Adapalene

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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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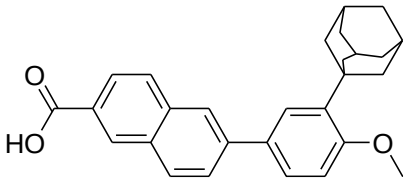
Adapalene



$C_{28}H_{28}O_3$ Mol. Wt. 412.5

Adapalene is 6-(4-Methoxy-3-tricyclo[3.3.1.1^{3,7}]dec-1-ylphenyl)naphthalene-2-carboxylic acid.

Adapalene contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{28}H_{28}O_3$, calculated on the dried basis.

Category. Topical retinoid.

Description. A white or almost white powder.

Identification

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

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

Appearance of solution. A 1.0 per cent w/v solution in *tetrahydrofuran* is clear (2.4.1) and not more intensely coloured than reference solution BYS6 (2.4.1).

Related substances. Determine by liquid chromatography (2.4.14).

Solvent Mixture. 20 volumes of *tetrahydrofuran,* 37 volumes of *acetonitrile* and 43 volumes of *water*.

Test solution. Dissolve 40.0 mg of the substance under examination in 10 ml of *tetrahydrofuran,* add 7 ml of the solvent mixture and dilute to 20.0 ml with *tetrahydrofuran*.

Reference solution (a). Dissolve 20 mg of *adapalene IPRS* in 5 ml of *tetrahydrofuran* and dilute to 10.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with *tetrahydrofuran.* Dilute 1.0 ml of the solution to 100.0 with the solvent mixture.

Reference solution (b). Dissolve 2.4 mg of *adapalene impurity C IPRS* in 2 ml of *tetrahydrofuran* and dilute to 20.0 with *tetrahydrofuran*. Dilute 2.0 ml of the solution to 20.0 ml with the solvent mixture. To 2.0 ml of the solution, add 2.0 ml of reference solution (a) and dilute to 20.0 ml with the solvent mixture.

Reference solution (c). Dissolve the contents of a vial of *adapalene for peak identification IPRS* (containing impurities A, C and D) in 0.5 ml of *tetrahydrofuran* and dilute to 1.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with phenyl group bonded to porous silica (5 µm),
- column temperature: 30°,
- mobile phase: A. a 0.1 per cent v/v solution of *glacial acetic acid* in *water*,
  B. a mixture of 65 volumes of *acetonitrile* and 35 volumes of *tetrahydrofuran*,
- a gradient programme using the conditions given below,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 270 nm,
- injection volume: 25 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	50	50
2.5	50	50
40	28	72
42	28	72
42.6	50	50
50	50	50

Name	Relative retention time	Correction factor
Adapalene impurity A[1]	0.3	0.7
Adapalene impurity C[2]	0.9	7.0
Adapalene (Retention time: about 20 minutes)	1.0	---
Adapalene impurity D[3]	1.9	1.4

[1]2,2'-binaphthalene-6,6'-dicarboxylic acid,

[2]1-(2-methoxyphenyl)tricyclo[3.3.1.1^{3,7}]decane,

[3]1.1'-[4.4'-bis(methoxy)biphenyl-3,3'-diyl]bis(tricyclo[3.3.1.1^{3,7}]decane).

Inject reference solution (c) to identify the peaks due to adapalene impurity A, C and D.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to adapalene and adapalene impurity C is not less than 4.5 and the signal-to-noise ratio is not less than 10 for adapalene impurity C peak.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to adapalene impurity A is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent), the area of any peak corresponding to adapalene impurity C is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.15 per cent), the area of any peak corresponding to adapalene impurity D is not more than twice the area of the principal peak in the chromatogram

obtained with reference solution (a) (0.2 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 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 reference solution (a) (0.5 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Sulphated ash (2.3.18). Not more than 0.1 per cent, determined on 1.0 g.

Loss on drying (2.4.19). Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105° for 4 hours.

Assay. Determine by liquid chromatography (2.4.14) as described under Related substances with the following modifications.

Test solution. Dissolve 20.0 mg of the substance under examination in 50 ml of *tetrahydrofuran*, add 35 ml of the solvent mixture and dilute to 100.0 ml with *tetrahydrofuran*. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Reference solution. Dissolve 20.0 mg of *adapalene IPRS* in 50.0 ml of *tetrahydrofuran*, add 35 ml of the solvent mixture and dilute to 100.0 with *tetrahydrofuran*. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Inject the reference solution and the test solution.

Calculate the content of $C_{28}H_{28}O_3$.

Storage. Store protected from moisture, at a temperature not exceeding 30°.

Solubility.

Adapalene. Sparingly soluble in *tetrahydrofuran* and practically insoluble in *water* and *ethanol (95 per cent)*.