Colica Colic Granules

NR 01175/0383

UKPAR

TABLE OF CONTENTS

Lay summary                           Page 2

Scientific discussion                  Page 3

Steps taken for assessment             Page 13

Summary of Product Characteristics    Page 14

Product Information Leaflet           Page 15

Labelling                             Page 16
The Medicines and Healthcare Products Regulatory Agency (MHRA) granted A Nelson & Co Limited a Homeopathic Marketing Authorisation for the homeopathic medicinal product Colica Colic Granules (Homeopathic Marketing Authorisation number: NR 01175/0383) on 18 July 2014. This product is available without prescription and can be bought from pharmacies and other outlets.

Colica Colic Granules is a homeopathic medicinal product used within the homeopathic tradition for the symptomatic relief of colic in babies over one month of age. These indications are based on published *Materia medica* references. The active ingredients are *Citrullus colocynthis* 30C and *Dioscorea villosa* 30C.

No new or unexpected safety concerns arose from this application and it was, therefore, decided that a Homeopathic Marketing Authorisation could be granted.
COLICA COLIC GRANULES

NR 01175/0383

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction ........................................ Page 4

Pharmaceutical assessment ......................... Page 5

Non-clinical assessment ........................... Page 8

Clinical assessment ................................ Page 9

Overall conclusions and risk assessment ........ Page 12
INTRODUCTION

The MHRA granted a Homeopathic Marketing Authorisation for the homeopathic medicinal product Colica Colic Granules (NR 01175/0383) on 18 July 2014. This product is on the General Sales List (GSL).

The application was submitted in accordance with Article 16.2 of Directive 2001/83/EC, as amended, under the National Rules Authorisation Scheme. Colica Colic Granules contain the homeopathic stocks *Citrullus colocynthis* 30C and *Dioscorea villosa* 30C. It is used for the symptomatic relief of colic in babies over one month of age.

*Citrullus colocynthis* and *Dioscorea villosa* are established homeopathic remedies and their traditional use in homoeopathy is well documented. In support of this application to authorise Colica Colic Granules published *Materia medica* references for the individual stocks have been provided.
PHARMACEUTICAL ASSESSMENT

HERBAL SUBSTANCE: CITRULLUS COLOCYNTHIS

Scientific/Latin name: Citrullus colocynthis L.
Plant family: Cucurbitaceae

Manufacture
The Citrullus colocynthis plants are cultivated in Germany. The ripe fruit are harvested by hand in the autumn and then cleaned, dried and peeled. The fruit’s seed are also removed.

The herbal substance is produced in line with the Guideline on Good Agricultural and Collection Practice (GACP).

Control of the Herbal Substance
The Citrullus colocynthis is described in the German Homeopathic Pharmacopoeia (GHP) and its quality is satisfactorily controlled in line with the GHP monograph.

Container Closure System
Satisfactory details of the container closure system are provided.

Stability
Confirmation is given that the herbal substance will be tested prior to being used to make the homeopathic stock.

ACTIVE INGREDIENT
(HOMEOPATHIC STOCK): CITRULLUS COLOCYNTHIS MOTHER TINCTURE

Extraction solvent: Ethanol 86 % (m/m)
General properties: A light yellow to yellow liquid

Manufacture
A satisfactory description of the manufacturing process of the homeopathic stock has been provided. The homeopathic stock is prepared according to method 4a of the GHP. The in-process controls are satisfactorily detailed. Certificates of Analysis for the ethanol and purified water used in the manufacture of the homeopathic stock have been provided.

Control of Homeopathic Stock
A satisfactory specification with appropriate tests and limits has been provided for the homeopathic stock.

Appropriate analytical procedures are used to control the quality of the homeopathic stock. As the analytical methods are compendial additional validation is not required.

Certificates of Analysis have been provided for batches of the homeopathic stock, demonstrating satisfactory compliance with the proposed specifications.
Container Closure System
Satisfactory details of the container closure system are provided.

Stability
Stability studies have been carried out and the results support the proposed shelf life of the homeopathic stock.

HERBAL SUBSTANCE: **Dioscorea villosa**

Scientific/Latin name: *Dioscorea villosa* L.
Plant family: Dioscoreaceae

Manufacture
The *Dioscorea villosa* plants are hand collected from the wild in the USA. The plants are collected during Spring, after flowering, and immediately conserved in ethanol.

The herbal substance is produced in line with the Guideline on Good Agricultural and Collection Practice (GACP) without use of fertilisers, pesticides, herbicides or growth promoters.

Control of the Herbal Substance
The *Dioscorea villosa* is described in the GHP and its quality is satisfactorily controlled in line with the GHP monograph.

Container Closure System
Satisfactory details of the container closure system are provided.

Stability
A shelf-life for the herbal substance is not necessary because it is collected and used in the fresh state and is tested according to the monograph for the herbal drug in the GHP prior to tincture manufacture.

ACTIVE INGREDIENT
(HOMEOPATHIC STOCK): **Dioscorea villosa** Mother Tincture

Extraction solvent: Ethanol 86 % (m/m)
General properties: A yellow liquid with a faintly aromatic odour

Manufacture
A satisfactory description of the manufacturing process of the homeopathic stock has been provided. The homeopathic stock is prepared according to method 3a of the GHP. The in-process controls are satisfactorily detailed. Certificates of Analysis for the ethanol and purified water used in the manufacture of the homeopathic stock have been provided.
Control of Homeopathic Stock
A satisfactory specification with appropriate tests and limits has been provided for the homeopathic stock.

Appropriate analytical procedures are used to control the quality of the homeopathic stock. As the analytical methods are in accordance with the GHP monograph or the European Pharmacopoeia (Ph Eur) additional validation is not required.

Certificates of Analysis have been provided for batches of the homeopathic stock, demonstrating satisfactory compliance with the proposed specifications.

Container Closure System
Satisfactory details of the container closure system are provided.

Stability
Stability studies have been carried out and the results support the proposed shelf life of the homeopathic stock.

HOMEOPATHIC MEDICINAL PRODUCT: COLICA COLIC GRANULES

Description and Composition
The oral granules contain *Citrullus colocynthis* 30C and *Dioscorea villosa* 30C and the pharmaceutical excipients lactose, xylitol, maize starch and pregelatinised maize starch. The excipients are considered to be compatible with the homeopathic stocks.

The excipients used comply with their respective Ph Eur monographs. Certificates of Analysis for the excipients have been provided by the suppliers.

Manufacture
A flow diagram outlining the various stages of the manufacturing process and the in-process controls is provided.

The critical steps of the process have been validated satisfactorily.

Control
The finished product specification is detailed and the tests and limits used were found to be satisfactory for a product of this nature.

Satisfactory details have been provided on all analytical procedures and these analytical procedures are valid.

Certificates of Analysis have been presented for batches of the drug product demonstrating little inter-batch variation.

Container Closure System
The product is presented in packs of 12 or 24 sachets each containing 300mg of granules. The sachets are made of laminated paper coated with polyethylene and aluminium and are stored in a cardboard carton.
The components of the primary packaging system comply with current legislation relating to materials and articles intended to come into contact with foodstuffs.

**Stability**
Stability studies were conducted under ICH conditions on product batches in the container type proposed for marketing. The results of the stability study support the 3 year shelf for the product when the storage precaution ‘Do not store above 25°C’ is applied.

**Summary of Product Characteristics, Labels and Patient Information Leaflet**
The product literature for this product is pharmaceutically satisfactory.

A user consultation with target patient groups on the PIL has been performed on the basis of a bridging report making reference to Nelsons Colica Colic Granules. The bridging report submitted by the applicant has been found acceptable.

**CONCLUSION**
There are no objections to the granting of a Homeopathic Marketing Authorisation from a quality point of view.
NON-CLINICAL AND CLINICAL SAFETY ASSESSMENT

The safety data which must be submitted by the applicant is set out in Schedule 1A – Part 1 and Part 2 of Statutory Instrument 2006 No.1952 The Medicines for Human Use [National Rules for Homeopathic Products) Regulations 2006. Point 4 of Part 2 states the conditions under which the applicant is not required to provide any data on the safety of the product. In such cases one of the following must apply:

a. The product is intended to be administered orally and is derived from a stock which is commonly present in food.

b. The product is derived from a stock present in a licensed medicinal product (i.e. product has a marketing authorisation, certificate of registration, herbal registration or product licence) and that the product is available via general sales, provided the product has the same degree of dilution and route of administration as the licensed product.

c. The product is derived from a stock diluted to at least $10^{24}$ and is not a material of biological origin.

The applicant has applied to authorise a 30C potency of *Citrullus colocynthis* and a 30C potency of *Dioscorea villosa*, diluted to $10^{60}$. Therefore, criteria c is fulfilled and no further information is required to establish the safety of the stocks to be included in the finished product.

As this product contains the excipient lactose appropriate warnings relating to lactose are included in the SmPC, PIL and product labels.

**CONCLUSION**

There are no objections to the granting of a Homeopathic Marketing Authorisation from a non-clinical point of view.
CLINICAL ASSESSMENT (NON SAFETY)

LEGAL STATUS
General sales list (GSL) status has been applied for and is applicable for the dilutions of *Citrullus colocynthis* 30C and *Dioscorea villosa* 30C to be authorised.

INDICATION
The applicant has proposed the following indication:

“A homeopathic medicinal product used within the homeopathic tradition for the symptomatic relief of colic in babies over one month of age”

This indication is acceptable.

EVIDENCE SUPPORTING THE PROPOSED INDICATION
Schedule 1A Parts 1 and 3 of SI 2006 No. 1952 The Medicines for Human Use (National Rules for Homeopathic Products) Regulations 2006 specifies the data that must be provided to support the use of the product in the indications sought.

The applicant must provide one of the following: published scientific literature, homeopathic provings and/or study reports in relation to the product which is the subject of the application. An evaluation of the data must be provided, including an explanation as to how the data establishes that the product to be authorised has a recognised level of efficacy in the indications sought. The data provided must be sufficient to demonstrate that UK homeopathic practitioners would accept the usage of the product within the homeopathic tradition for the indications sought.

The applicant has provided published homeopathic provings in the form of *Materia Medica* references to support the combination of *Citrullus colocynthis* and *Dioscorea villosa* in the indications sought.

Statements from UK homeopathic practitioners endorsing the use of the product within the UK homeopathic tradition have also been provided. The statements are satisfactory.

CONCLUSION
The applicant has provided published *Materia Medica* references to help demonstrate the use of the individual stocks in the indications sought. An expert statement has been provided to help justify the combination of homeopathic stocks to be used in the indications sought.

There are no objections to the granting of a Homeopathic Marketing Authorisation from a clinical point of view.
OVERALL CONCLUSION AND RISK ASSESSMENT

QUALITY
The quality data submitted with this application are satisfactory.

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

CLINICAL
The applicant has provided published homeopathic provings as supporting evidence to fulfil the requirements for this type of application. These relate to the indications sought and are, therefore, acceptable.

PRODUCT LITERATURE
The SmPC, PIL and labels for the product are satisfactory.

RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified.
COLICA COLIC GRANULES

NR 01175/0383

STEPS TAKEN FOR ASSESSMENT

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received an application under the Homeopathic National Rules Scheme (Article 16.2) on 28 October 2010</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 8 November 2010</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application and a meeting of the Advisory Board on the Registration of Homeopathic products (ABRH) on 15 February 2011 the MHRA requested further information relating to the dossier on 24 February 2011, 14 January 2014 and 20 January 2014</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the dossier on 1 December 2011, 17 January 2014, 31 January 2014, 26 February 2014, 6 March 2014, 1 April 2014, 2 May 2014 and 10 June 2014</td>
</tr>
<tr>
<td>5</td>
<td>A National Rules Marketing Authorisation was granted on 18 July 2014</td>
</tr>
</tbody>
</table>
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.