Vitamin B Compound Tablets
(nicotinamide, thiamine hydrochloride and riboflavin)

PL 20416/0281

UKPAR

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LAY SUMMARY

Vitamin B Compound Tablets
(nicotinamide, thiamine hydrochloride and riboflavin)

This is a summary of the Public Assessment Report (PAR) for Vitamin B Compound Tablets (PL 20416/0281). It explains how the application for Vitamin B Compound Tablets was assessed and its authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use Vitamin B Compound Tablets.

For practical information about using Vitamin B Compound Tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Vitamin B Compound Tablets and what are they used for?
This medicine is the same as Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited), which are already authorised in the UK. The licence holder (Dalkeith Laboratories Limited) for Vitamin B Compound Tablets BPC has agreed that its own scientific data can be used as a basis for the grant of an identical licence for Vitamin B Compound Tablets (informed consent).

Vitamin B Compound Tablets are used, in adults, the elderly and children over 12 years, to prevent Vitamin B deficiencies, as a nutritional supplement in the elderly and to help recovery after illness or surgery.

How do Vitamin B Compound Tablets work?
Vitamin B Compound Tablets contain the active ingredients nicotinamide, thiamine hydrochloride and riboflavin (Vitamins B₃, B₁ and B₂). Vitamins are essential nutrients for the functioning of the body.

How are Vitamin B Compound Tablets used?
Vitamin B Compound Tablets are taken by mouth. The tablets should be swallowed whole with water.

If this medicine is prescribed by a doctor, he/she will decide what dose the patient needs to take. The patient should always take the tablets exactly as the doctor has advised. The dose will be on the pharmacist’s label. If unsure, the patient should ask your doctor or pharmacist.

The patient should take the tablets for as long as advised unless he/she experiences any problems. In that case, the patient should check with the doctor.

The usual doses are as follows:

Adults, the elderly and children over 12 years:
One to three tablets daily.

The tablets are not recommended for children under 12.

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

Vitamin B Compound Tablets can be obtained without a prescription.
What benefits of Vitamin B Compound Tablets have been shown in studies?
The application for Vitamin B Compound Tablets is considered to be identical to the previously authorised licence for Vitamin B Compound Tablets BPC (PL 17496/0002), with the same benefits and risks. So, no new studies have been provided for Vitamin B Compound Tablets. However, reference is made to the studies for Vitamin B Compound Tablets BPC (PL 17496/0002).

What are the possible side effects from Vitamin B Compound Tablets?
Like all medicines, Vitamin B Compound Tablets can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Vitamin B Compound Tablets, see section 4 of the package leaflet.

For the full list of restrictions, see the package leaflet.

Why are Vitamin B Compound Tablets approved?
No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Vitamin B Compound Tablets outweigh their risks; and the grant of a Marketing Authorisation was recommended.

What measures are being taken to ensure the safe and effective use of Vitamin B Compound Tablets?
A Risk Management Plan has been developed to ensure that Vitamin B Compound 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 Vitamin B Compound 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/reviewed continuously.

Other information about Vitamin B Compound Tablets.
A Marketing Authorisation was granted in the UK on 14 August 2015.

The full PAR for Vitamin B Compound Tablets follows this summary.

For more information about treatment with Vitamin B Compound Tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in September 2015.
Vitamin B Compound Tablets
(nicotinamide, thiamine hydrochloride and riboflavin)

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Crescent Pharma Limited a Marketing Authorisation for the medicinal product Vitamin B Compound Tablets (PL 20416/0281) on 14 August 2015. The product is a pharmacy (P) medicine indicated:

- for the prophylaxis of Vitamin B deficiencies;
- as a nutritional supplement in the elderly;
- as an aid to convalescence after illness or surgery.

The application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited) which was granted in the UK on 23 March 2000. Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited) cross-refers to Vitamin B Compound Tablets BPC (PL 05544/5927R; Sussex Pharmaceuticals Limited), which was granted in August 1989 following the review of PLR 05544/5927. PLR 05544/5927 was granted in March 1984 following a Change of Ownership procedure of PLR 01378/5950, which was first granted in the UK to UAC/Seward in September 1975.

Vitamin B Compound Tablets contain the active ingredients, nicotinamide, thiamine (as thiamine hydrochloride) and riboflavin (Vitamins B3, B1 and B2). Thiamine is phosphorylated in the body and acts as a co-enzyme in carbohydrate metabolism. Riboflavin is also phosphorylated to give co-enzymes in the respiratory chain and oxidative phosphorylation. Nicotinamide is also active in the respiratory chain.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to those of the previously granted cross-reference product.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 20416/0281

PROPRIETARY NAME(S): Vitamin B Compound Tablets

ACTIVE(S):
- Nicotinamide
- Thiamine hydrochloride
- Riboflavin

COMPANY NAME: Crescent Pharma Limited

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

LEGAL STATUS: P

1. INTRODUCTION
This is an informed consent application for Vitamin B Compound Tablets (PL 20416/0281) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited) which was granted a Marketing Authorisation in the UK on 23 March 2000. Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited) cross-refers to Vitamin B Compound Tablets BPC (PL 05544/5927R; Sussex Pharmaceuticals Limited), which was originally granted a Product Licence of Right in September 1975. The application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1. Name
The proposed name of the product is Vitamin B Compound Tablets. The product has been named in line with current requirements.

2.2. Strength, pharmaceutical form, route of administration, container and pack sizes
Each tablet contains 15 mg nicotinamide, 1 mg thiamine hydrochloride and 1 mg riboflavin. The product is packaged in polypropylene or high-density polyethylene tablet containers, in pack sizes of 28, 100 and 1000 tablets.

The proposed shelf life for the product is 3 years, with the special storage conditions ‘Do not store above 25°C’. Store in the original container. Keep the container tightly closed.’

The packaging, proposed shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

2.3. Legal status
The product is available as a pharmacy (P) medicine.

2.4. Marketing Authorisation Holder/Contact Persons/Company
Crescent Pharma Limited, Units 3 & 4, Quidhampton Business Units, Polhampton Lane, Overton, Hants RG25 3ED.

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

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.
2.6. Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7. Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch sizes are stated.

2.8. Finished product/shelf-life specification
The proposed finished product specification is consistent with the details registered for the cross-reference product.

2.9. Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10. TSE Compliance
With the exception of lactose, none of the excipients contain materials of animal or human origin. The supplier of lactose monohydrate has confirmed that the milk used in the production of lactose is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the supplier has confirmed that no ruminant material other than calf rennet is used during the production of lactose.

This is consistent with the cross-reference product.

2.11. Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula and utilises the same processes as the reference product Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited).

3. EXPERT REPORT
The applicant cross-refers to the data for Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited) to which this application is claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See Section 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The proposed SmPC is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The PIL has been prepared in line with the details registered for the cross-reference product.

User-testing of the PIL for Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited) has previously been accepted based on the bridging report provided making reference to the successful user-testing of the PIL for Folic Acid Tablets 5mg (PL 17496/0017; Dalkeith Laboratories Limited) as the ‘parent PIL’
User-testing of the PIL for Vitamin B Compound Tablets (PL 20416/0281) has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited) as the ‘parent PIL’.

**Carton and label**
The proposed text is consistent with that for the cross-reference product. The Marketing Authorisation Holder has committed to submitting mock-ups to the relevant regulatory authorities for approval before marketing the product.

7. **CONCLUSION**
The data submitted with the application is acceptable. The grant of a Marketing Authorisation is recommended.
NON-CLINICAL ASSESSMENT

As this is an informed consent application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

The grant of a Marketing Authorisation is recommended.
CLINICAL ASSESSMENT

As this is an informed consent application 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.

An acceptable Risk Management Plan (RMP) has been submitted. A summary of safety concerns is listed in the following table.

<table>
<thead>
<tr>
<th>Summary of safety concerns</th>
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</thead>
<tbody>
<tr>
<td><strong>Important identified risks</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Important potential risks</strong></td>
</tr>
<tr>
<td><strong>Missing information</strong></td>
</tr>
</tbody>
</table>

Routine risk minimisation is provided through the Summary of Product Characteristics and the Patient Information Leaflet and this is sufficient.

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

QUALITY
The data for this application is consistent with those previously assessed for the cross-reference product 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
This application is identical to the previously granted licence for Vitamin B Compound Tablets BPC (PL 17496/0002; Dalkeith Laboratories Limited).

SAFETY
No new safety data were supplied or required for this application. Nicotinamide, thiamine hydrochloride and riboflavin have well-established safety profiles. No new or unexpected safety concerns arose from this application.

PRODUCT LITERATURE
The SmPC and PIL are satisfactory, and consistent with those for the cross-reference product. The labelling text complies with statutory requirements and is satisfactory.

BENEFIT/RISK ASSESSMENT
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. Extensive clinical experience with nicotinamide, thiamine hydrochloride and riboflavin is considered to have demonstrated the therapeutic value of the compounds. The benefit/risk assessment is, therefore, considered to be positive.
Vitamin B Compound Tablets
(nicotinamide, thiamine hydrochloride and riboflavin)

PL 20416/0281

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Marketing Authorisation application on 17 December 2014.
2. Following standard checks and communication with the applicant the MHRA considered the application valid on 24 December 2014.
3. Following assessment of the application the MHRA requested further information relating to the dossier on 18 March 2015 and 16 July 2015.
4. The applicant responded to the MHRA’s request, providing further information on the 22 June 2015 and 21 July 2015.
5. The application was granted on 14 August 2015.
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 Marketing Authorisation Holder has submitted a text version only and has committed to submitting mock-up livery to the relevant regulatory authorities for approval before packs are marketed.

<table>
<thead>
<tr>
<th>Crescent Pharma logo</th>
<th>Each tablet contains Nicotinamide 15 mg, Thiamine Hydrochloride 1 mg, Riboflavin 1 mg. Also contains lactose. Please read the leaflet provided before use.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vitamin B Compound Tablets</strong>&lt;br&gt;(Nicotinamide, thiamine, riboflavin)</td>
<td><strong>For oral use. Swallow with a drink of water.</strong>&lt;br&gt;<strong>Adults, the elderly and children over 12 years:</strong> Take one to three tablets daily, or as instructed by your doctor. Not recommended for use in children under 12 years.&lt;br&gt;<strong>KEEP OUT OF THE SIGHT AND REACH OF CHILDREN</strong>&lt;br&gt;Do not store above 25°C. Store in the original container. Keep the container tightly closed.</td>
</tr>
<tr>
<td>28/100/1000* Tablets</td>
<td><strong>Product Licence holder:</strong>&lt;br&gt;Crescent Pharma Ltd.&lt;br&gt;Polhampton Lane, Overtown,&lt;br&gt;Hampshire, RG26 3ED, UK&lt;br&gt;BAR CODE (if aplic) BN: ) To be&lt;br&gt;EXP: ) overprinted&lt;br&gt;PL 20416/0281</td>
</tr>
</tbody>
</table>

Include **Vitamin B Compound Tablets** in Braille for patient packs if there is no accompanying outer carton.

* = relevant pack size will be included
## Outer carton text (for use where relevant with tablet container)

<table>
<thead>
<tr>
<th>Vitamin B Compound Tablets</th>
<th>For patient packs Vitamin B Compound Tablets to appear in braille also on front of carton</th>
</tr>
</thead>
<tbody>
<tr>
<td>28/100/1000* Tablets</td>
<td></td>
</tr>
</tbody>
</table>

**For patient packs Vitamin B Compound Tablets to appear in braille also on front of carton**

| Crescent Pharma logo | Each tablet contains Nicotinamide 15 mg, Thiamine Hydrochloride 1 mg & Riboflavin 1 mg. Also contains lactose. Please read the leaflet provided before use. For oral use. Swallow with a drink of water. Adults, the elderly and children over 12 years: Take one to three tablets daily, or as instructed by your doctor. Not recommended for use in children under 12 years. KEEP OUT OF THE SIGHT AND REACH OF CHILDREN Do not store above 25°C. Store in the original container. Keep the container tightly closed. Product Licence holder: Crescent Pharma Ltd, Polhampton Lane, Overton, Hampshire, RG25 3ED, UK PL 20416/0281 | 28/100/1000* Tablets |
|----------------------|----------------------------------------------------------------------------------------|
| Vitamin B Compound Tablets | 28/100/1000* Tablets |
| Crescent Pharma logo | Include an area 70 x 35mm for dispensary label (unless is OTC pack) |

**BAR CODE**

BN: } To be EXP: } overprinted

* = relevant pack size will be included