Aciclovir Oral Suspension

Published on: 07 February, 2024 **Last date for comments:** 22 March, 2024

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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
First draft published on IPC website for public comments	February 7, 2024
Last date for comments	**March 22, 2024**
Monograph revisions proposed for inclusion in	**IP 2026**
Tentative effective date of monograph revisions	**July, 2026**
Draft revision published on IPC website for public comments	--
Further follow-up action as required.	

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Change **to:** **Aciclovir Oral Suspension**

Acyclovir Oral Suspension

Aciclovir Oral Suspension is a suspension of Aciclovir in a suitable flavoured vehicle.

Aciclovir Oral Suspension contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of aciclovir, $C_8H_{11}N_5O_3$.

Usual strengths. 200 mg per 5 ml; 400 mg per 5 ml.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (a).

Tests

pH (2.4.24). 4.0 to 7.0.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 20 volumes of *dimethyl sulphoxide* and 80 volumes of *water*.

Test solution. Disperse a quantity of the suspension containing 0.5 g of Aciclovir in 20 ml of *dimethyl sulphoxide,* dilute to 100.0 ml with the solvent mixture, filter. Dilute 2.0 ml of the filtrate to 10.0 ml with the solvent mixture.

Reference solution (a). A 0.01 per cent w/v solution of *aciclovir IPRS* in *dimethyl sulphoxide*. Dilute 2.0 ml of the solution to 100.0 ml with the solvent mixture.

Reference solution (b). Dissolve 5 mg of *aciclovir for system suitability A IPRS* in 1 ml of *dimethyl sulfoxide* and dilute to 5 ml with *water*.

Reference solution (c). Dissolve the content of a vial of *aciclovir for impurity C identification IPRS* in 200 µl of *dimethyl sulfoxide* and dilute to 1 ml with *water*.

Reference solution (d). Dissolve the content of a vial of *aciclovir for impurity G identification IPRS* in 1 ml of reference solution (b).

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Supelcosil LC-18-DB),
- mobile phase: A. a mixture of 99 volumes of a buffer solution prepared by dissolving 3.48 g of *dipotassium hydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 3.1 with *orthophosphoric acid* and 1 volume of *acetonitrile*,
  B. a mixture of 50 volumes of a buffer solution prepared by dissolving 3.48 g of *dipotassium hydrogen orthophosphate* in 1000 ml of *water,* adjusted to pH 2.5 with *orthophosphoric acid* and 50 volumes of *acetonitrile*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
5	100	0
27	80	20
40	80	20
40.1	100	0
50	100	0

Name	Relative retention time	Correction factor
Aciclovir impurity B[1]	0.4	---
Aciclovir impurity C[2]	0.9	2.2
Aciclovir (Retention time: about 13 minutes)	1.0	---
Aciclovir impurity K[3]	2.5	---
Aciclovir impurity G[4]	2.6	---

[1]2-amino-1,7-dihydro-6*H*-purin-6-one (guanine),
[2]2-amino-7-[(2-hydroxyethoxy)methyl]-1,7-dihydro-6Hpurin- e-one,
[3]2,2'-(methylenediazanediyl)bis[9-[(2-hydroxyethoxy) methyl]-1,9-dihydro-6H-purin-6-one],
[4]2-[(2-acetamido-6-oxo-1,6-dihydro-9H-purin-9-yl)methoxy]ethyl acetate.

Inject reference solution (c) and (d) to identify the peak due to aciclovir impurity C and peaks due to acyclovir impurity B, G, and K respectively.

Inject reference solution (c) and (d). The test is not valid unless the resolution between the peaks due to aciclovir impurity C and aciclovir is not less than 1.5 in the chromatogram obtained with reference solution (c) and between the peaks due to aciclovir impurity K and aciclovir impurity G is not less than 1.5 in the chromatogram obtained with reference solution (d).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution the area of any peak corresponding to aciclovir impurity B is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 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) (0.2 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 reference solution (a) (2.0 per cent). Ignore any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Other tests. Comply with the tests stated under Oral Liquids.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. 20 volumes of *dimethyl sulphoxide* and 80 volumes of *water*.

Test solution. Disperse a quantity of the suspension containing 25 mg of Aciclovir in 10 ml of *dimethyl sulphoxide* and dilute to 25.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (a). Dissolve 25 mg of *aciclovir IPRS* in 10 ml of *dimethyl sulphoxide* and dilute to 25.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (b). Dissolve the content of a vial of *aciclovir for impurity C identification IPRS* in 200 µl of *dimethyl sulfoxide* and dilute to 1 ml with *water (NOTE- Prepare the solution immediately before use).*

Use chromatographic system as described under Related substances.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to aciclovir impurity C and aciclovir is not less than 1.5.

Inject reference solution (a) and the test solution.

Determine the weight per ml of the oral solution (2.4.29) and calculate the content of $C_8H_{11}N_5O_3$.

Storage. Store protected from light, at a temperature not exceeding 30°. Do not freeze.