Lenalidomide 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.	

Lenalidomide Capsules

Lenalidomide Capsules contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of lenalidomide, $C_{13}H_{13}N_3O_3$.

Usual strengths. 5 mg; 10 mg; 15 mg; 25 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. 900 ml of *0.1 M hydrochloric acid*,
Speed and time. 50 rpm and 15 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate if necessary, with the dissolution medium.

Reference solution. A 0.00055 per cent w/v solution of *lenalidomide IPRS* in the dissolution medium.

Chromatographic system
- –a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- – mobile phase : a mixture of 85 volumes of *water*, 15 volumes of *acetonitrile* and 0.1 volume of *orthophosphoric acid,*
- –flow rate: 1ml per minute,
- –spectrophotometer set at 220 nm,
- –injection volume: 10 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 3000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injection is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{13}H_{13}N_3O_3$ in the medium.

Q. Not less than 75 per cent of the stated amount of $C_{13}H_{13}N_3O_3$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. Equal volumes of mobile phase A and mobile phase B.

Test solution. Disperse a quantity of the mixed contents of the capsules containing about 10 mg of Lenalidomide in the solvent mixture, with the aid of ultrasound for 20 minutes with intermittent shaking and dilute to 20.0 ml with the solvent mixture.

Reference solution. A 0.0001 per cent w/v solution of *lenalidomide IPRS* in the solvent mixture.

Chromatographic system
- –a stainless steel column 25 cm x 4.6 mm, packed with octylsilane bonded to porous silica (5µm) (Such as Ascentis C 8),
- –mobile phase A: a buffer solution prepared by dissolving 1.36 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 3.5 with *dilute orthophosphoric acid*,
  B: *acetonitrile,*
- –a gradient programme using the conditions given below,
- –flow rate: 1 ml per minute,
- –spectrophotometer set at 210 nm,
- –injection volume: 10 µl.

Time (in min)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	80	20
15	65	35
30	20	80
31	80	20
40	80	20

Name	Relative retention time	Correction factor
Lenalidomide impurity A[1*]	0.43	---
Lenalidomide	1.00	---
Lenalidomide impurity C[2]	2.09	1.39
Lenalidomide impurity B[3]	5.20	1.96

*Process impurity included for identification only, not to be included in total degradation product.
[1]3-Amino glutarimide hydrochloride,
[2]3-(4-nitro-1-oxo-1,3-dihydro-isoindol-2yl)-piperidine-2,6-dione,
[3]Methyl-2-bromomethyl-3-nitrobenzoate.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injection is not more than 5.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of the any peak corresponding to lenalidomide impurity B and lenalidomide impurity C, each of ,not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent), the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than 5 times the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent).

Uniformity of content. Complies with the test stated under Capsules.

Determine by liquid chromatography (2.4.14), as described under Assay with the following modification.

Test solution. Disperse the content of 1 capsule in *0.1M hydrochloric acid* with the aid of ultrasound for 20 minutes and dilute with *0.1M hydrochloric acid* to obtain a solution containing 0.01 per cent w/v of Lenalidomide and filter.

Inject the reference solution and the test solution.

Calculate the content of $C_{13}H_{13}N_3O_3$ in the Capsule.

Other tests. Comply with the tests stated under Capsules.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of the mixed contents of 20 capsules containing 25 mg of Lenalidomide in *0.1M hydrochloric acid*, with the aid of ultrasound for 20 minutes with intermittent shaking and dilute to 100.0 ml with *0.1M hydrochloric acid*. Dilute 10.0 ml of the solution to 25.0 ml with *0.1M hydrochloric acid.*

Reference solution. A 0.01per cent w/v solution of *lenalidomide IPRS* in *0.1M hydrochloric acid*.

Use the chromatographic system as described under Dissolution, using injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 3000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and test solution.
Calculate the content of $C_{13}H_{13}N_3O_3$ in the capsules.

Storage. Store at a temperature not exceeding 30°