Sodium Fusidate Tablets

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

<table>
<thead>
<tr>
<th>EAG ABS</th>
<th>Antibiotics</th>
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</thead>
<tbody>
<tr>
<td>Contact Details</td>
<td><a href="mailto:stephen.maddocks@mhra.gov.uk">stephen.maddocks@mhra.gov.uk</a></td>
</tr>
<tr>
<td></td>
<td><a href="mailto:peter.crowley@mhra.gov.uk">peter.crowley@mhra.gov.uk</a></td>
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<tr>
<td>Deadline for Comment</td>
<td>31st March 2020</td>
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<tr>
<td>Target Publication</td>
<td>BP 2021</td>
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<tr>
<td>Notes: New Monograph</td>
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</tbody>
</table>

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

Action and use

Antibacterial

**DEFINITION**

Sodium Fusidate Tablets contain Sodium Fusidate.

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

Content of sodium fusidate, C$_{31}$H$_{47}$NaO$_6$

95.0 to 105.0% of the stated amount.

**IDENTIFICATION**

To a quantity of powdered tablets containing the equivalent of 0.1 g of anhydrous fusidic acid add 5 mL of water and extract with three 10-mL quantities of dichloromethane. Wash the combined extracts with two 10-mL quantities of water, dry with anhydrous sodium sulfate, evaporate to dryness and dissolve the residue in 1 mL of dichloromethane. The infrared absorption spectrum of the resulting solution, Appendix II A, is concordant with the reference spectrum of fusidic acid (RS 166).

**TESTS**

Related substances

Carry out the method for liquid chromatography, Appendix III D, using the following solutions in Solution A.

Solution A 10 volumes of methanol, 40 volumes of a 0.5 % w/v solution of orthophosphoric acid and 50 volumes of acetonitrile.
(1) Disperse a quantity of the powdered tablets corresponding to 26 mg of Sodium fusidate in 8 mL of ethanol (70%) and filter (0.7 µm Whatman GFC filter is appropriate). Dilute to 10 mL with ethanol (70%).

(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase.

(3) Dissolve the contents of a vial of fusidic acid impurity mixture EPCRS in 1.0 mL of the solvent mixture.

(4) Dissolve 2 mg of fusidic acid for peak identification EPCRS in the solvent mixture and dilute to 1.0 mL.

(5) Dilute 1 volume of solution (2) to 10 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm x 4.6 mm) packed with end capped octadecylsilyl silica gel for chromatography (3.5 µm) (Waters Symmetry C18 is suitable).

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

(c) Use a flow rate of 1.0 mL/min.

(d) Use a column temperature of 30 °.

(e) Use a detection wavelength of 235 nm.

(f) Inject 20 µL of each solution.

MOBILE PHASE

**mobile phase A** 20 volumes of methanol, 40 volumes of a 0.05M solution of orthophosphoric acid and 40 volumes of acetonitrile.

**mobile phase B** 20 volumes of methanol, 10 volumes of a 0.05M solution of orthophosphoric acid and 70 volumes of acetonitrile.

<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>0-3</td>
<td>100</td>
<td>0</td>
<td>isocratic</td>
</tr>
<tr>
<td>3-28</td>
<td>100→0</td>
<td>0→100</td>
<td>linear gradient</td>
</tr>
<tr>
<td>28-33</td>
<td>0</td>
<td>100</td>
<td>isocratic</td>
</tr>
<tr>
<td>33-34</td>
<td>0→100</td>
<td>100→0</td>
<td>linear gradient</td>
</tr>
<tr>
<td>34-40</td>
<td>100</td>
<td>0</td>
<td>re-equilibration</td>
</tr>
</tbody>
</table>

When the chromatograms are recorded using the prescribed conditions, the relative retentions with reference to Fusidic acid (retention time about 18 minutes) are: impurity A, about 0.4; impurity B, about 0.5; impurity C, about 0.6; impurity D, about 0.63; impurity N about 0.65; impurity F, about 0.7; impurity G, about 0.8; impurity H, about 0.9; impurity I, about 0.96; impurity K, about 1.18; impurity L, about 1.23 and impurity M, about 1.4.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the resolution between the peaks due to impurities G and H is at-least 1.5.

LIMITS

Identify any peaks due to impurities C, D, F, G, I, K, L and M using the relative retention times and the chromatograms obtained with solutions (3) and (4).

Multiply the area of any peak corresponding to: impurities C and D by a factor of 0.7; impurity F by a factor of 0.3, and impurities I and K by a factor of 0.6.
In the chromatogram obtained with solution (1):

the area of any peak due to impurity M is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (1.0%);

the area of any peak due to impurity G is not greater than 0.9 times the area of the principal peak in the chromatogram obtained with solution (2) (0.9%);

the area of any peak due to impurity K is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.6%);

the area of any peak due to impurity C, D, F, I or L is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%);

the area of any peak due to impurity B is not greater than 0.4 times the area of the principal peak in the chromatogram obtained with solution (2) (0.4%);

the area of any peak due to impurity A is not greater than 0.3 times the area of the principal peak in the chromatogram obtained with solution (2) (0.3%);

the area of any other secondary peak is not greater than twice the area of the principal peak in the chromatogram obtained with solution (5) (0.2%);

the sum of the areas of any secondary peaks is not greater than 4.0 times the area of the principal peak in the chromatogram obtained with solution (2) (4.0%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.1%).

**ASSAY**

Weigh and powder 20 tablets. Carry out the method for liquid chromatography, Appendix III D, using the following solutions in Solution A under Related substances.

1. Disperse a quantity of the powdered tablets corresponding to 260 mg of sodium fusidate in 80 mL of ethanol (70%), dilute to 100 mL with ethanol (70%) and filter (0.7 µm Whatman GFC filter is appropriate). Dilute a suitable volume of the filtrate to produce a final solution containing 0.026% w/v sodium fusidate.

2. 0.03% w/v of diethanolamine fusidate BPCRS in the mobile phase.

**CHROMATOGRAPHIC CONDITIONS**

The chromatographic conditions under Related substances may be used with the following gradient program.

<table>
<thead>
<tr>
<th>MOBILE PHASE</th>
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<tbody>
<tr>
<td>Time (Minutes)</td>
</tr>
<tr>
<td>0-3</td>
</tr>
<tr>
<td>3-28</td>
</tr>
<tr>
<td>28-29</td>
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<tr>
<td>29-35</td>
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</tbody>
</table>
DETERMINATION OF CONTENT

Calculate the content of C_{31}H_{47}NaO_{6} in the Tablets using the declared content of C_{31}H_{48}O_{6} in diethanolamine fusidate BPCRS. Each mg of C_{31}H_{48}O_{6} is equivalent to 1.04 mg of C_{31}H_{47}NaO_{6}.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of Sodium Fusidate.

IMPURITIES

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