Pomalidomide

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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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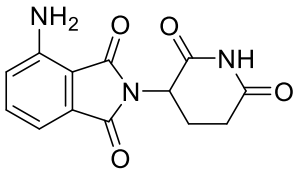
Pomalidomide



$C_{13}H_{11}N_3O_4$ Mol. Wt. 273.2

Pomalidomide is 4-amino-2-(2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione.

Pomalidomide contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{13}H_{11}N_3O_4$, calculated on the anhydrous basis.

Category. Anticancer.

CAUTION — Pomalidomide is cytotoxic; extra care required to prevent inhaling particles and exposing the skin to it.

Description. A Pale yellow to yellow colour powder.

Identification

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

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 reference solution.

Tests

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 80 volumes of *acetonitrile* and 20 volumes of *water*.

Test solution. Dissolve 25 mg of the substance under examination in the solvent and dilute to 50.0 ml with the solvent mixture.

Reference solution. A 0.005 per cent w/v solution of *pomalidomide IPRS* in the 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 × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Kromasil C18),
- column temperature: 25°,
- mobile phase: A. 0.1 per cent v/v solution of orthophosphoric acid in water,
  B. a mixture of 40 volumes of *water* and 60 volumes of *acetonitrile*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 5 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	65	35
2	65	35
22	40	60

40	20	80
41	65	35
50	65	35

Name	Relative retention time	Correction factor
Pomalidomide impurity B[1]	0.18	1.91
Pomalidomide impurity A[2]	0.57	2.44
Pomalidomide	1.0	---
Pomalidomide impurity C[3]	1.28	1.39

[1]3-amino-glutarimide hydrochloride,
[2]3-nitrophthalic anhydride,
[3]2-(2,6-dioxopiperidin-3yl)-4-nitro-isoindole-1,3-dione.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0, 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 any peak corresponding to pomalidomide impurity B, pomalidomide impurity A, and pomalidomide impurity C, each of, is not more than 1.5 times the area of the principal peak in the chromatogram obtained with the reference solution (0.15 per cent). the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.1 per cent) and the sum of the 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). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with the reference solution (0.05 per cent).

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

Water (2.3.43). Not more than 1.0 per cent, determined on 0.1 g.

Assay. Determine by liquid chromatography (2.4.14),

Solvent mixture. 80 volumes of *acetonitrile* and 20 volumes of *water*.

Test solution. Dissolve 25 mg of the substance under examination in the solvent mixture and dilute to 50.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 20.0 ml with the solvent mixture.

Reference solution. A 0.0125 per cent w/v solution of *pomalidomide IPRS* in the solvent mixture.

Chromatographic system
- a stainless steel column 25 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Kromasil C18),
- column temperature: 40°,
- mobile phase: A. 0.1 per cent v/v solution of orthophosphoric acid in *water*,
  B. a mixture of 40 volumes of *water* and 60 volumes of *acetonitrile*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 220 nm,
- injection volume: 5 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	65	35
10	30	70
11	30	70
11.1	65	35
16	65	35

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 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 the test solution.

Calculate the content of $C_{13}H_{11}N_3O_4$.

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

Solubility.

Pomalidomide. Soluble in *dimethylsulphoxide*.