GAMMADERM BATH & SHOWER EMOLLIENT

PL 19786/0003

UKPAR

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PL 19786/0003

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LAY SUMMARY

The MHRA today granted Linderma Limited a Marketing Authorisation (licence) for the medicinal product Gammaderm Bath and Shower Emollient (PL 19786/0003). This is a product for sale direct to the general public (GSL) used for the treatment of dry skin conditions such as inflammation of the skin caused by contact with metals such as zinc, or reaction to soaps and perfumes, dry itching skin, scaly skin and related dry skin conditions.

Gammaderm bath and shower Emollient acts by hydrating dry skin and leaving a thin barrier on it to reduce further water loss.

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

GAMMADERM BATH & SHOWER EMOLLIENT

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted a marketing authorisation for the medicinal product Gammaderm Bath and Shower Emollient on 30th October 2007. The product is a general sale list (GSL) product.

This is an abridged national application for Gammaderm Bath and Shower Emollient under Article 10.1 of Directive 2001/83/EC claiming to be a generic medicinal product of Oilatum Bath formula, Oilatum Emollient from Steifel Laboratories (PL 00174/5010R).

Gammaderm Bath and Shower Emollient for the treatment of contact dermatitis, atopic dermatitis, senile pruritis, ichthyosis and related skin conditions. The product is suitable for infant bathing. It is used for cleansing the skin in conditions where the use of soaps, soap substitutes, and other cleansers prove irritating.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

No DMF or Certificate of Suitability is submitted and none is required considering that liquid paraffin is a well-established active substance.

An appropriate specification based on the European Pharmacopoeia has 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.

Active liquid paraffin is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Appropriate stability data has been provided.

DRUG PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients, cetearyl octanoate, PPG-5-laureth-5, and laureth-2.

All excipients comply with satisfactory in-house specifications. 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

Specifications and certificates of analysis for all packaging materials have been provided. These are satisfactory.

The applicant has confirmed that all packaging that comes into direct contact with the

drug product complies with European Directive 90/128/EEC with respect to their contact with food.

Stability
Based on the results, a shelf-life of 3 years has been set, which is satisfactory. A precaution 'Do not store above 25°C' has been included.

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

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

PRECLINICAL ASSESSMENT

INTRODUCTION

This is an abridged national application for Gammaderm Bath and Shower Emollient under Article 10.1 of Council Directive 2001/83/EC claiming to be a generic medicinal product of Oilatum Bath formula, Oilatum Emollient. Gammaderm contains 48% weight for weight (w/w) liquid paraffin in a base of surfactants and emulsifiers and is intended for the treatment of dry scaling skin disorders by topical application.

The proposed dose is 30 to 40 ml in a "full bath" of water for adults, children and the elderly, with a recommendation to soak for twenty minutes. For infants, the dose is 2.5 ml in a "baby-bathful" of water. For a shower emollient, the instruction is to "apply sparingly to the affected areas, rinse and pat dry." The product can be applied daily and can also be used as a substitute for soap.

The excipients comprise cetearyl octanoate as a wetting agent, laureth-2 as an emulsifier and PPG-5-laureth-5 as a surfactant.

The applicant has provided written confirmation that the product has been on the market in Germany (since 1986) under the name of Linola®-Fett Ölbad and that the composition of the product in this application is identical to that of Linola®-Fett Ölbad.

GOOD LABORATORY PRACTICE (GLP) ASPECTS

No preclinical studies have been submitted.

PHARMACODYNAMICS

Emollients are well-established as part of the management of dry skin conditions. Their action is to hydrate the skin. Liquid paraffin works by forming an occlusive oily film on the surface thereby reducing transepidermal water loss through the stratum corneum.

TOXICOKINETICS

The PCER does not contain a discussion on the pharmacokinetics of liquid paraffin or any of the excipients because the route of application is topical. The statement is made that absorption does not occur but there were no supporting data presented. Further information was requested and a supplementary document was provided by the applicant.

The supplementary document contains a summary of a literature review on absorption of the active, as the manufacturer cannot provide any data. In a dermal study in the guinea pig, less than 0.1% of topically applied doses were found in the dermis. The same proportion of a topical dose in rats was recovered over ninety-six hours in faeces, urine, expired air or tissues. Human skin studies in vitro showed penetration of between 0 and 0.01% after fifty-four hours. A fourth study showed that penetration appeared to be limited to the stratum corneum and that it was not expected to increase in diseased skin. Two more studies have shown very low penetration with topical application.

A clinical case was reported in which an oleogranulomatous response in local lymph nodes occurred in a patient with Netherton's syndrome who used both emollient ointments and bath oils. The response was reversible upon reduction of the dose of mineral oil to 10 g per day.

Assessor's comment
The data show that absorption via normal skin is very low. The one clinical case where absorption was deemed to have led to sequelae showed that the effect was reversible at a dose considerably higher (10 g) than that likely to result from Gammaderm when used as directed. The additional data provide some reassurance on the question.

TOXICOLOGY

No studies have been conducted on the formulation or any of its constituents by the applicant. The literature has been reviewed and a summary presented in the PCER.

LIQUID PARAFFIN

Liquid paraffin is a clear, oily, colourless, flavourless and odourless mixture of highly purified aliphatic and alicyclic liquid hydrocarbons.

By the oral route, it is poorly absorbed and has been known to cause a foreign body granulomatous reaction. Excessive intake can cause anal seepage and irritation while chronic ingestion might impair absorption of fat-soluble vitamins. In feeding studies in rats, haematological changes and deposition of food grade liquid paraffins in the liver, spleen and lymph nodes were seen.

Following aspiration, lipoid pneumonia has been reported.

At the exposure levels likely with this formulation, there is no evidence of local toxicity upon topical application, and skin irritation or sensitisation have not been reported. There are also no reports of phototoxicity or photosensitisation.

Cetearyl octanoate

Wetting agent, is a 6:3:1 mixture of hexadecyl (2-ethyl hexanoate): octadecyl (2-ethyl hexanoate): isopropyl myristate.

The manufacturers report that it has an LD50 of >5g/kg in rats and is of low toxicity by the inhalation route. In rabbits, the Draize eye irritation and skin sensitisation tests were negative.

Cetearyl octanoate has an oral LD50 in rats of >8g/kg. It was free of irritant properties in rabbit modified Draize tests, primary skin irritation tests and hamster mucous membrane tests. It was also free of sensitising effects in a rabbit dermal study and was a constituent of a moisturiser that had no photosensitising effects in guinea pigs.

Laureth-2

Laureth-2, an emulsifier, is α-dodecyl-ω-hydroxypoly(oxyethylene)-2. It has been found to have an oral LD50 in the rat of >5g/kg and was negative in the Ames test. It

was non-irritant in dermal studies in mice and rabbits, and in the modified Draize eye test in the rabbit. In a dermal sensitisation test in the Guinea pig, it was also negative. A sub acute oral toxicity study in the rat revealed a no observed adverse effect dose (NOAED) of 100 mg/kg. A small clinical study is cited in which no irritancy was seen at a concentration of 10%.

PPG-5-laureth-5

PPG-5-laureth-5, a surfactant, is α-(dodecyl,tetradecyl)-ω-hydroxypoly(oxyethylene)-4,5-poly(oxypropylene)-5. It has an oral LD_{50} in the rat of >5.8 g/kg. Mild dermal irritancy was shown in rabbits and mice with a 100% concentration. A modified Draize test also at 100% resulted in mild, reversible conjunctival reactions. Clinical studies using solutions of 50% and over did not reveal any primary irritancy.

Assessor's comment

The PCER contains a brief review of the published data on the toxicity of liquid paraffin and the excipients. Liquid paraffin has been in use in many formulations for many years with few adverse outcomes and the content of Gammaderm is lower than that of the reference product. While some reports of irritation and sensitivity regarding the excipients have been found, the doses in question were much higher than those in Gammaderm and generally applied to industrial handling. Regarding the lack of consideration given to the possibility of greater sensitivity with skin lesions, the absence of reports of irritancy or sensitisation in the Periodic Safety Update Report for Linola®-Fett Ölbad would indicate that Gammaderm does not constitute a risk to human health at the dose proposed.

PRECLINICAL EXPERT REPORT

The Preclinical Expert Report was written by an individual who has had extensive experience of drug development and has participated in the invention and development of dermatological products. The PCER with the supplement is considered acceptable.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

Sections 4.6 and 5.3 of the SPC are acceptable.

CONCLUSION

The preclinical issues identified in this application have been satisfactorily resolved and there is no indication of any risks to human health from Gammaderm Bath and Shower Emollient if used as recommended. There is no objection to the grant of a licence from a preclinical point of view.

CLINICAL ASSESSMENT

1. INTRODUCTION
This national abridged application is submitted claiming to be a generic medicinal product of Oilatum Bath Formula/oilatum emollient Steifel laboratories PL 0174/5010R.

2. INDICATIONS
Satisfactory. Consistent with originator

3. DOSE & DOSE SCHEDULE
Satisfactory. Consistent with originator

4. TOXICOLOGY
No new data

5. CLINICAL PHARMACOLOGY
No new data

6. EFFICACY
No new data.

7. SAFETY
No new data.

8. EXPERT REPORTS
The expert report is written by qualified Pharmaceutical physician and is satisfactory.

9. PATIENT INFORMATION LEAFLET (PIL)
Satisfactory.

10. LABELLING
Satisfactory.

11. APPLICATION FORM (MAA)
Satisfactory.

12. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
Satisfactory.

13. DISCUSSION
This is a well established topical use. No topical bioavailability or comparative efficacy data is required

14. MEDICAL CONCLUSION
Marketing authorisation is recommended.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Gammaderm Bath and Shower Emollient lotion 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

The efficacy of Gammaderm Bath and Shower Emollient has been well documented in the past. No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with the originator product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable. Extensive clinical experience with Gammaderm Bath and Shower Emollient is considered to have demonstrated the therapeutic value of the product. The risk benefit is, therefore, considered to be positive.

GAMMADERM BATH & SHOWER EMOLLIENT

PL 19786/0003

STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application on 27th June 2003
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 19th September 2003
3	Following assessment of the application the MHRA requested information relating to the medical dossier on the 21st October 2003, 5th of January 2004 and quality dossiers on 14th October 2004 and 7th December 2006
4	The applicant responded to the MHRA's requests, providing further information on the clinical dossier on 5th November 2003, 19th January 2004 and on the quality dossier on 2nd August 2006 and 31st May 2007
5	The application was determined on 30th October 2007

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Gammaderm Bath and Shower Emollient

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Liquid Paraffin PhEur 48.0 % w/w.

For excipients see 6.1.

3 PHARMACEUTICAL FORM
Bath oil. Topical solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS
For the treatment of contact dermatitis, atopic dermatitis, senile pruritis, ichthyosis, and related skin conditions. The product is suitable for infant bathing. Cleansing the skin in conditions where the use of soaps, soap substitutes, and other cleansers proves irritating.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
The product is suitable for daily use.

As a bath oil, by adding to the bath and mixing thoroughly:

For adults, children, and the elderly: Add 30 to 40 ml to a full bath of water, soak for 10 to 20 minutes and pat dry.

For infants: Add 2.5 ml to a baby-bathful of water and apply gently over the whole of the body with a soft cloth or sponge and pat dry.

As a shower emollient:

For adults, children, and the elderly: Wet the skin, apply sparingly to the affected areas, rinse, and pat dry.

4.3 CONTRAINDICATIONS
Hypersensitivity to any of the ingredients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
If skin irritation should occur stop using the product.

Take care if the bath or shower tray becomes slippery.

Do not swallow the product; medical help should be sought if this occurs.

Avoid swallowing the diluted product or getting it into the nose.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
None known.

4.6 PREGNANCY AND LACTATION

There is no, or inadequate, evidence of the safety of Gammaderm Bath and Shower Emollient in human pregnancy or lactation, but it has been in wide use for many years without ill consequence.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None stated.

4.8 UNDESIRABLE EFFECTS

None stated.

4.9 OVERDOSE

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Liquid paraffin exerts its emollient effect by forming an occlusive film on the skin, thus re-hydrating the skin.

5.2 PHARMACOKINETIC PROPERTIES

Not applicable.

5.3 PRECLINICAL SAFETY DATA

There are no preclinical data of relevance to the prescriber other than that which is already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Cetearyl octanoate, PPG-5-laureth-5, Laureth-2

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

36 months.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25ºC.

6.5 NATURE AND CONTENTS OF CONTAINER

Polyethylene bottle, dropper device, and screw cap, covered with a 20 ml measure. Contents 200 ml and 400 ml.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

A 20 ml measure is supplied to aid patient compliance, graduated at 2.5 ml (for infant bathing) and at 5 ml, 10 ml, and 20 ml.

7 MARKETING AUTHORISATION HOLDER

Linderma Ltd

Canon Bridge House

Madley

Herefordshire HR2 9JF

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 19786/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
30/10/2007

10 DATE OF REVISION OF THE TEXT
30/10/2007

PATIENT INFORMATION LEAFLET

PATIENT INFORMATION LEAFLET
GAMMADERM BATH AND SHOWER EMOLLIENT

Please read this leaflet before you start your treatment. It contains important information about your medicine. If you have any questions or are unsure about anything, please consult your doctor or pharmacist. There is no, or inadequate, evidence of the safety of Gammaderm Bath and Shower Emollient in human pregnancy or lactation, but it has been in wide use for many years without ill consequence.

What is this medicine

Gammaderm Bath and Shower Emollient contains 48% w/w liquid paraffin in a base of agents intended to aid dispersal of the product and wetting of the skin, these are cetearyl octanoate, PPG-5-laureth-5, and Laureth 2.

Gammaderm Bath and Shower Emollient acts by hydrating dry skin and leaving a thin barrier on it to reduce further water loss.

The medicine is used by adding to the bath water, or by applying to the skin whilst in the shower.

It is also an alternative to soaps that can often be irritant to the skin.

It is available in plastic bottles of 200 ml, 400 ml, and is supplied with a 20 ml graduated measure.

The holder of the Marketing Authorisation is Linderma Ltd, Canon Bridge House, Madley, Herefordshire, HR2 9JF, UK, and the manufacturer of the product is Dr. August Wolff GmbH & Co, Sudbrackstrasse 56, 33611 Bielefeld, Germany

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What is this medicine used for

Gammaderm Bath and Shower Emollient is a bathing preparation used for the treatment of dry skin conditions such as contact dermatitis (inflammation of the skin caused by contact with metals such as zinc, or reaction to soaps and perfumes etc, atopic dermatitis (eczema – dry itching skin), senile pruritis (itching of the skin in older subjects), ichthyosis (scaly skin), and related dry skin conditions. The product is suitable for infant bathing. It can also be used for cleansing the skin in conditions where the use of soaps, soap substitutes, and other cleansers proves irritating.

Before using this medicine
You should not use the product if you are hypersensitive (allergic) to liquid paraffin or any of the excipients listed above. No interactions are known between Gammaderm Bath and Shower Emollient and other medicines which you may be taking.

How to use this medicine
Gammaderm Bath and Shower Emollient should only be used by adding to the bath or applying to the skin in the shower.

In order to maximise its effectiveness **do not** use soap or other skin cleansers whilst bathing or showering with Gammaderm Bath and Shower Emollient.

Take care to avoid slipping in the bath or shower.

Gammaderm Bath and Shower Emollient is suitable for daily use.

As a bath emollient:
For adults, children, and the elderly:
Add 30 to 40 ml, using the graduated measure supplied, to a full bath (about 8 inches or 20 cm) of water, mix thoroughly, soak for 10 to 20 minutes, and pat dry.

For infants: Add 2.5 ml, using the graduated measure supplied, to a baby-bathful of water, mix thoroughly, and apply gently over the whole of the body with a soft cloth or sponge and pat dry.

As a shower emollient:
For adults, children, and the elderly:

Wet the skin, apply sparingly to the affected areas (using up to 15 ml to 30 ml), rinse, and pat dry.

The product is for use on the skin only. Do not allow the diluted product to enter the mouth or nostrils. If you, or anyone else, should accidentally swallow a quantity of the product, tell your doctor at once, or go to the nearest hospital casualty department.

After using this medicine
Should a rash or skin irritation develop after using the product, or if you notice any other unexpected effect, stop using your medicine and inform your doctor or pharmacist.

Gammaderm®

Bath and Shower Emollient

Soothes, Smoothes
and rehydrates
dry, red, itchy skin

For external use only
200ml

Linderma

Marketing Authorisation holder:
Linderma Ltd, Canon Bridge House, Madley, Herefordshire, HR2 9JF
Marketed by LINDERMA LTD, Madley, Hereford, HR2 9JF
PL 19786/0003

Batch number: Expiry date:

Storing your medicine
Do not use the product after the expiry date printed on the pack.

Remember that your medicine has been prescribed for you. Do not give it to others, even if it seems that they are suffering from the same condition as you.

KEEP ALL MEDICINES OUT OF SIGHT AND REACH OF CHILDREN

If you have any medicine left over after completing the treatment, return it to your pharmacist for safe disposal.

This leaflet was last revised on 16th April 2007

Distributed in the UK by:-
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