Folic Acid Oral Solution

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

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<th>EAG MC3</th>
<th>Medicinal Chemicals 3</th>
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<tr>
<td>Contact Details</td>
<td><a href="mailto:adrian.evans@mhra.gov.uk">adrian.evans@mhra.gov.uk</a></td>
</tr>
<tr>
<td></td>
<td><a href="mailto:hina.ashraf@mhra.gov.uk">hina.ashraf@mhra.gov.uk</a></td>
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Action and use

Vitamin B component.

DEFINITION

Folic Acid Oral Solution is a solution of Folic Acid in a suitable vehicle.

The oral solution complies with the requirements stated under Oral Liquids and with the following requirements.

Content of folic acid, \( \text{C}_{19}\text{H}_{19}\text{O}_{6} \)

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for thin-layer chromatography, Appendix III A, using the following solutions.

1. Dilute a quantity of the oral solution containing 20 mg of Folic Acid with sufficient of a mixture of 2 volumes of 13.5M ammonia and 9 volumes of methanol to produce 100 mL.

2. 0.02% w/v of folic acid BPCRS in a mixture of 2 volumes of 13.5M ammonia and 9 volumes of methanol.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating silica gel \( G \)

(b) Use the mobile phase as described below.

(c) Apply 2 µL of each solution.

(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine immediately under ultraviolet light (365 nm).

MOBILE PHASE

20 volumes of 13.5M ammonium and 20 volumes of propan-1-ol and 60 volumes of ethanol (96%).

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (2) shows two clearly separated spots.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) is similar in position, colour and size to that in the chromatogram obtained with solution (2).

B. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

ACIDITY

pH, 5.5 to 6.5, Appendix V L.

Related substances

Carry out the method for liquid chromatography, Appendix III D, using the following solutions protected from light.

(1) Dilute a quantity of the oral solution containing 2.5 mg of folic acid with 2.5 mL of a 2.86% w/v solution of sodium carbonate and dilute to 50 mL with the mobile phase. Dilute 10 mL of this solution to 25 mL of the mobile phase.

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

(3) To 1 mL of a solution containing 0.004% w/v of folic acid impurity A EPCRS and 0.0012% of folic acid impurity D EPCRS in a solution of 2.86% w/v solution of sodium carbonate, dilute to 5mL with the same solution, then to 100 mL with the mobile phase.

(4) Mix 1 mL of a solution of 0.02% w/v of folic acid impurity D EPCRS in 2.86% w/v solution of sodium carbonate with 1 mL of solution containing 0.002% of folic acid BPCRS in the mobile phase and dilute to 10 mL with the mobile phase.

(5) Dilute 1 volumes of solution (2) to 10 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm x 4 mm) packed with octylsilyl silica gel for chromatography (5µm) (Merck Lichrospher 100 RP 8 is suitable).

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

(c) Use a flow rate of 0.6 mL per minute.

(d) Use a ambient column temperature.
(e) Use a detection wavelength of 280 nm.

(f) Inject 25 µL of each solution.

(g) For solution (1) allow the chromatography to run for three times the retention time of folic acid.

MOBILE PHASE

10 volumes of methanol and 90 volumes of a solution containing 1.116 w/v% of potassium dihydrogen phosphate and 0.55% w/v of dipotassium hydrogen phosphate.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4), the resolution between the peaks due to folic acid and impurity D is at least 4.0.

Under the prescribed conditions, the relative retention time with reference to folic acid (retention time = about 8.5 min) are: impurity A, about 0.5; impurity D, about 1.3.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (2%);

the area of any peak corresponding to impurity D is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.6%);

the area of any secondary peak is not greater than two times 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 3 times the principal peak in the chromatogram obtained with solution (2) (3%).

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

ASSAY

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

(1) Dilute a quantity of the oral solution containing 2.5mg of folic acid with 2.5 mL of a 2.86% w/v solution of sodium carbonate and dilute to 125 mL with the mobile phase.

(2) Dilute 25 mg of folic acid BPCS with 25 mL of a 2.86% w/v solution of sodium carbonate and dilute to 500 mL with the mobile phase. Dilute 10 mL of this solution to 25 mL of the mobile phase.

(3) Mix 1 mL of a solution of 0.02% w/v of folic acid impurity D EPCS in 2.86% w/v solution of sodium carbonate with 1 mL of solution containing 0.002% of folic acid BPCS in the mobile phase and dilute to 10 mL with the mobile phase.
CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under related substances may be used, with an injection volume of 10 µL.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the resolution between the peaks due to folic acid and impurity D is at least 4.0.

DETERMINATION OF CONTENT

Calculate the content of C_{19}H_{19}N_{7}O_{6}, in the oral solution from the chromatograms obtained and using the declared content of C_{19}H_{19}N_{7}O_{6}, in folic acid BPCRS.

IMPURITIES

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