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 in the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

Buffer: 6.8 g/L of monobasic potassium phosphate
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 in *Diluent*, from the *Standard stock solution*
Sample stock solution: Transfer an equivalent of about 250 mg of primidone, from finely powdered Tablets (NLT 20), based on the label claim, to a 250-mL volumetric flask. Add about 125 mL of methanol, sonicate for about 15 min, and shake by mechanical means until all the solid is dispersed (usually 20 min). Allow the solution to cool to room temperature, and dilute with methanol to volume. Pass a portion of this solution through a PTFE (or equivalent) filter of 0.45-µm pore size, and discard the first 5 mL of filtrate.
Sample solution: 0.05 mg/mL of primidone in *Diluent*, from the *Sample stock solution*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 10-cm; 3-µm packing L1
Column temperature: 35°
Flow rate: 1.3 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Column efficiency: NLT 3000 theoretical plates
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 the *Sample solution*
r_S = peak response of the *Standard solution*
C_S = concentration of USP Primidone RS in the *Standard solution* (mg/mL)
C_U = concentration of primidone in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

PERFORMANCE TESTS

- **DISSOLUTION** ⟨**711**⟩

Medium: Water; 900 mL
Apparatus 2: 50 rpm
Time: 60 min
Standard solution: USP Primidone RS in *Medium*
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 and 280 nm and beyond 257 nm.]
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**, **Diluent**, and **Chromatographic system:** Proceed 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 in *Diluent*, from *Primidone related compound A stock solution*
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 and 2 µg/mL of USP Primidone RS in *Diluent*, from the *Primidone related compound A solution* and the *Standard stock solution,* respectively
Standard solution: 2 µg/mL of USP Primidone RS in *Diluent*, from the *Standard stock solution*
Sample solution: Transfer an equivalent of about 250 mg of primidone, from finely powdered Tablets (NLT 20), based on the label claim, to a 250-mL volumetric flask. Add about 90 mL of methanol, sonicate for about 15 min, and shake by mechanical means until all the solid is dispersed (usually 20 min). Allow the solution to cool to room temperature, and dilute with water to volume. Pass a portion of this solution through a PTFE (or equivalent) filter of 0.45-µm pore size, and discard the first 5 mL of filtrate.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
System suitability
Samples: *System suitability solution* and *Standard solution*
[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*
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 impurity from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Primidone RS in the *Standard solution* (µg/mL)

C_U = concentration of primidone in the *Sample solution* (µg/mL)
F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

[NOTE—Disregard impurity peaks that are less than ●0.05%.● (RB 1-Nov-2011)]

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Primidone related compound A[a]	0.5	0.76	0.1
Primidone	1.0	—	—
Phenobarbital	1.6	1.4	0.1
Primidone related compound C[b]	1.9	0.92	0.1
●2-Cyano-2-phenylbutyramide[c]	2.2	—	—● (RB 1-Nov-2011)
2-Phenylbutyric acid	4.1	0.91	0.1
●Phenylpropyl-primidone[c]	11.4	—	—● (RB 1-Nov-2011)
Any individual unspecified degradation product	—	1.0	0.1
Total impurities	—	—	●0.5● (RB 1-Nov-2011)

[a] 2-Ethyl-2-phenylmalonamide.

[b] 2-Phenylbutyramide.

●[c] Process impurities controlled in the drug substance. Included for identification purposes only. Not reported for the drug product and not included in *Total impurities*.● (RB 1-Nov-2011)

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **LABELING:** Tablets intended solely for veterinary use are so labeled.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Primidone RS
  USP Primidone Related Compound A RS
  2-Ethyl-2-phenylmalonamide.
  $C_{11}H_{14}N_2O_2$ 206.24