UK Public Assessment Report

Folic Acid 5 mg Tablets

PL 20416/0290

Crescent Pharma Limited
Lay Summary
Folic Acid 5 mg Tablets
(folic acid)

This is a summary of the Public Assessment Report (PAR) for Folic Acid 5 mg Tablets (PL 20416/0290). It explains how Folic Acid 5 mg Tablets were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Folic Acid 5 mg Tablets.

For practical information about using Folic Acid 5 mg Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Folic Acid 5 mg Tablets and what are they used for?
This medicine is the same as Folic Acid Tablets BP 5 mg, which are already authorised (PL 17496/0017). The company that makes Folic Acid Tablets BP 5 mg, Dalkeith Laboratories Limited, has agreed that its scientific data can be used as a basis for the grant of an identical licence for Folic Acid 5 mg Tablets (PL 20416/0290).

Folic Acid 5 mg Tablets are used for the treatment of certain types of anaemia. They are also used to help prevent the breakdown of red blood cells, which can occur as a result of renal (kidney) dialysis or certain other conditions.

How do Folic Acid 5 mg Tablets work?
Folic Acid 5 mg Tablets contain the active substance folic acid, which is necessary for the normal production of blood cells. Folic acid is the chemical name for Vitamin B9.

How are Folic Acid 5 mg Tablets used?
Folic Acid 5 mg Tablets should be swallowed with a drink of water. The prescribing doctor will decide on how many tablets should be taken. The usual dose in adults, the elderly and children over 1 year of age, is one tablet daily for up to 4 months. After this period the prescribing doctor may reduce the dose to one tablet every few days.

Please read Section 3 of the package leaflet for further information.

Folic Acid 5 mg Tablets can only be obtained with a prescription.

What benefits of Folic Acid 5 mg Tablets have been shown in studies?
Folic Acid 5 mg Tablets are considered identical to the previously granted marketing authorisation for Folic Acid Tablets BP 5 mg (PL 17496/0017), with the same benefits and risks. No new studies have been provided for Folic Acid 5 mg Tablets (PL 20416/0290) but reference is made to the studies for Folic Acid Tablets BP 5 mg (PL 17496/0017).

What are the possible side effects from Folic Acid 5 mg Tablets?
Like all medicines, this medicine can cause side effects, although not everybody gets them.

For information about side effects that may occur with using Folic Acid 5 mg Tablets, please refer to the package leaflet or the Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency website.
Why are Folic Acid 5 mg Tablets approved?
No new or unexpected safety concerns arose from this application. It was, therefore, considered that the benefits of Folic Acid 5 mg Tablets outweigh the risks, and the grant of this marketing authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Folic Acid 5 mg Tablets?
A Risk Management Plan (RMP) has been developed to ensure that Folic Acid 5 mg Tablets are used as safely as possible. Based on this plan, safety information has been included in the SmPC and the package leaflet for Folic Acid 5 mg Tablets, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients and healthcare professionals will be monitored and reviewed continuously as well.

Other information about Folic Acid 5 mg Tablets
The marketing authorisation was granted in the UK on 16 April 2015.

For more information about taking Folic Acid 5 mg Tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in June 2015.

The full PAR for Folic Acid 5 mg Tablets follows this summary.
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I Introduction

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation to Crescent Pharma Limited for the medicinal product Folic Acid 5 mg Tablets (PL 20416/0290) on 16 April 2015. Folic acid is necessary for the normal production and maturation of blood cells, and is used in the treatment of nutritional megaloblastic anaemias, e.g. following gastrectomy and the megaloblastic anaemia of pregnancy. It may also be used prophylactically in chronic haemolytic states or in renal dialysis.

Folic Acid 5 mg Tablets are a prescription-only medicine (legal status POM).

This application was submitted as an abridged simple application, according to Article 10c of Directive 2001/83/EC, as amended. The application cross-refers, and claims to be identical, to Folic Acid Tablets BP 5 mg, which was granted to Dalkeith Laboratories Limited on 09 August 2000 (PL 17496/0017).

This medicinal product contains the active substance folic acid.

No new data have been submitted and none are required for this simple application, as the data are identical to that of the previously granted, cross-referred product.
II Quality aspects

II.1 Introduction
This is a simple, piggyback (informed consent) application for Folic Acid 5 mg Tablets submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to Folic Acid Tablets BP 5mg (PL 17496/0017). The current application is considered valid.

Folic Acid 5 mg Tablets contain the active substance folic acid at a strength of 5 mg. The excipients present in the tablets are lactose, pregelatinised maize starch, sucrose and stearic acid. The qualitative and quantitative composition of these excipients is identical to that of the reference product.

The tablets are packed into:
- High-density polypropylene (HDPP) tablet containers with low-density polyethylene (LDPE) lids in pack sizes of 50, 100, 500 or 1000 tablets
- Aluminium/polyvinyl chloride/polyvinylidene chloride (Al/PVC/PVdC) blisters enclosed in an outer carton, in pack sizes of 28 or 56 tablets, or
- Al/PVC/PVdC blisters enclosed in an outer carton – “Burgopackaging” format, containing 28 tablets.

This packaging is identical to that of the cross-reference product.

II.2 Drug Substance
Folic acid
The drug substance specification is identical to that of the cross-reference product and is acceptable.

II.3 Medicinal Product
Pharmaceutical development
A quality expert statement was provided by an appropriately qualified person, confirming that the chemical and pharmaceutical data supporting the application are identical to those of the cross-reference product.

Manufacture of the product
The proposed manufacturing sites are consistent with those registered for the cross-reference product. Evidence of Good Manufacturing Practice (GMP) compliance has been provided, which is identical to that of the cross-reference product.

The proposed composition is identical to that of the reference product and is acceptable.

The proposed manufacturing process is identical to that of the cross-reference product and is acceptable.
None of the excipients are sourced from animal or human origin, except for lactose. A declaration has been provided by the suppliers of lactose stating that the lactose is of animal origin and is derived from milk that has been collected from healthy animals in the same way as milk for human consumption. This satisfies the requirements of the Note for Guidance (NfG) on the reduction of transmission of spongiform encephalopathy (EMA/410/01 rev.3), which is acceptable.

**Finished Product Specification**
The proposed finished product specification is identical to that of the cross-reference product and is acceptable.

**Stability of the product**
The proposed shelf-life for Folic Acid 5 mg Tablets is 36 months. This shelf life is identical to that of the cross-reference product.

**II.4 Discussion on chemical, pharmaceutical and biological aspects**
The quality data for this application are consistent with those previously assessed for the marketing authorisation for Folic Acid Tablets BP 5mg (PL 17496/0017) and, as such, have been judged to be satisfactory. The grant of a marketing authorisation is recommended.

**III Non-clinical aspects**
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data has been supplied and none are required.

The grant of a marketing authorisation is recommended.

**IV Clinical aspects**
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

**Risk Management Plan (RMP)**
The applicant has submitted an RMP, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Folic Acid 5 mg Tablets.

A summary of safety concerns, as approved in the RMP, are listed below:
### Summary table of safety concerns

<table>
<thead>
<tr>
<th>Important identified risks</th>
<th>Hypersensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Use in patients with Addisonian pernicious anaemia (Vitamin B12 deficiency)</td>
</tr>
<tr>
<td></td>
<td>Use in patients with malignant disease</td>
</tr>
<tr>
<td></td>
<td>Use in patients with rare hereditary problems of fructose or galactose intolerance, the LAPP lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Important potential risks</th>
<th>Drug interactions with anticonvulsants or lithium</th>
</tr>
</thead>
</table>

| Missing information | None identified |

### Summary table of risk minimisation measures

<table>
<thead>
<tr>
<th>Important identified risks</th>
<th>Summary of Routine Risk Minimisation Activities</th>
<th>Summary of Additional Risk Minimisation Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity</td>
<td>Routine pharmacovigilance activities, Contraindication, Hypersensitivity to folic acid or any of the ingredients, included in SmPC Section 4.3</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Adverse event, Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnoea, and anaphylactic reactions (including shock), included in SmPC Section 4.8</td>
<td></td>
</tr>
<tr>
<td>Use in Addisonian pernicious anaemia (Vitamin B12 deficiency)</td>
<td>Routine pharmacovigilance activities, Contraindication, Addisonian pernicious anaemia (Vitamin B12 deficiency), included in SmPC Section 4.3 Warning, Should not be used in the treatment of pernicious anaemia or other vitamin B12 deficiency states until adequate amounts of hydroxocobalamin have been administered parenterally (may precipitate subacute combined degeneration of the spinal cord), included in SmPC Section 4.4</td>
<td>N/A</td>
</tr>
<tr>
<td>Use in malignant disease</td>
<td>Routine pharmacovigilance activities, Contraindication, malignant disease, included in SmPC Section 4.3 Warning, The treatment of megaloblastic anaemias of malignant disease should be approached individually and folic acid tablets are unlikely to be the most suitable agent, included in SmPC Section 4.4</td>
<td>N/A</td>
</tr>
</tbody>
</table>
The grant of a marketing authorisation is recommended.

V  User consultation
A letter from the MA Holder of the cross-reference product, Dalkeith Laboratories Limited, has been provided allowing Crescent Pharma Limited to refer to the user test report submitted for Folic Acid Tablets BP 5mg (PL 17496/0017). The proposed leaflet mock-up for Folic Acid 5 mg Tablets has the same layout as the leaflet currently registered for Folic Acid Tablets BP 5mg (PL 17496/0017). This is acceptable.

VI  Overall conclusion, benefit/risk assessment and recommendation
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. The benefit-risk assessment is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), package leaflet and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference product. In accordance with Directive 2012/84/EU, the current approved UK versions
of the SmPC and package leaflet text for this product are available on the Medicines and Healthcare products Regulatory Agency website.

The currently approved labelling text is listed below:
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BLISTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Folic Acid 5 mg Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains Folic Acid 5 mg.

3. LIST OF EXCIPIENTS

Also contains lactose and sucrose (see leaflet for further information).

4. PHARMACEUTICAL FORM AND CONTENTS

28 tablets
56 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use as directed by the doctor.
Please read the leaflet provided before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C. Store in the original package.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Crescent Pharma Ltd.
Polhampton Lane, Overton,
Hampshire, RG25 3ED, UK.
12. MARKETING AUTHORISATION NUMBER(S)

PL 20416/0290

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Folic Acid 5 mg Tablets

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

1. NAME OF THE MEDICINAL PRODUCT

Folic Acid 5 mg Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Crescent Pharma Ltd

3. EXPIRY DATE

EXP

4. BATCH NUMBER

BN

5. OTHER
PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

TABLET CONTAINER

1. NAME OF THE MEDICINAL PRODUCT

Folic Acid 5 mg Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains Folic Acid 5 mg.

3. LIST OF EXCIPIENTS

Also contains lactose and sucrose.

4. PHARMACEUTICAL FORM AND CONTENTS

50 tablets
100 tablets
500 tablets
1000 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use as directed by the doctor.
Please read the leaflet provided before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25°C. Keep the container tightly closed.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE
11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Crescent Pharma Ltd,
Pollhampton Lane, Overton,
Hampshire, RG25 3ED, UK.

12. MARKETING AUTHORISATION NUMBER(S)

PL 20416/0290

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE


16. INFORMATION IN BRAILLE

Folic Acid 5 mg Tablets
# Annex - Table of content of the PAR update
Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

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<th>Scope</th>
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<th>Date of end of procedure</th>
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<th>Assessment report attached Y/N (version)</th>
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