

## **EXO-DERM EMOLLIENT OINTMENT**

**PL 06166/0004**

**UKPAR**

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## **EXO-DERM EMOLLIENT OINTMENT**

**PL 06166/0004**

### **LAY SUMMARY**

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Forest Tosara Limited a Marketing Authorisation (licence) for the medicinal product Exo-Derm Emollient Ointment (PL 06166/0004) on 5<sup>th</sup> April 2007. This is a medicine available to the general public (GSL).

Exo-Derm Emollient Ointment contains the active ingredients white soft paraffin and emulsifying wax which are both common emollient materials. The medicine is used as a moisturising and protective ointment for irritated, dry or scaling skin conditions, and can also be used in the treatment of certain skin diseases.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of using Exo-Derm Emollient Ointment outweigh the risk, hence a Marketing Authorisation has been granted.

## **EXO-DERM EMOLLIENT OINTMENT**

**PL 06166/0004**

### **SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

Based on the review of the data on quality, safety and efficacy, the UK granted Forest Tosara Limited a Marketing Authorisation for the medicinal product Exo-Derm Emollient Ointment (PL 06166/0004) on 5<sup>th</sup> April 2007. This is a medicinal product available to the general public (GSL).

The application was submitted as a bibliographic application, for actives of well-established use, according to Article 10(a) of Directive 2001/83/EC (as amended).

Exo-Derm Emollient Ointment contains the active ingredients white soft paraffin and emulsifying wax which are both common emollient materials. The medicine is used as a moisturising and protective ointment for irritated, dry or scaling skin conditions.

## **PHARMACEUTICAL ASSESSMENT**

### **ACTIVE SUBSTANCE**

#### **Emulsifying wax**

Physical form: An almost white or pale yellow waxy solid, with an odour that is faint and characteristic

Solubility: Practically insoluble in water, partially soluble in alcohol

The active substance emulsifying wax is a well known material and is the subject of a BP monograph.

Synthesis of the drug substance from the designated starting material, with acceptable in-process controls and intermediate specifications, is satisfactory and controlled by the BP monograph. Satisfactory specifications are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Confirmation has been provided that the materials used are not derived from animals or animals susceptible to BSE and TSE and therefore comply with the TSE requirements.

An appropriate active substance specification has been provided which is in line with the British Pharmacopeia monograph.

The analytical methods used are those detailed in the European Pharmacopoeia.

Active emulsifying wax is stored in appropriate packaging. It is packed in to 20kg polyethylene bags. Specifications and certificates of analysis have been provided for the packaging material. The polyethylene bags in direct contact with the drug substance satisfy Directive 2002/72/EC (as amended), and are suitable for contact with foodstuffs.

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

No stability data has been presented on the basis that this is a pharmacopoeial product, which is acceptable. The emulsifying wax is considered to be stable for at least one year when stored unopened in ambient conditions. It has been confirmed that the emulsifying wax is tested to the pharmacopoeia specification prior to manufacture of the finished product.

**ACTIVE SUBSTANCE****White soft paraffin**

Physical form:	A white or almost white, translucent, soft unctuous mass, slightly fluorescent in daylight when melted.
Solubility:	Practically insoluble in water, in alcohol and in glycerol. Soluble in methylene chloride

The active substance white soft paraffin is a well known material and is the subject of a European Pharmacopoeia monograph.

Synthesis of the drug substance from the designated starting material, with acceptable in-process controls and intermediate specifications, is satisfactory and controlled by the EP monograph. Satisfactory specifications are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Confirmation has been provided that the materials used are not derived from animals or animals susceptible to BSE and TSE and therefore comply with the TSE requirements.

An appropriate active substance specification has been provided which is in line with the European Pharmacopoeia monograph. An additional in house test for identification is included and is satisfactory.

The analytical methods used are those detailed in the European Pharmacopoeia.

Active white soft paraffin is stored in appropriate packaging. It is packed in lacquer lined, open top drums, with a lid fitted with a lever clamp and tamper evident seal. Specifications and certificates of analysis have been provided for the packaging material. The primary packaging in direct contact with the drug substance satisfies Directive 2002/72/EC (as amended), and is suitable for contact with foodstuffs.

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

No stability data has been presented on the basis that this is a pharmacopoeial product, which is acceptable. The white soft paraffin has a two year shelf-life. It has been confirmed that the white soft paraffin is tested to the pharmacopoeia specification prior to manufacture of the finished product.

**DRUG PRODUCT****Composition**

The finished product is a simple emollient of white soft paraffin and emulsifying wax as the active substances and the single pharmaceutical excipient, liquid paraffin. Appropriate justification for the inclusion of the excipient has been provided. The components of the finished product are standard materials used for the preparation of topical pharmaceutical products.

The excipient, liquid paraffin complies with an appropriate in house specification, which is in compliance with the European Pharmacopoeia monograph with the exception of the viscosity. A satisfactory certificate of analysis has been provided for the excipient.

There are no materials of human or animal origin contained in or used in the manufacturing process for the proposed product.

There were no novel excipients used and no overages.

**Pharmaceutical development**

Details of the pharmaceutical development of the drug product have been supplied and are satisfactory.

**Manufacture**

A description and flow-chart of the manufacturing method has been provided.

In-process controls have been provided and are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on validation batches. The results are satisfactory.

**Finished product specification**

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described but validation data has not been presented for the release methods as they are considered standard pharmacopoeia methods. This is acceptable. Batch data have been provided that comply with the release specification and are comparable.

**Container Closure System**

Three types of primary packaging are proposed for the marketed product:

1. 40ml white polypropylene Snaplock jar with white polyethylene Snaplock cap (30g)
2. 180ml white polypropylene Securitub with white polyethylene wadless Securipot lid (125g)
3. 700ml white polypropylene Securitub with white polyethylene wadless Securipot lid (500g)

Specifications and Certificates of Analysis for all packaging components used have been provided. These are satisfactory. All primary product packaging complies with EU legislation, Directive 2002/72/EC (as amended), and is suitable for contact with foodstuffs.

**Stability**

Finished product stability studies have been conducted in accordance with current guidelines and results were within the proposed specification limits. Based on the results, a shelf-life of 24 months has been set, which is satisfactory. An in-use shelf-life of 28 days has also been set. Storage conditions are “Do not store above 25 degrees”, “Keep container tightly closed”.

**Bioequivalence Studies**

There was no bioequivalence study carried out to support this application. The legal basis of the application is that it is a bibliographic application, therefore a bioequivalence study is not required.

**Product Information**

The approved SPC and labelling are satisfactory. There is no package leaflet for the finished product as all information has been included on the label.

**Conclusion**

All pharmaceutical issues have been resolved and the quality grounds for this application are considered adequate. It is recommended that a Marketing Authorisation is granted.

## **PRECLINICAL ASSESSMENT**

The application was submitted as a bibliographic application, for actives of well-established use, according to Article 10(a) of Directive 2001/83/EC (as amended).

No new preclinical data have been supplied with this application and none are required for an application of this type. A preclinical expert report has been written by a suitably qualified person and is satisfactory.

## **CLINICAL ASSESSMENT**

### **INDICATIONS**

Exo-Derm Emollient Ointment is indicated for use as a moisturising and protective ointment for irritated, dry or scaling skin conditions. It can also be used in the treatment of skin diseases such as eczema or psoriasis, as an adjunct to therapies containing other agents.

### **TOXICOLOGY**

No new data has been submitted and none are required for this type of application.

A pre-clinical expert report has been provided by an appropriately qualified consultant. Based on the literature, currently no evidence is available that suggests that pharmacopoeial grades of mineral oil and petroleum waxes used in skin care applications are likely to cause local or systemic toxic effects.

### **CLINICAL PHARMACOLOGY**

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

### **EFFICACY**

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

A bibliography has been submitted that adequately supports the efficacy for a product of this nature.

### **SAFETY**

No formal safety data are presented and none are required for this type of application.

A bibliography has been presented and supports the clinical safety of the product. The ingredients in the product are accepted as being well established, the majority of the undesirable effects associated with the ingredients are skin reactions and hypersensitivity reactions, and occur very rarely.

### **EXPERT REPORT**

A satisfactory expert report is provided, and has been prepared by an appropriately qualified expert. An appropriate CV for the expert has been supplied.

### **PRODUCT INFORMATION:**

#### **Summary of Product Characteristics**

The approved SPC is satisfactory.

#### **Patient Information Leaflet**

No PIL has been provided. All relevant information will be displayed on the product label.

#### **Labelling**

Colour mock-ups of the labelling have been provided. The labelling is satisfactory and contains all the information that would normally be presented in the PIL. The information presented is consistent with the final SPC.

**DISCUSSION AND RECOMMENDATION**

This is a bibliographic application. No clinical study has been undertaken to demonstrate that the efficacy for this formulation of emulsifying ointment will be comparable to the formulations described in the literature. However, given the nature of the product and the mechanism of action, this is acceptable. It is accepted that the ingredients used in this medicinal product are well established and have been used in combination for many years for the proposed indication.

Providing that the ingredients used in this medicinal product are of a suitable pharmaceutical grade and the formulation as a whole is of a suitable quality there is little reason to suggest that the safety profile of this product should be different to that of other similar products.

Sufficient clinical information has been submitted to support this application. All issues have been adequately addressed by the applicant. A Marketing Authorisation may, therefore, be granted on medical grounds.

## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

The important quality characteristics of Exo-Derm Emollient Ointment 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 an application of this type.

### **EFFICACY**

Emollients containing the combination of ingredients used in this medicinal product have been available in the UK for much more than ten years. Their use is well established with recognised efficacy and acceptable safety.

The applicant has submitted an adequate literature review for this bibliographic application. The literature review confirms the therapeutic effectiveness of a white soft paraffin- emulsifying wax emollient preparation and no new safety issues have arisen.

### **PRODUCT LITERATURE**

The approved SPC and labelling are satisfactory. No Patient Information Leaflet has been provided as the labelling includes all the information that would normally be present in the PIL.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with white soft paraffin-emulsifying wax combination emollient preparations is considered to have demonstrated the therapeutic value of the drug product. The risk benefit is, therefore, considered to be positive.

## **EXO-DERM EMOLLIENT OINTMENT**

**PL 06166/0004**

### **STEPS TAKEN FOR ASSESMENT**

- 1 The MHRA received the marketing authorisation application on 5<sup>th</sup> November 2004
- 2 Following standard checks and communication with the applicant the MHRA considered the application valid on 13<sup>th</sup> December 2004
- 3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 18<sup>th</sup> May 2005
- 4 The applicant responded to the MHRA's request, providing further information for the quality sections on 5<sup>th</sup> August 2005
- 5 Following assessment of the response the MHRA requested further information relating to the quality sections on 25<sup>th</sup> November 2005, and further information relating to the quality dossier was also requested on 1<sup>st</sup> December 2005
- 6 The applicant responded to the MHRA's request, providing further information for the quality sections on 12<sup>th</sup> April 2006
- 7 Following assessment of the response the MHRA requested further information relating to the quality sections on 12<sup>th</sup> April 2006
- 8 The applicant responded to the MHRA's request, providing further information for the clinical sections on 16<sup>th</sup> June 2006, and further information relating to the quality sections on 15<sup>th</sup> August 2006
- 9 Following assessment of the response the MHRA requested further information relating to the quality sections on 2<sup>nd</sup> November 2006
- 10 The applicant responded to the MHRA's request, providing further information for the quality sections on 20<sup>th</sup> February 2007
- 11 The application was determined on 5<sup>th</sup> April 2007

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1 NAME OF THE MEDICINAL PRODUCT

Exo-Derm Emollient Ointment

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Emulsifying Wax 20% w/w

White Soft Paraffin 30% w/w

For a full list of excipients, see section 6.1

### 3 PHARMACEUTICAL FORM

Ointment

An off-white waxy ointment with a smooth consistency and a very weak fatty odour.

### 4 CLINICAL PARTICULARS

#### 4.1 THERAPEUTIC INDICATIONS

Exo-Derm Emollient Ointment is an emollient, moisturising and protective ointment for use in irritated, dry or scaling skin conditions.

#### 4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Cutaneous use.

Adults, children and the elderly:

Exo-Derm Emollient Ointment should be applied to the skin as often as required.

#### 4.3 CONTRAINDICATIONS

Hypersensitivity to any of the ingredients.

#### 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

If symptoms persist consult your doctor.

In the rare event of a skin reaction, treatment should be discontinued.

#### 4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

None known

#### 4.6 PREGNANCY AND LACTATION

The safety of Exo-Derm Emollient Ointment during pregnancy and lactation has not been established but is not considered to constitute a hazard during these periods.

#### 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None stated

#### 4.8 UNDESIRABLE EFFECTS

Very rarely skin sensitivity reactions, including mild skin irritation, may occur.

#### 4.9 OVERDOSE

No case of overdose has been reported. If large amounts are swallowed accidentally, this may cause anal seepage and irritation. Symptomatic treatment should be provided.

### 5 PHARMACOLOGICAL PROPERTIES

#### 5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Emollients and Protectives

ATC Code: D02A C

Massaged into the skin, the emollient white soft paraffin permits rehydration of dry skin by forming an occlusive barrier within the skin surface, thus reducing drying from evaporation of water that diffuses from the underlying areas. The ingredients of emulsifying wax have skin softening properties.

## **5.2 PHARMACOKINETIC PROPERTIES**

Not applicable

## **5.3 PRECLINICAL SAFETY DATA**

There are no preclinical data of relevance to the prescriber, which are additional to safety data already included in other sections of the SPC.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 LIST OF EXCIPIENTS**

Liquid paraffin

### **6.2 INCOMPATIBILITIES**

Not applicable

### **6.3 SHELF LIFE**

2 years

Once opened, use within 28 days.

### **6.4 SPECIAL PRECAUTIONS FOR STORAGE**

Do not store above 25°C.

Keep container tightly closed.

### **6.5 NATURE AND CONTENTS OF CONTAINER**

30g: White polypropylene tub with white polyethylene tamper-evident cap.

125g: White polypropylene tub with white polyethylene tamper-evident cap.

500g: White polypropylene tub with white polyethylene tamper-evident screw-on lid.

### **6.6 SPECIAL PRECAUTIONS FOR DISPOSAL**

No special requirements

## **7 MARKETING AUTHORISATION HOLDER**

Forest Tosara Ltd  
Baldoyle Industrial Estate  
Grange Road  
Dublin 13  
Ireland

## **8 MARKETING AUTHORISATION NUMBER(S)**

PL 06166/0004

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

05/04/2007

## **10 DATE OF REVISION OF THE TEXT**

05/04/2007

## LABELLING

Label pack size 30g

<p>BN</p> <p>EXP</p> <p>Use within 28 days of opening.</p> <p>PEEL HERE</p>	<p>Moisturising and protective ointment for irritated, dry or scaling skin conditions.</p> <p><b>Exo-Derm Emollient</b> Ointment White Soft Paraffin 30% w/w Emulsifying Wax 20% w/w</p> <p>30g</p>	<p>Topical Ointment containing: White Soft Paraffin 30% w/w, Emulsifying Wax 20% w/w. Other ingredients: Liquid Paraffin.</p> <p>MA Holder: Forest Tosara Ltd.</p> <p>KEEP OUT OF THE REACH AND SIGHT OF CHILDREN. DO NOT STORE ABOVE 25°C. PROFESSIONAL SAMPLE - NOT FOR RESALE</p>	<p>3558</p> <p>PL 06166/0004</p>
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<p>Before use: Do not use if sensitive to any of the ingredients.</p> <p>Directions: Adults and Children: Apply to the affected area as needed by rubbing in gently.</p> <p>FOR EXTERNAL USE ONLY. Side effects: Occasionally skin irritation or an allergic skin reaction may occur. If this happens, stop using the ointment.</p> <p>If symptoms persist or you notice anything unusual, talk to your doctor or pharmacist.</p> <p>Keep container tightly closed.</p> <p>Do not use after the expiry date.</p>	<p>MA Holder: Forest Tosara Ltd., Baldoyle Industrial Estate, Dublin 13, Ireland</p> <p>Manufacturer: Forest Laboratories UK Ltd., Bourne Road, Bexley, Kent, DA5 1NX, UK</p> <p>Text revised: November 2006</p>
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Label pack size 125g

<p>Marketing Authorisation Holder: Forest Tosara Limited, Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland. Manufacturer: Forest Laboratories UK Ltd, Bourne Road, Bexley, Kent, DA5 1NX, UK.</p>	<p>Topical Ointment containing: White Soft Paraffin 30% w/w, Emulsifying Wax 20% w/w</p>	 <p><b>Exo-Derm Emollient ointment</b> White Soft Paraffin 30% w/w Emulsifying Wax 20% w/w</p>	<p>Directions: Adults and Children: Apply to the affected area as needed by rubbing in gently. <b>FOR EXTERNAL USE ONLY.</b> Side effects: Occasionally skin irritation or an allergic skin reaction may occur. If this happens, stop using the ointment. If symptoms persist or you notice anything unusual, talk to your doctor or pharmacist. Use within 28 days of opening. Keep container tightly closed. <b>KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.</b> DO NOT STORE ABOVE 25°C. Do not use after the expiry date.</p>	<p>EAN Code: 5014398001902</p>
<p>BN MAN EXP</p>	<p>Other ingredients: Liquid Paraffin.  Before use: Do not use if sensitive to any of the ingredients. Text revised: November 2006. PL 06166/0004</p>		<p>125g</p>	

Label pack size 500g

<p>Marketing Authorisation Holder: Forest Tosara Limited, Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.</p>	<p>Topical Ointment containing: White Soft Paraffin 30% w/w, Emulsifying Wax 20% w/w.</p>	 <p><b>Exo-Derm Emollient ointment</b> White Soft Paraffin 30% w/w Emulsifying Wax 20% w/w</p>	<p>Directions: Adults and Children: Apply to the affected area as needed by rubbing in gently. <b>FOR EXTERNAL USE ONLY.</b> Side effects: Occasionally skin irritation or an allergic skin reaction may occur. If this happens, stop using the ointment. If symptoms persist or you notice anything unusual, talk to your doctor or pharmacist. Use within 28 days of opening. Keep container tightly closed. <b>KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.</b> DO NOT STORE ABOVE 25°C. Do not use after the expiry date.</p>	<p>EAN Code: 5014398001919</p>
<p>BN MAN EXP</p>	<p>Other ingredients: Liquid Paraffin.  Before use: Do not use if sensitive to any of the ingredients. Text revised: November 2006. PL 06166/0004</p>		<p>500g</p>	