Thalidomide Capsules

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

Thalidomide Capsules

Thalidomide Capsules contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of thalidomide, $C_{13}H_{10}N_2O_4$.

Usual strengths. 50 mg; 100 mg; 200 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests

Dissolution (2.5.2).
Apparatus No.2 (Paddle),
Medium: 4000 ml of a buffer solution prepared by diluting 1.0 ml of 50 per cent w/v solution of *polyoxyethylene (23) lauryl ether* to 4000 ml with *0.225 M hydrochloric acid,*
Speed and time. 75 rpm for 60 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Solution A. A 1 per cent v/v solution of *orthophosphoric acid* in *water.*

Internal standard solution. A 0.0375 per cent w/v solution of *phenacetin* in *acetonitrile.* Transfer 20.0 ml of the solution to a 100-ml volumetric flask, add 10.0 ml of solution A and dilute to volume with *water* and mix.

Test solution. Dilute the filtrate, with the dissolution medium to obtain a solution having similar concentration as obtained in the reference solution. To 20.0 ml of the solution, add 5.0 ml of internal standard solution..

Reference solution. A 0.0125 per cent w/v solution of *thalidomide IPRS* in *acetonitrile.* Transfer10.0 ml of the solution to a 100-ml volumetric flask, add 10.0 ml of solution A and dilute to volume with *water*. To 20.0 ml of the solution, add 5.0 ml of internal standard solution.

Chromatographic system
- a stainless steel column 15 cm x 3.9 mm, packed with octadecylsilane bonded to porous or non porous silica (4 µm) (Such as Nova-Pak C18),
- mobile phase: a mixture of 15 volumes of *acetonitrile*, 85 volumes of *water* and 0.1 volume of *orthophosphoric acid,*
- flow rate: 1 ml per minute,
- spectrophotometer set at 237 nm,
- injection volume: 20 µl.

Inject the reference solution and the test solution.

Calculate the content of $C_{13}H_{10}N_2O_4$ in the medium, using ratio of peak area of thalidomide to that of peak area of phenacetin (internal standard).

Q. Not less than 70 per cent of the stated amount of $C_{13}H_{10}N_2O_4$.

Microbial contamination (2.2.9). Total aerobic viable count is not more than 1000 CFU per g and total combined mold and yeasts count is not more than 100 CFU per g. 1 g is free from *Escherichia coli.*

Other tests. Comply with the tests stated under Capsules.

Assay. Determine by liquid chromatography (2.4.14).

Solution A. A 1 per cent v/v solution of *orthophosphoric acid* in *water.*

Internal standard solution. A 0.15 per cent w/v solution of *phenacetin* in *acetonitrile.*

Test solution. Weigh and transfer a quantity of the mixed contents of 20 capsules containing about 50 mg of Thalidomide, to a 100-ml volumetric flask, add 80 ml of *acetonitrile* and sonicate for 20 minutes to dissolve and dilute to volume with *acetonitrile*. To 20.0 ml of the solution, add 5.0 ml of internal standard solution and 10.0 ml of solution A dilute to 100.0 ml with *water.*

Reference solution. A 0.1 per cent w/v solution of *thalidomide IPRS* in *acetonitrile.* Transfer 10.0 ml of the solution to a 100-ml volumetric flask, add 5.0 ml of internal standard solution and 10.0 ml of solution A and dilute to volume with *water*.

Use chromatographic system as described under Dissolution.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to thalidomide and phenacetin (internal standard) is not less than 3.0, the tailing factor is not more than 2.0 and the relative standard deviation for peak area ratio due to thalidomide and phenacetin (internal standard) for the replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{13}H_{10}N_2O_4$ in the capsules, using ratio of peak area of thalidomide to that of peak area of phenacetin (internal standard).

Storage. Store protected from light and moisture, at a temperature not exceeding 30°.