noise ratio:** NLT 10, *Sensitivity solution*▲ (USP 1-Dec-2022)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any individual degradation product in the portion of Tablets taken:

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

r_U = peak response of each ▲degradation product▲ (USP 1-Dec-2022) from the *Sample solution*

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

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

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

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

Acceptance criteria: See *Table 1*.

[NOTE— ▲The reporting threshold is 0.05%.▲ (USP 1-Dec-2022)]

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Primidone related compound A▲▲ (USP 1-Dec-2022)	0.5	0.76	0.1
Primidone	1.0	—	—
Phenobarbital	1.6	1.4	0.1
Primidone related compound C[a]	1.9	0.92	0.1
2-Cyano-2-phenylbutyramide▲[b]▲ (USP 1-Dec-2022) [c]	2.2	—	—
2-Phenylbutyric acid▲[d]▲ (USP 1-Dec-2022)	4.1	0.91	0.1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Phenylpropyl primidone[c,▲e▲] (USP 1-Dec-2022)	11.4	—	—
Any individual unspecified degradation product	—	1.0	0.1
Total ▲degradation products▲ (USP 1-Dec-2022)	—	—	0.5

[a] 2-Phenylbutyramide.

[b] 2-Cyano-2-phenylbutanamide.

[c] ▲Process impurity included in the table for identification only. Process impurities are controlled in the drug substance, and are not to be reported or included in the total degradation products for the drug product.▲ (USP 1-Dec-2022)

[d] 2-Phenylbutanoic acid.

[e] 5-Ethyl-5-phenyl-2-(1-phenylpropyl)dihydropyrimidine-4,6 (1*H*,5*H*)-dione.

ADDITIONAL REQUIREMENTS

Change to read:

• **Packaging and Storage:** Preserve in well-closed containers. ▲Store at controlled room temperature.▲ (USP 1-Dec-2022)

• **Labeling:** Tablets intended solely for veterinary use are so labeled.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Primidone RS

USP Primidone Related Compound A RS

2-Ethyl-2-phenylmalonamide.

$C_{11}H_{14}N_2O_2$ ▲206.25▲ (USP 1-Dec-2022)

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

Topic/Question	Contact	Expert Committee
PRIMIDONE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

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