HYDRODERM CREAM
PL 20685/0015

UKPAR

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HYDRODERM CREAM
PL 20685/0015

LAY SUMMARY

The MHRA granted Ferndale Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Hydroderm Cream (PL 20685/0015). This is a General Sales List medicine (GSL).

Hydroderm Cream is used to treat red, inflamed, damaged, dry or chapped skin in adults and children, and to protect raw skin areas; it can also be applied to the skin before having a bath to prevent the skin from drying further.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Hydroderm Cream outweigh the risks; hence a Marketing Authorisation has been granted.

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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 Hydroderm Cream (PL 20685/0015) on 8th November 2007. The product is a General Sales List (GSL) product for sale to the general public.

This application was submitted as an abridged application according to Article 10a of Directive 2001/83/EC, as amended, and was submitted with a complete bibliography in support of well-established use.

The product contains the active ingredients white soft paraffin and liquid paraffin; these are emollients and are used extensively to treat dry skin conditions. Emollients may also be used in the treatment of skin diseases such as eczema or psoriasis; they can be used as an adjunct to topical steroids, where a steroid-sparing effect is desirable. It can be used to space treatment with topical steroid or as a diluent for topical steroids, and as a follow-up to treatment with topical steroids. For adults, elderly and children, the cream is applied to the dry skin areas as often as is required and rubbed well into the skin.

As the active ingredients are drug substances for which safety and efficacy is well established it is not considered necessary to conduct additional non-clinical or clinical studies to support this application.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE (WHITE SOFT PARAFFIN)

rINN: White Soft Paraffin, White Petroleum Jelly
Chemical Name: Petrolatum
Other name: Bentley Wax (BW 1832)
Physical form: Semi-solid
Molecular formula: C 20 to C 50- mixture of straight and branched chain paraffin's.
Molecular weight: 500 (mass average molecular weight)
Stereoisomerism/chirality: No
Polymorphism: No
Structure: NA

No DMF or certificate of suitability has been submitted and none is required considering that white soft paraffin is a well-established active substance.

An appropriate specification based on the British Pharmacopoeia has been provided.

An adequate description of the manufacturing process and a flow diagram has been provided.

Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Satisfactory batch analysis data has been provided and complies with the proposed specification.

Appropriate stability data have been generated that support the retest period for the drug substance when stored in the proposed packaging.

DRUG SUBSTANCE (LIQUID PARAFFIN)

rINN: Liquid Paraffin
Chemical Name: Refined Mineral Oil
Molecular formula: A mixture of liquid saturated hydrocarbons.
Physical form: Liquid Oil
Stereoisomerism/chirality:NA
Polymorphism: NA
Structure: NA

Synthesis of the drug substance is in accordance with GMP and complies with the European Pharmacopoeia, this is satisfactory. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis. No DMF or certificate of suitability has been 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.

Satisfactory batch analysis data has been provided and complies with the proposed specification.

Appropriate stability data have been generated that support the retest period for the drug substance when stored in the proposed packaging.

DRUG PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients, namely chlorocresol, cetostearyl alcohol, isopropyl alcohol and cetomacgrogol 1000.All excipients used in the manufacture of the cream are routinely tested for compliance with their respective British Pharmacopoeial monograph; with the exception of cetostearyl alcohol which complies with the European Pharmacopoeial monograph.

Satisfactory certificates of analysis have been provided for all excipients.

None of the excipients used are novel or contain material of animal or human origin.

Manufacture

A full description and a detailed flow-chart of the manufacturing method has been provided. A Good Manufacturing Practice (GMP) certificate has been provided for the manufacturing site.

A satisfactory batch formula has been provided for the manufacture of the product. The manufacturing process has been validated and appropriate in-process controls are applied. Process validation has been carried out on three batches of the product and the results were 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 and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification.

Container Closure System

Product is packaged in either polyethylene jars or polypropylene pump dispensers or tubes composed of aluminium. Specifications and certificates of analysis for all packaging types used have been provided and are satisfactory. The product is packaged in pack sizes of 500g for the polyethylene jars or polypropylene pump dispensers and sizes of 10g and 50g for the aluminium tubes.

Stability

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 2years has been set, which is satisfactory. Storage conditions are “Do not store above 25 degrees” and “Do not freeze”.

Conclusion

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

PRECLINICAL ASSESSMENT

1. GOOD LABORATORY PRACTICE (GLP) ASPECTS

As this is a bibliographic application, no preclinical studies have been submitted. Preclinical data published in the literature have been reviewed for the Preclinical Expert Report (PCER) and generally do not make any reference to GLP. Hence, compliance with the regulations cannot be verified.

2 PHARMACODYNAMICS

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

White soft paraffin is a bleached semi-solid mixture of hydrocarbons, mainly saturated aliphatic compounds, obtained from petroleum. The active complies with the British Pharmacopoeial monograph. Liquid paraffin is a clear, oily, colourless, flavourless and odourless mixture of highly purified aliphatic and cyclic liquid hydrocarbons, also obtained from petroleum. The active complies with the European Pharmacopoeial monograph.

3 TOXICOKINETICS

The PCER does not contain a discussion on the pharmacokinetics of liquid paraffin, white soft paraffin or any of the excipients. Reference is made to a review of fifty papers on the toxicology of mineral oil and petroleum waxes in toiletries and cosmetics. The review confirms that only minimal absorption of the actives occurs.

4 TOXICOLOGY

The literature has been reviewed and a selective and brief summary presented in the PCER. Additional information is provided in the supporting documentation of the application.

Most of the toxicity data reviewed referred to liquid paraffin rather than white soft paraffin but some lifetime studies on the toxicity of petroleum waxes, of which white soft paraffin is one, have been conducted in mice, rats and rabbits by the oral or topical routes. The data do not indicate any carcinogenic risks. Various mineral oils have been tested for correlation between their polycyclic aromatic hydrocarbon (PAH) content and mutagenicity or carcinogenicity. In general, a higher PAH content was found to be associated with mutagenicity and carcinogenicity. It is argued that petroleum waxes are likely to share this correlation between PAH content and mutagenicity or carcinogenicity. Hence, it has been inferred that the highly refined grades of petroleum waxes used as medicinal emollients would have a low PAH content and are not considered to present a mutagenic or carcinogenic risk. This is a reasonable assumption.

At the exposure levels likely with this formulation, there is no evidence of local toxicity upon topical application. However, no consideration is given to the potential for skin irritation or sensitisation or for phototoxicity or photosensitisation of inflamed or damaged skin.

5 EXCIPIENTS

All the excipients comply with either British or European Pharmacopoeial monographs. However, no consideration is given in the PCER to the potential for irritation or sensitisation or for phototoxicity or photosensitisation resulting from the excipients being applied to inflamed or damaged skin.

Assessor's comment

The applicant has provided a brief review of literature and noting the long-term safety in use of the actives and excipients. Both actives have been in use in many formulations for many years with few adverse outcomes.

6 PRECLINICAL EXPERT REPORT

The Preclinical Expert Report was written by an appropriately qualified person.

7. ENVIRONMENTAL RISK ASSESSMENT (ERA)

A satisfactory justification as to why an ERA statement was not provided.

8 SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

This is satisfactory.

9 CONCLUSION

The actives in this formulation are well-known and it is unlikely that they will pose a risk to human health. It is recommended that a Marketing Authorisation be granted.

CLINICAL ASSESSMENT

DOSE & DOSE SCHEDULE

Adults, Elderly and Children

The cream should be applied to the dry skin areas as often as is required and rubbed well into the skin.

TOXICOLOGY

A pre-clinical expert report was written by a suitable qualified person. No new toxicology data have been submitted or are required. A literature review has been conducted and the conclusion is that there is no evidence to suggest that pharmacopoeial grades of mineral oil and petroleum waxes used in skin care applications are likely to cause local or systemic toxic effects.

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CLINICAL PHARMACOLOGY

No new pharmacology data has been submitted.

EFFICACY

No formal efficacy data derived from studies of patients have been provided for this application and none are required.

SAFETY

No formal safety data have been provided for this application and none are required.

EXPERT REPORT

A satisfactory Clinical Expert Report has been submitted with appropriate CV.

SUMMARY OF PRODUCT CHARACTERISTICS

This is satisfactory.

PATIENT INFORMATION LEAFLET

This is satisfactory.

LABELLING

This is satisfactory.

MAA

The MAA form is satisfactory.

DISCUSSION

This is a national abridged bibliographical application for Hydroderm Cream.
Liquid paraffin and white soft paraffin are well established as constituents of emollient creams and ointments for the treatment of dry skin conditions.
The pre-clinical and expert reports review the published literature and both recommend the approval of the applicant product under the conditions specified in the SPC.

RECOMMENDATIONS

The efficacy and safety of the product are satisfactory for the grant of a product licence.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Hydroderm Cream 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 applications of this type.

EFFICACY

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory.

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 and liquid paraffin is considered to have demonstrated the therapeutic value of the compounds. The risk benefit is, therefore, considered to be positive.

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 28th October 2003
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 1st August 2005.
3	Following assessment of the applications the MHRA requested further information relating to the quality dossiers on 17th January 2006 and 8th March 2006.
4	The applicant responded to the MHRA's requests, providing further information on 27th June 2006 and 31st July 2007 for the quality sections.
5	The applications were determined on 8th November 2007

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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Hydroderm Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

White Soft Paraffin Ph Eur 8.5% w/w

Liquid Paraffin Ph Eur 5.0% w/w

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cream.

A smooth white cream.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Hydroderm Cream is an emollient, moisturising and protective cream for the symptomatic treatment of red inflamed, damaged, dry or chapped skin, the protection of raw skin areas and as a pre-bathing emollient for dry/eczematous skin to alleviate drying areas. Hydroderm Cream can be used as an adjunct to topical steroids, where a steroid-sparing effect is desirable. It can be used to space treatment with topical steroids. Hydroderm Cream can also be used as a follow-up to treatment with topical steroids.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Adults, Elderly and children

The cream should be applied to the dry skin areas as often as is required and rubbed well into the skin.

4.3 CONTRAINDICATIONS

There are no absolute contra-indications to the use of the cream other than hypersensitivity to any of the ingredients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

One of the ingredients in Hydroderm Cream, cetostearyl alcohol, may cause local skin reactions (e.g. contact dermatitis).

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

None known. No interaction studies have been undertaken.

4.6 PREGNANCY AND LACTATION
No special precautions or dosage requirements are indicated for use during pregnancy or lactation.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
None known.

4.8 UNDESIRABLE EFFECTS
Rarely, mild skin reactions have been observed.

4.9 OVERDOSE
Not applicable.

5 PHARMACOLOGICAL PROPERTIES
5.1 PHARMACODYNAMIC PROPERTIES
ATC Code: D02A C

Emollients and Protectives

The ingredients provide emollient or moisturising action on dry or chapped skin.

5.2 PHARMACOKINETIC PROPERTIES
Not applicable due to topical administration and direct action on the skin.

5.3 PRECLINICAL SAFETY DATA
There are no pre-clinical data of relevance to the prescriber that are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS
6.1 LIST OF EXCIPIENTS
Chlorocresol
Cetomacrogol 1000
Cetostearyl alcohol
Isopropyl alcohol
Anhydrous sodium dihydrogen phosphate
Dilute phosphoric acid
Purified water

6.2 INCOMPATIBILITIES
None known.

6.3 SHELF LIFE
2 years.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Do not store above 25°C.

Store in the original container.

6.5 NATURE AND CONTENTS OF CONTAINER

Aluminium epoxy-phenolic resin lined tubes with polypropylene screw cap containing 10 g cream for use as a professional sample only.

Aluminium epoxy-phenolic resin lined tubes with polypropylene screw cap containing 50 g cream.

HDPE jar with polypropylene screw cap containing 500 g cream.

HDPE bottle with polypropylene pump dispenser containing 500 g cream.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Ferndale Pharmaceuticals Limited
12 York Place
Leeds
LS1 2DS
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

20685/00015

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

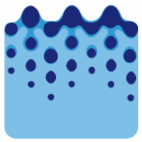
08/11/2007

10 DATE OF REVISION OF THE TEXT

08/11/2007

PATIENT INFORMATION LEAFLET

What you should know about



Hydroderm® CREAM

White Soft Paraffin Ph Eur 8.5% w/w
Liquid Paraffin Ph Eur 5% w/w

Please read this leaflet carefully before you start to use this medicine.

This leaflet only gives a summary of the information available on your medicine.

If you have any questions or are not sure about anything, ask your doctor or pharmacist.

What is in your medicine?
The name of your medicine is Hydroderm Cream. It contains the active ingredients white soft paraffin Ph Eur 8.5% w/w and liquid paraffin Ph Eur 5% w/w. It also contains the following ingredients: chlorocresol, cetomacrogol, cetostearyl alcohol, dilute phosphoric acid, sodium dihydrogen phosphate, isopropyl alcohol and purified water.

The cream is available in a pump dispenser or securitub containing 500g, or in tubes containing 50g.

Hydroderm Cream is an emollient, moisturising and protecting cream. It helps to soothe, smooth and hydrate the skin and prevents moisture loss.

The marketing authorisation for Hydroderm Cream is held by:
Ferndale Pharmaceuticals Ltd, 12 York Place, Leeds LS1 2DS, England.

The manufacturer of Hydroderm Cream is:
Bioglan AB, PO Box 50310, SE-202 13 Malmö, Sweden

What is your medicine for?
Hydroderm Cream is used to treat red, inflamed, damaged, dry or chapped skin in adults and children, and to protect raw skin areas. If you suffer from eczema and your skin is dry, the cream can be applied before having a bath to prevent your skin from drying any further.

Hydroderm Cream can also be used during or after treatment with topical steroid creams, gels or ointments.

Before using your medicine
Do not use Hydroderm Cream if you, or your child, have ever had an allergic reaction to it or any of its ingredients. Tell your doctor so that he or she can give you, or your child, another medicine.

How to use your medicine
Hydroderm Cream is for external use only.

Always follow the instructions of your doctor or pharmacist. Check the label for directions on how to use your medicine. Ask your doctor or pharmacist if you are not sure.

Unless your doctor has given you different advice, the cream should be thinly applied to cover the affected area completely, massaging gently and thoroughly into the skin. Your doctor will tell you when, how often and for how long you should use the cream.

If you forget to use your cream at the right time, use the usual amount as soon as you remember, then carry on as before.

Your cream contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).

If your condition worsens, or your symptoms persist beyond the period of treatment specified by your doctor, you should consult your doctor or pharmacist.

After using your medicine
As with all medicines, Hydroderm Cream can have undesirable side effects. Rarely, a few people may suffer from mild skin reactions such as itching, and a rash after using the cream. If this occurs you should tell your doctor as soon as possible.

If you experience any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Keeping your medicine safe
Do not use any medicine after the expiry date stated on the packaging.

Keep your medicine in a safe place where children cannot see it or reach it. Your medicine could harm them.

Your cream should be stored below 25°C, and kept in its original container.

This leaflet does not contain the complete information on Hydroderm Cream. If you have any questions or are not sure about anything ask your doctor or pharmacist.

This information applies only to Hydroderm Cream.

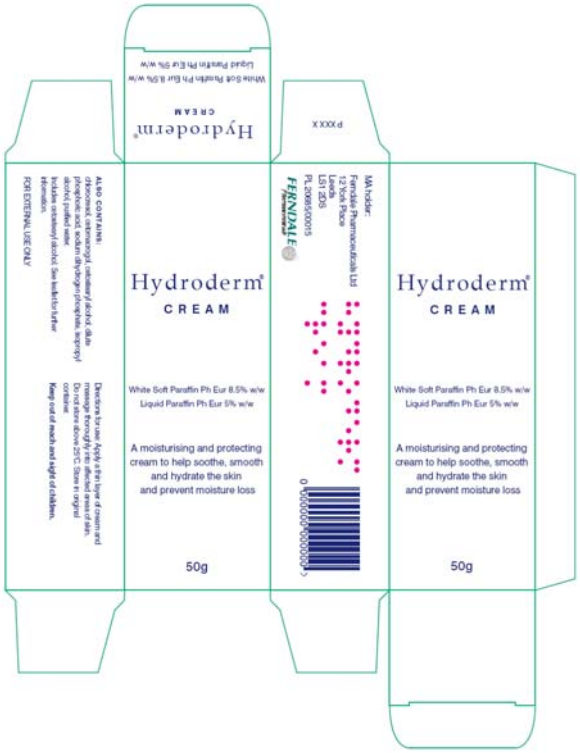
Date of preparation or last review: June 2007
PXXXXX
PL 20685/00015

FERNDALE Pharmaceuticals
12 York Place, Leeds LS1 2DS, England.

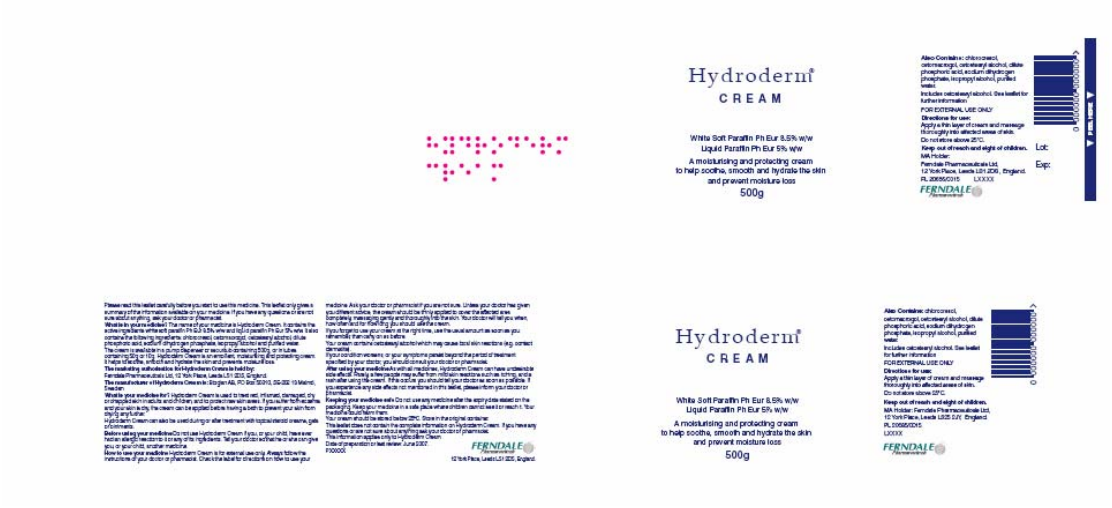
LABELLING
PL 20685/0015

CARTON-
10g

CARTON-
50g



CARTON-
500g


Hydroderm
CREAM
White Soft Paraffin Ph Eur 8.5% w/w
Liquid Paraffin Ph Eur 5% w/w
A moisturising and protecting cream
to help soothe, smooth and hydrate the skin
and prevent moisture loss
500g
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