# 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>3</td>
</tr>
<tr>
<td>Steps taken for assessment</td>
<td>12</td>
</tr>
<tr>
<td>Summary of Product Characteristics</td>
<td></td>
</tr>
<tr>
<td>Product Information Leaflet</td>
<td></td>
</tr>
<tr>
<td>Labelling</td>
<td></td>
</tr>
</tbody>
</table>
ZEROZOLE

PL 18962/0005

UKPAR

LAY SUMMARY

The MHRA today granted Zeroderma Ltd a Marketing Authorisation (licence) for the medicinal product Zerozole (PL 18962/0005). This is a product for sale direct to the general public (GSL).

Zerozole is a bath oil the active ingredients of which have emollient and local anaesthetic properties. It is recommended for the treatment of dry skin conditions including those associated with dermatitis and eczema.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Zerozole outweigh the risks, hence Marketing Authorisation has been granted.
ZEROZOLE

PL 18962/0005

UKPAR

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction Page 4
Pharmaceutical assessment Page 5
Preclinical assessment Page 7
Clinical assessment (including statistical assessment) Page 10
Overall conclusions and risk benefit assessment Page 11
**INTRODUCTION**

Based on the review of the data on quality, safety and efficacy the UK granted a marketing authorisation for the medicinal product Zerozole on 10th May 2007. The product is a general sale list (GSL) used for the treatment of itchy dry skin conditions such as dermatitis and eczema.

This application was submitted as a bibliographic application according to Article 10a of Directive 2001/83/EC.

Zerozole contain the active ingredients Soya bean oil, a purified mixture of glycerides present as linoleic, linolenic, oleic, palmitic and stearic acids with other acids present in trace quantities. It acts as an emollient and is used primarily in topical pharmaceutical formulations. And macrogol 4 lauryl ether (Laureth-4), which has local anaesthetic and antipruritic actions. It is an effective infiltration and conduction anaesthetic.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

No DMF or Certificate of Suitability is submitted and none is required considering that the actives are well-established substances.

An appropriate specifications based on the European Pharmacopoeia have been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Actives soya bean oil and macrogol 4 lauryl ether are stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

DRUG PRODUCT

Other ingredients
Other ingredients consist of pharmaceutical excipients, Butylated Hydroxytoluene (E321), Propylene Glycol and Perfume oil (Balneum A167139).

All excipients used comply with their respective European Pharmacopoeia monograph with the exception of Perfume oil (Balneum A167139) which complies with in-house specification. Satisfactory certificates of analysis have been provided for all excipients. None of the excipients used contain material of animal or human origin.

Manufacture
In-process controls are satisfactory based on process validation data and controls on the finished product.

Finished product specification
The finished product specification is satisfactory. Test methods have been described and have been adequately validated as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System
The product is packaged in to HDPE bottles with polypropylene screw caps. Specifications and certificates of analysis for all packaging materials have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with food.
Stability
Based on the results, a shelf-life of 2 years has been set, which is satisfactory. A precaution ‘Do not store above 25°C’ has been included.

SPC, PIL, Labels
The SPC, and Label are pharmaceutically acceptable.

Conclusion
It is recommended that Marketing Authorisation is granted for this application.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.
CLINICAL ASSESSMENT

1 INTRODUCTION
This is an abridged national, bibliographical, application made under Article 10a of Directive 2001/83/EC and is for the Marketing Authorisation of Zerozole. Zerozole is a cutaneous solution containing the active ingredients soya bean oil and macrogol lauryl ether (Laureth-4). The formulation is based on that of Balneum Plus, (Crookes Healthcare, PL 00327/0110) and contains the same proportion of soya bean oil. However the other active ingredient in Zerozole is macrogol lauryl ether (Laureth-4) whereas Balneum Plus contains mixed polyethylene lauryl ethers.

2 BACKGROUND
Zerozole bath oil is an emollient and antipruritic agent for the topical treatment of dry skin conditions including those associated with dermatitis and eczema. The active ingredients are soya bean oil and macrogol lauryl ether, Laureth-4. Soya bean oil is a purified mixture of glicerides present as linoleic, linolenic, oleic, palmitic and stearic acids with other acids present in trace quantities. The additional active ingredient macrogol lauryl ether, is a mixture of ethers of mixed macrogols with linear fatty alcohols, mainly lauryl alcohol. The excipients are butylated hydroxytoluene, propylene glycol, and perfume oil (Balneum A167139). Zerozole is indicated as an emollient cleansing agent which is added to the bath for the relief of dry skin conditions including those associated with eczema or dermatitis. It also has local anaesthetic properties.

3 INDICATIONS
Zerozole is a bath oil the active ingredients of which have emollient and local anaesthetic properties. It is recommended for the treatment of dry skin conditions including those associated with dermatitis and eczema.

4 DOSE & DOSE SCHEDULE
After shaking the bottle, Zerozole should be added to the bath water and mixed well. Frequency and duration of the application should be adjusted according to the type and severity of the condition, adults should use the bath oil frequently (at least 3 times per week) whilst neonates and infants should be treated daily.

Dosage

The following quantities are recommended: (if the skin requires considerable moisturising, 2-3 times these quantities can be used).

Adults (including the elderly)

For full bath (~100L) 20ml.

For partial bath (~5L) 2.5ml.

Neonates and children

For bath (~25L) 5ml.
For neonates and children daily application is recommended.

Method of administration

A partial bath may be required when condition is localised eg. the arm.

Zerozole can also be used in the shower. In this case the preparation should first be evenly applied over the body without dilution. Subsequently the excess is removed under the shower. Only pat dry the skin as vigorous wiping and rubbing decreases the therapeutic effect.

5 TOXICOLOGY
No new data has been submitted

6 CLINICAL PHARMACOLOGY

6.1 PHARMACOKINETICS
No new data are submitted and none are required for this type of application.

6.2 BIOEQUIVALENCE
Not applicable.

7 EFFICACY
No new data are submitted and none are required for this type of application

8 SAFETY
No new data are submitted and none is required for this type of application.

9 EXPERT REPORT
An expert report has been provided by a suitably qualified consultant and it was acceptable.

10 PATIENT INFORMATION LEAFLET (PIL)
No Patient Information leaflet has been submitted with this Application. This is acceptable provided the additional patient information can be accommodated on the Label.

11 LABELLING
This is satisfactory

12 APPLICATION FORM (MAA)
This is satisfactory.
13 SUMMARY OF PRODUCT CHARACTERISTICS
This is satisfactory.

14. DISCUSSION
Soya bean based bath oils have become widely used as emollient cleansers with moisturising and protective properties and are suitable for all age groups. Zerozole is similar to the currently approved cleansing, emollient, antipruritic product Balneum Plus. It contains the same quantity of the active ingredient, soya oil, however the other active ingredient in Zerozole is macrogol lauryl ether (Laureth-4) whereas Balneum Plus contains mixed polyethylene lauryl ethers. There are also some differences in the excipients though all are substances for which there is extensive clinical experience and none of these differences should not impact on efficacy or safety. Zerozole cannot be regarded as “essentially similar” to Balneum Plus as defined by the EEC guidelines. However, there is sufficient similarity between the products for a Licence to be granted for Zerozole for the same indications as Balneum Plus and a bibliographical application under Article 10a of Directive 2001/83/EC is appropriate. The pharmaco-toxicological and clinical literature reviews support the approval of this product.

15 MEDICAL CONCLUSION
Overall, there is no clinical objection to grant a Marketing Authorisation for this application. No new or unexpected safety concerns arose from this application.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Zerozole are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for application of this type.

EFFICACY
No new or unexpected safety concerns arise from this application.

The SPC and labelling are satisfactory.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable. Extensive clinical experience with Zerozole is considered to have demonstrated the therapeutic value of the product. The risk benefit is, therefore, considered to be positive.
# STEPS TAKEN FOR ASSESSMENT

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 4\textsuperscript{th} April 2002</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 25\textsuperscript{th} June 2002</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested information relating to the medical dossier on the 12\textsuperscript{th} July 2002, and quality dossiers on 19\textsuperscript{th} July 2002</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the clinical dossier on 11\textsuperscript{th} August 2003 and on the quality dossier on 11\textsuperscript{th} August 2003</td>
</tr>
<tr>
<td>5</td>
<td>The application was determined on 10\textsuperscript{th} May 2007</td>
</tr>
</tbody>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Zerozole

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Soya bean oil, refined 83.45% w/w
Macrogol 4 lauryl ether (Laureth-4) 15.0% w/w
For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM
Cutaneous Solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Zerozole is a bath oil the active ingredients of which have emollient and local anaesthetic properties. It is recommended for the treatment of dry skin conditions including those associated with dermatitis and eczema.

4.2 Posology and method of administration
After shaking the bottle, Zerozole should be added to the bath water and mixed well. Frequency and duration of the application should be adjusted according to the type and severity of the condition, adults should use the bath oil frequently (at least 3 times per week) whilst neonates and infants should be treated daily.

Dosage

The following quantities are recommended: (if the skin requires considerable moisturising, 2-3 times these quantities can be used).

Adults (including the elderly)

For full bath (~100L) 20ml.

For partial bath (~5L) 2.5ml.

Neonates and children

For bath (~25L) 5ml.

For neonates and children daily application is recommended.

Method of administration

A partial bath may be required when condition is localised eg. the arm.
Zerozole can also be used in the shower. In this case the preparation should first be evenly applied over the body without dilution. Subsequently the excess is removed under the shower. Only pat dry the skin as vigorous wiping and rubbing decreases the therapeutic effect.

4.3 Contraindications
Sensitivity to any of the ingredients.

4.4 Special warnings and precautions for use
As Zerozole deposits a film of oil over skin, care should be taken to avoid slipping, especially in the bath or shower.

Contact with the eyes should be avoided and if it occurs the eyes should be washed out with copious amounts of clean water.

Ingestion of the bath oil should be avoided.

4.5 Interaction with other medicinal products and other forms of interaction
None known.

4.6 Pregnancy and lactation
No special precautions are recommended.

4.7 Effects on ability to drive and use machines
None known

4.8 Undesirable effects
None known.

4.9 Overdose
In the event of oral ingestion the occurrence of symptoms are very unlikely owing to the low toxicity of the ingredients. No specific antidote or treatment is recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Soya bean oil is a purified mixture of glycerides present as linoleic, linolenic, oleic, palmitic and stearic acids with other acids present in trace quantities. It acts as an emollient and is used primarily in topical pharmaceutical formulations. Macrogol 4 lauryl ether (Laureth-4) has local anaesthetic and antipruritic actions. It is an effective infiltration and conduction anaesthetic.

5.2 Pharmacokinetic properties
Although it has been suggested that local anaesthetics in general have little effect over the intact stratum corneum because of their inability to penetrate this barrier this seems to apply only to the pure substance without a fatty base.

5.3 Preclinical safety data
There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Butylated hydroxytoluene (E321)
Propylene glycol
Perfume oil (Balneum A167139).

6.2 Incompatibilities
None known.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Container: HDPE bottle with polyethylene or polypropylene cap containing 250ml or 500ml of solution.

6.6 Special precautions for disposal
None stated.

7 MARKETING AUTHORISATION HOLDER
Zeroderma Ltd
Manor House
Victors Barn
Northampton Road
Brixworth
Northamptonshire NN6 9DQ

8 MARKETING AUTHORISATION NUMBER(S)
PL 18962/0005.

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
10/05/2007

10 DATE OF REVISION OF THE TEXT
10/05/2007
LABELLING

SOOTHING BATH OIL

For soothing acclaim of the mind and body

For external use only

KEEP OUT OF REACH OF CHILDREN

Zerozole

scented

50ml

[Braille text]

[Image of the product label]

[Braille text]

[Image of the product label]

UKPAR Zerozole

PL 18962/0005