Aciclovir Dispersible Tablets

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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.	

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Change **to:** **Aciclovir Dispersible Tablets**

Acyclovir Dispersible Tablets

Aciclovir Dispersible Tablets contain Aciclovir in a suitable dispersible base.

Aciclovir Dispersible Tablets contain 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; 400 mg; 800 mg.

Identification

A. To a quantity of the powdered tablets containing 0.1 g of Aciclovir, add 60 ml of *0.1 M sodium hydroxide* and disperse with the aid of ultrasound for 15 minutes. Add a sufficient quantity of *0.1 M sodium hydroxide* to produce 100 ml, mix well and filter. To 15 ml of the filtrate, add 50 ml of *water* and 5.8 ml of *2 M hydrochloric acid* and dilute 100 ml with *water*. Dilute 5 ml of the solution to 50 ml with *0.1 M hydrochloric acid* and mix well. When examined the solution in the range 230 nm to 350 nm (2.4.7), shows an absorption maximum at about 255 nm and a broad shoulder at about 274 nm.

B. 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

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

Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, suitably diluted with the dissolution medium if necessary, at the maximum at about 255 nm (2.4.7). Calculate the content of $C_8H_{11}N_5O_3$ in the medium from the absorbance obtained from a solution of known concentration of *aciclovir IPRS* in the dissolution medium.

Q. Not less than 80 per cent of the stated amount of $C_8H_{11}N_5O_3$.

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 powdered tablets containing 25 mg of Aciclovir in *dimethyl sulphoxide* with the aid of mechanical shaker for 15 minutes and dilute to 10.0 ml with *dimethyl sulphoxide.* Dilute 2.0 ml of the solution to 5.0 ml with the solvent mixture.

Reference solution (a). A 0.001 per cent w/v solution of *aciclovir IPRS* in *dimethyl sulphoxide.* Dilute 2.0 ml of the solution to 10.0 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) *(NOTE- Prepare the solution immediately before use)*.

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 aciclovir 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 Tablets.

Assay. Determine by liquid chromatography (2.4.14).

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

Test solution. Weigh and powder 20 tablets. Disperse a quantity of powder containing 25 mg of Aciclovir in *dimethyl sulphoxide* with the aid of mechanical shaker and dilute to 10.0 ml with *dimethyl sulphoxide*. Dilute 1.0 ml of the solution to 25.0 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 *acyclovir 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.

Calculate the content of $C_8H_{11}N_5O_3$ in the tablets.

Labelling. The label states that the tablets should be dispersed in water immediately before use.