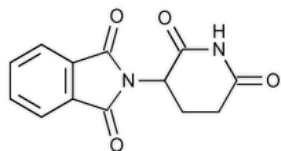


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# Thalidomide



$C_{13}H_{10}N_2O_4$  258.23

1*H*-Isoindole-1,3(2*H*)-dione, 2-(2,6-dioxo-3-piperidiny)-, (±)-;

(±)-*N*-(2,6-Dioxo-3-piperidyl)phthalimide;

α-(*N*-Phthalimido)glutarimide CAS RN®: 50-35-1; UNII: 4Z8R6ORS6L.

## DEFINITION

Thalidomide contains NLT 98.0% and NMT 101.5% of thalidomide ( $C_{13}H_{10}N_2O_4$ ), calculated on the anhydrous basis.

## IDENTIFICATION

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197K

Add the following:

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

## ASSAY

Change to read:

### PROCEDURE

**Solution A:** Transfer 1 mL of phosphoric acid into a 100-mL volumetric flask and dilute with water to volume.

**Mobile phase:** Acetonitrile, water, and phosphoric acid (15: 85: 0.1)

**Internal standard solution:** 1.5 mg/mL of phenacetin in acetonitrile

**Standard stock solution:** 1 mg/mL of [USP Thalidomide RS](#) in acetonitrile. Sonicate to dissolve, if necessary.

**Standard solution:** 0.1 mg/mL of [USP Thalidomide RS](#) and 0.075 mg/mL of phenacetin prepared as follows. Transfer 10.0 mL of *Standard stock solution* and 5.0 mL of *Internal standard solution* to a 100-mL volumetric flask, add 10.0 mL of *Solution A*, and dilute with water to volume.

**Sample stock solution:** 1 mg/mL of Thalidomide in acetonitrile. Sonicate to dissolve, if necessary.

**Sample solution:** 0.1 mg/mL of Thalidomide and 0.075 mg/mL of phenacetin prepared as follows. Transfer 10.0 mL of *Sample stock solution* and 5.0 mL of *Internal standard solution* to a 100-mL volumetric flask, add 10.0 mL of *Solution A*, and dilute with water to volume.

### Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

**Mode:** LC

**Detector:** UV 237 nm

**Column:** 3.9-mm × 15-cm; 4-μm packing [L1](#)

**Flow rate:** 1 mL/min

**Injection volume:** 20 μL

### System suitability

**Sample:** *Standard solution*

### Suitability requirements

**Resolution:** NLT 3.0 between thalidomide and phenacetin

▲ ▲ (USP 1-Dec-2020)

**Tailing factor:** NMT 2.0

**Relative standard deviation:** NMT 1.0% for the response ratio of thalidomide to phenacetin

## Analysis

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of thalidomide ( $C_{13}H_{10}N_2O_4$ ) in the portion of Thalidomide taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

$R_U$  = peak response ratio of thalidomide to phenacetin from the *Sample solution*

$R_S$  = peak response ratio of thalidomide to phenacetin from the *Standard solution*

$C_S$  = concentration of [USP Thalidomide RS](#) in the *Standard solution* (mg/mL)

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

**Acceptance criteria:** 98.0%–101.5% on the anhydrous basis

## IMPURITIES

### • ORGANIC IMPURITIES

**Solution A:** Acetonitrile, water, and phosphoric acid (5: 95: 0.1)

**Solution B:** Acetonitrile, water, and phosphoric acid (15: 85: 0.1)

**Solution C:** Acetonitrile and water (80:5)

**Mobile phase:** See [Table 1](#).

**Table 1**

| Time<br>(min) | Solution A<br>(%) | Solution B<br>(%) |
|---------------|-------------------|-------------------|
| 0             | 100               | 0                 |
| 15            | 50                | 50                |
| 20            | 100               | 0                 |
| 30            | 100               | 0                 |

**Diluent A:** Acetonitrile, water, and phosphoric acid (50: 50: 0.1)

**Diluent B:** Transfer 1 mL of phosphoric acid into a 100-mL volumetric flask and dilute with water to volume.

**Standard stock solution A:** 1 mg/mL of phthalic acid prepared as follows. Transfer 100 mg of phthalic acid to a 100-mL volumetric flask, dissolve in 85 mL of *Solution C*, and dilute with acetonitrile to volume.

**Standard stock solution B:** 0.1 mg/mL of phthalic acid prepared as follows. Transfer *Standard stock solution A* to a suitable volumetric flask and dilute with acetonitrile to volume.

**Standard stock solution C:** 1 mg/mL of [USP Thalidomide RS](#) in acetonitrile. Sonicate to dissolve, if necessary.

**Standard stock solution D:** 0.002 mg/mL of phthalic acid and 0.02 mg/mL of [USP Thalidomide RS](#) prepared as follows. Pipet 2.0 mL of *Standard stock solution B* and 2.0 mL of *Standard stock solution C* into a 100-mL volumetric flask, and dilute with *Diluent A* to volume.

**Standard solution:** 0.0002 mg/mL of phthalic acid and 0.002 mg/mL of [USP Thalidomide RS](#) prepared as follows. Pipet 10.0 mL of *Standard stock solution D* into a 100-mL volumetric flask, add 10.0 mL of *Diluent B*, and dilute with water to volume.

**Sample stock solution:** 2 mg/mL of Thalidomide in *Diluent A*. Sonicate to dissolve, if necessary.

**Sample solution:** 0.2 mg/mL of Thalidomide prepared as follows. Pipet 10.0 mL of *Sample stock solution* into a 100-mL volumetric flask, add 10.0 mL of *Diluent B*, and dilute with water to volume.

## Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

**Mode:** LC

**Detector:** UV 218 nm

**Column:** 3.9-mm × 15-cm; 4-μm packing [L1](#)

**Flow rate:** 2 mL/min

**Injection volume:** 200 μL