Pomalidomide 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.	

Pomalidomide Capsules

Pomalidomide Capsules contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of pomalidomide, $C_{13}H_{11}N_3O_4$.

Usual strengths. 1 mg; 2 mg; 3 mg; 4mg.

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

Identification

A. 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.

B. Disperse a quantity of the mixed contents of the capsules containing 4 mg of pomalidomide in a mixture of 80 volumes of *acetonitrile* and 20 volumes of *water*, with the aid of ultrasound for 10 minutes with intermittent shaking and dilute to 100.0 ml with a mixture of 80 volumes of *acetonitrile* and 20 volumes of *water*. Dilute 1.0 ml of the solution to 20.0 ml with a mixture of 80 volumes of *acetonitrile* and 20 volumes of *water*. When examined in the range of 200 nm to 400 nm (2.4.7), the resulting solution shows maximum at about 226 nm and 238 nm.

Tests

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium: 900 ml of *0.1M hydrochloric acid*,
Speed and time. 50 rpm for 45 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

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

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. A 0.22 per cent w/v solution of *pomalidomide IPRS* in the solvent mixture. Dilute the solution with the dissolution medium to obtain a solution containing 0.00011 per cent w/v solution of pomalidomide.

Chromatographic system
- a stainless steel column 25 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Kromasil),
- column temperature: 25°,
- mobile phase: A. 0.17 per cent w/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: 100 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 tailing factor is not more than 2.0, the relative standard deviation of replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

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

Q. Not less than 60 per cent of the stated amount of $C_{13}H_{11}N_3O_4$.

Related substances. Determine by liquid chromatography (2.4.14).

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

Test solution. Disperse a quantity of mixed contents of capsules containing 10 mg of Pomalidomide in the solvent mixture with the aid of ultrasound for 10 minutes with intermittent shaking and dilute to 50.0 ml with the solvent mixture, filter.

Reference solution. A 0.0001 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),
- column temperature: 25°,
- mobile phase: A. 0.17 per cent w/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: 20 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

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0, the relative standard deviation of 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 secondary peak is not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.5 per cent) and the sum of the areas of all the secondary peaks is not more than 4 times the area of the principal peak in the chromatogram obtained with the reference solution (2.0 per cent).

Uniformity of dosage units. (2.5.4). Comply with the tests stated under Capsules.

Other tests. Comply with the tests stated under Capsules.

Assay. Determine by liquid chromatography (2.4.14).

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

Test solution. Disperse a quantity of the mixed contents of 20 capsules containing 20 mg of Pomalidomide in the solvent mixture with the aid of ultrasound for 10 minutes with intermittent shaking and dilute to 200.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 25.0 ml with the solvent mixture, filter.

Reference solution. A 0.002 per cent w/v solution of *pomalidomide IPRS* in the solvent mixture.

Use the chromatographic system as described under Dissolution, with the following modifications.

– injection volume: 20 µl.

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 $C_{13}H_{11}N_3O_4$ in the capsules.

Storage. Store at a temperature not exceeding 30°.