**Aciclovir Dispersible Tablets**

**General Notices**

Dispensable Aciclovir Tablets

*Details for the public consultation of this monograph are as follows:*

<table>
<thead>
<tr>
<th>EAG/Panel/Working Party</th>
<th>Medicinal Chemicals 1</th>
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</thead>
<tbody>
<tr>
<td>Contact Details</td>
<td><a href="mailto:helen.coms@mhra.gov.uk">helen.coms@mhra.gov.uk</a></td>
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<tr>
<td>Deadline for Comment</td>
<td>31 March 2021</td>
</tr>
<tr>
<td>Target Publication Date (subject to change)</td>
<td>BP 2022</td>
</tr>
<tr>
<td>Notes</td>
<td>Revised monograph</td>
</tr>
</tbody>
</table>

If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required.

**Related substances**: Specified impurities, solutions (3) to (5), system suitability, and correction factor revised as per European Pharmacopoeia monograph.

**Action and use**

Purine nucleoside analogue; antiviral (herpesviruses).

**DEFINITION**

Aciclovir Dispersible Tablets contain Aciclovir in a suitable dispersible basis.

*The tablets comply with the requirements stated under Tablets and with the following requirements.*

**Content of aciclovir, C₈H₁₁N₅O₃**

95.0 to 105.0% of the stated amount.

**IDENTIFICATION**

A. To a quantity of the powdered tablets containing 0.1 g of Aciclovir add 60 mL of 0.1mol sodium hydroxide and disperse with the aid of ultrasound for 15 minutes. Add sufficient 0.1mol sodium hydroxide to produce 100 mL, mix well and filter. To 15 mL of the filtrate add 50 mL of water, 5.8 mL of 2mol hydrochloric acid and sufficient water to produce 100 mL. To 5 mL of the resulting solution add sufficient...
0.1M hydrochloric acid to produce 50 mL and mix well. The light absorption, Appendix II B, in the range 230 to 350 nm of the final solution exhibits a maximum at 255 nm and a broad shoulder at about 274 nm.

B. In the Assay, the chromatogram obtained with solution (1) shows a principal peak with the same retention time as the peak due to aciclovir in the chromatogram obtained with solution (2).

**TESTS**

**Related substances**

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in a solvent mixture of 1 volume of dimethyl sulfoxide and 4 volumes of water unless otherwise indicated.

1. Shake a quantity of the powdered tablets containing 25 mg of Aciclovir with 10 mL of dimethyl sulfoxide for 15 minutes and filter. Dilute 2 volumes of the filtrate to 5 volumes with the solvent mixture.

2. Dilute 1 volume of solution (1) to 100 volumes and further dilute 1 volume of this solution to 5 volumes.

3. Dissolve 5 mg of aciclovir for system suitability A EPCRS in 1 mL of dimethyl sulfoxide and dilute to 5 mL with water. Prepare the solution immediately before use.

4. Dissolve the contents of a vial of aciclovir for impurity C identification EPCRS in 200 µL of dimethyl sulfoxide and dilute to 1 mL with water.

5. Dissolve the contents of a vial of aciclovir for impurity G identification EPCRS in 1 mL of solution (3).

**CHROMATOGRAPHIC CONDITIONS**

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with octadecylsilica silica gel for chromatography (5 µm) (Supelcosil LC-18-DB is suitable).

(b) Use gradient elution and the mobile phase described below.

(c) Use a flow rate of 1 mL per minute.

(d) Use an ambient column temperature.

(e) Use a detection wavelength of 254 nm.

(f) Inject 10 µL of each solution.

**MOBILE PHASE**

*Phosphate buffer solution pH 3.1* Dissolve 3.48 g of dipotassium hydrogen orthophosphate in 1000 mL of water and adjust to pH 3.1 with orthophosphoric acid.

*Phosphate buffer solution pH 2.5* Dissolve 3.48 g of dipotassium hydrogen orthophosphate in 1000 mL of water and adjust to pH 2.5 with orthophosphoric acid.

**Mobile phase A** 1 volume of acetonitrile and 99 volumes of phosphate buffer solution pH 3.1.

**Mobile phase B** 50 volumes of acetonitrile and 50 volumes of phosphate buffer solution pH 2.5.

<table>
<thead>
<tr>
<th>Time (Minutes)</th>
<th>Mobile phase A (% v/v)</th>
<th>Mobile phase B (% v/v)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>100</td>
<td>0</td>
<td>isocratic</td>
</tr>
<tr>
<td>5-27</td>
<td>100→80</td>
<td>0→20</td>
<td>linear gradient</td>
</tr>
<tr>
<td>Time (Minutes)</td>
<td>Mobile phase A (% v/v)</td>
<td>Mobile phase B (% v/v)</td>
<td>Comment</td>
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<td>---------------</td>
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<td>------------------------</td>
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</tr>
<tr>
<td>27-40</td>
<td>80</td>
<td>20</td>
<td>isocratic</td>
</tr>
<tr>
<td>40-46</td>
<td>80→100</td>
<td>20→0</td>
<td>linear gradient</td>
</tr>
</tbody>
</table>

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (4), the *resolution* between the peaks due to impurity C and aciclovir is at least 1.5.

in the chromatogram obtained with solution (5), the *resolution* between the peaks due to impurity K and impurity G is at least 1.5.

LIMITS

Identify any peak in solution (1) corresponding to impurity C using the chromatogram obtained with solution (4) and multiply the area of this peak by a correction factor of 2.2.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity B is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than 10 times the area of the principal peak in the chromatogram obtained with solution (2) (2.0%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

Weigh and finely powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in a mixture of 1 volume of *dimethyl sulfoxide* and 4 volumes of *water*, unless otherwise indicated.

1. Shake a quantity of the powdered tablets containing 25 mg of Aciclovir in 10 mL of *dimethyl sulfoxide* and filter. Dilute 2 volumes of the filtrate to 5 volumes and further dilute 1 volume to 10 volumes.

2. Dissolve 25 mg of aciclovir BPCS in 10 mL of *dimethyl sulfoxide*. Dilute 2 volumes to 5 volumes and further dilute 1 volume to 10 volumes.

3. Dissolve the contents of a vial of aciclovir for peak identification 1 EPCS (containing impurities C and I) in 200 µL of *dimethyl sulfoxide* and dilute to 1.0 mL with *water*. Prepare the solution immediately before use.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.
SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between the peaks due to impurity C and aciclovir is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of C₈H₁₁N₅O₃ in the tablets using the declared content of C₈H₁₁N₅O₃ in aciclovir BPCS.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Aciclovir.