Aciclovir Intravenous Infusion

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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 Infusion**

Aciclovir Infusion; Acyclovir Infusion; Acyclovir Sodium Infusion

Aciclovir Infusion is a sterile solution containing aciclovir sodium, prepared by dissolving Aciclovir Sodium for Infusion with suitable diluent as recommended by the manufacturer.

The infusion complies with the requirements stated under Parenteral Preparation and with the following requirements.

Tests

Bacterial endotoxins (2.2.3). Not more than 4.37 Endotoxin Units per ml of acyclovir, determined on 25 mg per ml solution of Aciclovir.

Storage. The constituted solution should be used immediately after preparation but, in any case, within the period recommended by the manufacturer.

Aciclovir Sodium for Infusion

Aciclovir Sodium for Infusion is a sterile material, prepared from Aciclovir with the aid of a suitable alkali. It may contain excipients. It is supplied in a sealed container.

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

The contents of the sealed container comply with the requirements stated under Parenteral Preparations (Powders for Injections) and with the following requirements.

Usual strength. 500 mg per vial.

Description. A white or almost white, crystalline powder.

Identification

A. Dissolve a quantity of the powder in *0.1M hydrochloric acid* and dilute with the same solvent to obtain 0.0015 per cent w/v solution of Aciclovir. 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 the reference solution (a).

C. It gives reaction (A) of sodium salts (2.3.1).

Tests

Appearance of solution. Dissolve a quantity of powder in sufficient *water for injections* to produce a solution containing 2.5 per cent w/v solution of Aciclovir (solution A). The solution is not more opalescent than opalescence standard OS2 (2.4.1), and not more intensely coloured than reference solution BYS5 (2.4.1).

pH (2.4.24). 10.7 to 11.7, determined in solution A.

Related substances. Determine by liquid chromatography (2.4.14).

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

Test solution. Dissolve a quantity of the powder containing 25 mg of Aciclovir in 10.0 ml of *dimethyl sulphoxide* and dilute to 25.0 ml with the solvent mixture, filter.

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).

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 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).

Assay. Determine by liquid chromatography (2.4.14).

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

Test solution. Mix the content of 10 containers. Disperse a quantity of powder 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.

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

Labelling. The label states the quantity of aciclovir sodium in the sealed container in terms of the equivalent amount of Aciclovir.