Ascorbic Acid 50 mg Tablets
Ascorbic Acid 100 mg Tablets
Ascorbic Acid 200 mg Tablets
Ascorbic Acid 500 mg Tablets

PL 20416/0286
PL 20416/0287
PL 20416/0288
PL 20416/0289

UKPAR

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lay Summary</td>
<td>2</td>
</tr>
<tr>
<td>Scientific Discussion</td>
<td>4</td>
</tr>
<tr>
<td>Steps Taken for Assessment</td>
<td>11</td>
</tr>
<tr>
<td>Steps Taken After Initial Authorisation</td>
<td>12</td>
</tr>
<tr>
<td>Summary of Product Characteristics</td>
<td>13</td>
</tr>
<tr>
<td>Patient Information Leaflet</td>
<td>14</td>
</tr>
<tr>
<td>Labelling</td>
<td>15</td>
</tr>
</tbody>
</table>
LAY SUMMARY

This is a summary of the public assessment report (PAR) for Ascorbic Acid 50 mg Tablets, Ascorbic Acid 100 mg Tablets, Ascorbic Acid 200 mg Tablets and Ascorbic Acid 500 mg Tablets (PL 20416/0286-0289). It explains how Ascorbic Acid 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 Ascorbic Acid Tablets.

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

What are Ascorbic Acid Tablets and what are they used for?

These medicines are the same as Ascorbic Acid 50mg, 100mg, 200mg and 500mg Tablets BP, which are already authorised to Dalkeith Laboratories Ltd. Dalkeith Laboratories Ltd has agreed that these Marketing Authorisations can be used as a basis for the grant of identical Marketing Authorisations for Ascorbic Acid Tablets (informed consent).

Ascorbic acid is the chemical name for vitamin C. Ascorbic Acid 50 mg Tablets and Ascorbic Acid 100 mg Tablets are used to treat patients with scurvy or they can be used by people who are at risk of vitamin C deficiency. Ascorbic Acid 200 mg Tablets and Ascorbic Acid 500 mg Tablets are used to treat vitamin C deficiency including the prevention and treatment of scurvy.

How do Ascorbic Acid Tablets work?
The tablets can be used to supplement the amount of vitamin C in the diet and increase the levels in the body.

How are Ascorbic Acid Tablets used?
For the 50 mg tablets the usual dose for the treatment of scurvy is 2 tablets, three times a day,
and the usual dose to prevent possible vitamin C deficiency is 1 tablet, twice a day. For the 100 mg tablets the usual dose for the treatment of scurvy is 1 tablet, three times a day, and the usual dose to prevent possible vitamin C deficiency is 1 tablet per day. For the 200 mg tablets the usual dose is 1 or 2 tablets a day in divided doses for adults and children over 12 and ½ to 1 tablet a day for children aged 4 to 12. For the 500 mg tablets the usual dose is 1 to 5 tablets a day in divided doses for adults and children over 12 and ½ to 2½ tablets a day.

If the tablets are given by a doctor they may suggest a different dose.

The tablets can be obtained without a prescription.

**What benefits of Ascorbic Acid Tablets have been shown in studies?**
Ascorbic Acid Tablets are considered to be identical to previously authorised medicinal products, with the same benefits and risks. Therefore, no new studies have been provided for Ascorbic Acid Tablets but reference is made to the Marketing Authorisations owned by Dalkeith Laboratories Ltd.

**What are the possible side effects from Ascorbic Acid Tablets?**
Like all medicines ascorbic acid can cause side effects, although not everybody gets them. Diarrhoea and passing water (urinating) frequently can occur if patients take a dose that is too high. Patients with glucose-6-phosphate dehydrogenase deficiency taking this medicine may develop a type of anaemia (symptoms include headache, tiredness, shortness of breath, jaundice).

For the full list of all side effects reported with Ascorbic Acid Tablets, see section 4 of the package leaflet. For the full list of restrictions, see the package leaflet.

**Why are Ascorbic Acid Tablets approved?**
The MHRA decided that the benefits of Ascorbic Acid Tablets are greater than their risks and recommended that they be approved for use.

**What measures are being taken to ensure the safe and effective use of Ascorbic Acid Tablets?**
A Risk Management Plan has been developed to ensure Ascorbic Acid Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Ascorbic Acid 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/healthcare professionals will be monitored and reviewed continuously.

**Other information about Ascorbic Acid Tablets**
Marketing Authorisations were granted in the UK on 17 April 2015.

This summary was last updated in June 2015.

The full PAR for Ascorbic Acid Tablets follows this summary.
ASCORBIC ACID 50 MG TABLETS
ASCORBIC ACID 100 MG TABLETS
ASCORBIC ACID 200 MG TABLETS
ASCORBIC ACID 500 MG TABLETS

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction Page 5
Pharmaceutical Assessment Page 6
Non-clinical Assessment Page 8
Clinical Assessment Page 9
Overall Conclusion and Benefit/Risk Assessment Page 10
INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Crescent Pharma Limited Marketing Authorisations for the medicinal products Ascorbic Acid 50 mg Tablets, Ascorbic Acid 100 mg Tablets, Ascorbic Acid 200 mg Tablets and Ascorbic Acid 500 mg Tablets (PL 20416/0286-0289) on 17 April 2015. These are General Sales List (GSL) medicines.

Ascorbic Acid 50 mg and 100 mg Tablets are indicated for the treatment of scurvy and for prophylactic use in cases where vitamin C deficiency might be expected to occur. Ascorbic Acid 200 mg and 500 mg Tablets are indicated for use in treating vitamin C deficiency including the treatment and prevention of scurvy.

These applications were submitted as abridged applications, according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to the Marketing Authorisations owned by Dalkeith Laboratories Ltd for Ascorbic Acid 50mg and 100mg Tablets BP (PL 17496/0012-0013; authorised on 23 October 2000), Ascorbic Acid 200mg Tablets BP (PL 17496/0014; authorised on 18 September 2000) and Ascorbic Acid 500mg Tablets BP (PL 17496/0015; authorised on 8 January 2001). These cross reference products refer to Marketing Authorisations owned by Sussex Pharmaceutical Ltd for Ascorbic Acid Tablets BP 50mg and 100mg (PL 05544/5900R-5901R; authorised on 20 April 1989), Ascorbic Acid Tablets BP 200mg (PL 05544/5902R; authorised on 21 April 1989) and Ascorbic Acid Tablets BP 500mg (PL 05544/0025; authorised on 7 March 1984).

Ascorbic acid is essential for the synthesis of collagen and intercellular material involved in conversion of folic acid to folinic acid.

Ascorbic acid coupled with dehydroascorbic acid, to which it is reversibly oxidised, has a variety of functions in cellular oxidation processes. Vitamin C is required in several important hydroxylations, including the conversion of proline to hydroxyproline (and thus in collagen formation e.g. for intercellular substances during wound healing); the formation of the neurotransmitters 5-hydroxytryptamine from tryptophan and noradrenaline from dopamine; and the biosynthesis of carnitine from lysine and methionine. Vitamin C appears to have an important role in metal ion metabolism, including the gastrointestinal absorption of iron and its transport between plasma and storage organs. There is also evidence that vitamin C is required for normal leukocyte function and that it participates in the detoxification of numerous foreign substances by the hepatic microsomal system.

Deficiency in vitamin C leads to scurvy, which may be manifested by weakness, fatigue, dyspnoea, aching bones, perifollicular hyperkeratoses, petechiae and ecchymoses, swelling and bleeding of gums, hypochromic anaemia and other haemopoietic disorders, together with reduced resistance to infection (and impaired wound healing).

No new data were submitted nor were necessary for these simple applications, as the data are identical to those provided for the previously authorised products.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 20416/0286-0289

PROPRIETARY NAME: Ascorbic Acid 50 mg Tablets, Ascorbic Acid 100 mg Tablets, Ascorbic Acid 200 mg Tablets and Ascorbic Acid 500 mg Tablets

ACTIVE: Ascorbic acid

COMPANY NAME: Crescent Pharma Limited

E.C. ARTICLE: Article 10c of Directive 2001/83/EC, as amended

LEGAL STATUS: GSL

1. INTRODUCTION
These are abridged applications for Ascorbic Acid 50 mg Tablets, Ascorbic Acid 100 mg Tablets, Ascorbic Acid 200 mg Tablets and Ascorbic Acid 500 mg, submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Ascorbic Acid 50mg, 100mg, 200mg and 500mg Tablets BP (PL 17496/0012-0015). The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Names
The names of the products are acceptable.

2.2 Strengths, pharmaceutical form, route of administration, container and pack sizes
The tablets have the same strengths, form and route of administration as the reference products.

The tablets are packaged in polypropylene containers with low density polyethylene caps.

Pack sizes of 28, 100, 500 and 1000 tablets are authorised for the 50 mg and 100 mg tablets; pack sizes of 28, 100 and 500 tablets are authorised for the 200 mg tablets; and pack sizes of 28, 50, 100 and 500 tablets are authorised for the 500 mg tablets. Not all pack sizes may be marketed. The products have a shelf life of 3 years.

2.3 Legal status
The tablets have General Sales List status.

2.4 Marketing Authorisation Holder
The Marketing Authorisation Holder is Crescent Pharma Limited, Units 3 & 4, Quidhampton Business Units, Polhampton Lane, Overton, Hants RG25 3ED, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

2.5 Manufacturers
The manufacturing sites are identical to those of the reference products and are acceptable.
2.6 Qualitative and quantitative composition
The products’ compositions are identical to those of their respective reference products and are acceptable.

2.7 Manufacturing process
The manufacturing process is identical to that of the reference products and is acceptable.

2.8 Finished product/shelf-life specification
The finished product specifications are identical to those of the reference products and are acceptable.

2.9 Drug substance specification
The drug substance specification is identical to that of the reference products and is acceptable.

2.10 TSE Compliance
The stearic acid and magnesium stearate used in the product are confirmed to be of vegetable origin and the lactose monohydrate is sourced from milk from animals suitable for human consumption, in accordance with current requirements.

2.11 Bioequivalence
No bioequivalence data are required to support these simple abridged applications because the products are identical to products that are already authorised.

3. EXPERT REPORTS
These are acceptable.

4. PRODUCT NAMES AND APPEARANCE
The names of the products are acceptable. The appearance of the tablets is in line with the reference products and is acceptable.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The Summaries of Product Characteristics are identical to those of the reference products, apart from the necessary administrative updates to reflect the change in Marketing Authorisations, and are acceptable.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
The PIL and labels are identical to those of the reference products, apart from the necessary administrative updates to reflect the change in Marketing Authorisations, and are acceptable.

7. CONCLUSION
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA).

The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

The Risk Management Plan is considered adequate. Routine risk minimisation is provided through the Summaries of Product Characteristics and the Patient Information Leaflets and this is sufficient.

The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with the data previously assessed for the Marketing Authorisations for Ascorbic Acid 50mg, 100mg, 200mg and 500mg Tablets BP (PL 17496/0012-0015) and, as such, have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for this type of application.

EFFICACY
The products are identical to those previously authorised; therefore, no efficacy data are needed.

SAFETY
No new or unexpected safety concerns arose from these applications.

PRODUCT LITERATURE
The SmPCs, PILs and labels are identical to those previously approved, apart from the necessary administrative updates to reflect the change in Marketing Authorisation.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s products are identical to the reference products. The benefit/risk balance is therefore considered to be positive.
STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Marketing Authorisation Applications on 17 October 2014.
2. Following standard checks and communication with the applicant the MHRA considered the applications valid on 19 November 2014.
3. Following assessment of the applications the MHRA requested further information relating to the dossiers on 17 February 2015.
4. The applicant responded to the MHRA’s requests, providing further information on 16 March 2015.
5. The applications were granted on 17 April 2015.
## STEPS TAKEN AFTER INITIAL AUTHORISATION

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<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
</tr>
</thead>
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SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
LABELLING

The following text is the approved label text for Ascorbic Acid 50 mg Tablets. This label text is identical to the text for Ascorbic Acid 100 mg Tablets, Ascorbic Acid 200 mg Tablets and Ascorbic Acid 500 mg Tablets, with the exception of differences in the product names, Marketing Authorisation numbers, strengths, instructions for use, method of administration and pack sizes. No label mock-ups have been provided. In accordance with medicines legislation, the products shall not be marketed in the UK until approval of the label mock-ups has been obtained.
PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING TABLET CONTAINER

1. NAME OF THE MEDICINAL PRODUCT

Ascorbic Acid 50 mg Tablets

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains Ascorbic Acid 50 mg.

3. LIST OF EXCIPIENTS

Also contains sucrose and lactose.

4. PHARMACEUTICAL FORM AND CONTENTS

28 tablets
100 tablets
500 tablets
1000 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Tablets for oral use. The tablets may be sucked, chewed or swallowed with a drink of water. 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 and store in the original package in order to protect from light and moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE
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<tbody>
<tr>
<td><strong>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Crescent Pharma Ltd, Polhampion Lane, Overton, Hampshire, RG25 3ED, UK.</td>
</tr>
<tr>
<td><strong>12. MARKETING AUTHORISATION NUMBER(S)</strong></td>
<td>PL 20416/0286</td>
</tr>
<tr>
<td><strong>13. BATCH NUMBER</strong></td>
<td>BN</td>
</tr>
<tr>
<td><strong>14. GENERAL CLASSIFICATION FOR SUPPLY</strong></td>
<td>GSL</td>
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<tr>
<td><strong>15. INSTRUCTIONS ON USE</strong></td>
<td>Dose: Adults, the elderly and children: For the treatment of scurvy: Take 2 tablets three times a day. To prevent vitamin C deficiency: Take 1 tablet twice a day.</td>
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<td><strong>16. INFORMATION IN BRAILLE</strong></td>
<td>Ascorbic Acid 50 mg Tablets</td>
</tr>
</tbody>
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