Adapalene Gel

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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.	

Adapalene Gel

Adapalene Gel contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of adapalene, $C_{28}H_{28}O_3$.

Usual strength. 0.1 per cent w/w

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

pH (2.4.24). 4.0 to 6.0.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 60 volumes of *acetonitrile* and 40 volumes of *tetrahydrofuran*.

Test solution. Disperse a quantity of the gel containing 5 g of Adapalene in 10 ml of *tetrahydrofuran*, with the aid of ultrasound for 10 minutes, add 10 ml of *acetonitrile*, further sonicate for 10 minutes. Cool to room temperature and dilute to 25.0 with *acetonitrile* and filter.

Reference solution (a). Dissolve 25 mg of *adapalene IPRS* in 20 ml of *tetrahydrofuran* with the aid of ultrasound for 10 minutes and dilute to 50.0 with *acetonitrile*. Dilute 4.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 200.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Hypersil BDS C18)
- column temperature: 40°,
- mobile phase: A. a mixture of 43 volumes of *acetonitrile*, 36 volumes of *tetrahydrofuran*, 21 volumes of *water*, and 0.02 volume of *trifluoroacetic acid*.

  B. a mixture of equal volumes of a buffer solution prepared by dissolving 6.8 g of *potassium dihydrogen orthophosphate* in 1000 ml *water*, adjusted to pH 3.5 with *orthophosphoric acid* and mobile phase A.
- flow rate: 1 ml per minute,
- spectrophotometer set at 235 nm,
- injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	0	100
4	0	100
30	55	45
65	55	45
68	0	100
80	0	100

Name	Relative retention time
Adapalene related compound A[1*]	0.5
Adapalene	1.0
Adapalene related compound B[2*]	1.3

[*]Process impurity included for identification only and not included in the calculation of total degradation products,
[1]Methyl 6-bromo-2-naphthoate,
[2]Methyl 6-[3-adamant-1-yl)-4-methoxyphenyl]-2-naphthoate.

Inject reference solution (a) and (b). The test is not valid unless the tailing factor is not more than 2.0 in the chromatogram obtained with reference solution (a) and the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (b).

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any other secondary peak is not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent) and the sum of areas of all the secondary peaks is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent). Ignore any peak with an area less than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 percent).

Other tests. Comply with the tests stated under Gels.

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of the gel containing 2 g of Adapalene in 25 ml of *tetrahydrofuran* with the aid of ultrasound, add 25 ml of *acetonitrile*, and further sonicate for 20 minutes. Cool to room temperature and dilute to 100.0 with the mobile phase and filter.

Reference solution. Dissolve 25 mg of *adapalene IPRS* in 1 ml of *tetrahydrofuran*, with the aid of ultrasound, dilute to 100.0 with the mobile phase. Dilute 2.0 ml of the solution to 25.0 ml with the mobile phase.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Hypersil BDS C18)
- mobile phase: a mixture of 43 volumes of *acetonitrile,* 36 volumes of *tetrahydrofuran*, 21 volumes of *water*, and 0.02 volume of *trifluoroacetic acid,*
- flow rate: 1 ml per minute,
- spectrophotometer set at 235 nm,
- injection volume: 20 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 $C_{28}H_{28}O_3$ in the gel.

Microbial contamination (2.2.9). Total aerobic viable count is not more than 10^2 CFU per g and total combined molds and yeast count is not more than 10^1 CFU per g. 1 g is free from Escherichia coli, Salmonella species, Staphylococcus aureus and Pseudomonas aeruginosa.

Storage. Store at a temperature not exceeding 30º. Do not freeze.