Lenalidomide

Published on: 19 December, 2022 **Last date for comments:** 17 February, 2023

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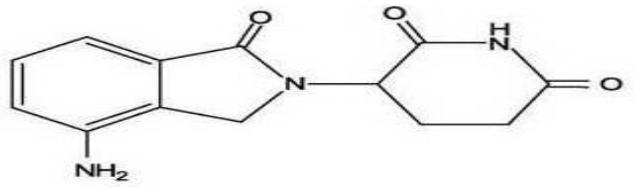
Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls 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

Description	Details
Document version	1.0
Monograph proposed for inclusion	IP Addendum 2024
Tentative effective date of monograph	July, 2024
First draft published on IPC website for public comments	19 December, 2022
Draft revision published on IPC website for public comments	-
Further follow-up action as required.	

Lenalidomide



$C_{13}H_{13}N_3O_3$ Mol Wt. 259.3

Lenalidomide is 3-(4-Amino-1, 3-dihydro-1-oxo-2H-isoindol-2-yl)-2,6-piperidinedione.

Lenalidomide contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{13}H_{13}N_3O_3$, calculated on the anhydrous basis.

Category. Antineoplastic.

Description. Off white to pale yellow powder.

CAUTION- Lenalidomide is cytotoxic; Extra care required to prevent inhaling and exposing the skin to it.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *lenalidomide IPRS* or with the reference spectrum of lenalidomide.

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

Tests

Related substances. Determine by liquid chromatography (2.4.14).

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

Test solution. Dissolve 25 mg of substance under examination in 10 ml of the solvent mixture with the aid of ultrasound for 20 minutes and dilute to 50.0 ml with the solvent mixture.

Reference solution. A 0.005 per cent w/v solution of *lenalidomide IPRS* in solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octylsilane bonded to porous silica (5 µm)(Such as Zorbax C8),
- sample temperature: 5º,
- 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
35	80	20

Name	Relative retention time	Correction factor
Lenalidomide impurity A[1]	0.43	2.44
Lenalidomide	1.00	---
Lenalidomide impurity C[2]	2.09	1.39
Lenalidomide impurity B[3]	5.20	1.96

[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 injections 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 A, B and C, each of, is not more than 1.5 times the area of the principle peak in the chromatogram obtained with the reference solution (0.15 per cent), the area of any other secondary peak is not more than of the area of the principal peak in the chromatogram obtained with the reference solution (0.1 per cent) and the sum of areas of all the secondary peaks is not more than 10 times the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent).

Heavy metals (2.3.13). 1.0 g complies with the limit test for heavy metals method B (20 ppm).

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Water (2.3.43). Not more than 4.5 per cent, determined on 0.2 g.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Dissolve 25.0 mg of substance under examination in *0.1M hydrochloric acid* and dilute to 100.0 ml with *0.1M hydrochloric acid*.

Reference solution. A 0.025 per cent w/v solution of *lenalidomide IPRS* in *0.1M hydrochloric acid*.

Chromatographic system
- a stainless steel column 250 mm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm)(Such as Kromasil),
- mobile phase: a mixture of 85 volumes water, 15 volumes of acetonitrile and 0.1 volume of *orthophosphoric acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 220 nm,
- Injection volume: 5 µl.

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 injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

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

Storage: Store protected from light and moisture , at temperature not exceeding 30º.

2.4.26. Solubility.

Insert before **Lenvatinib Mesylate.** Page 282

Lenalidomide. Soluble in *dimethylsulphoxide*