HYDROCORTISONE CREAM 1%
PL 13606/0181-2
PL 13606/0191

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency granted Co-pharma Ltd, Marketing Authorisations for the medicinal product, Hydrocortisone Cream 1% (PL 13606/0181) and its duplicate licences (PL 13606/0182 and PL 13606/0191) on 13th September 2011. This is a P licensed medicine, available only from pharmacies, under the supervision of a pharmacist.

This cream is used to treat the following conditions:

- irritant dermatitis (inflammation of the skin)
- contact allergic dermatitis
- insect bite reactions
- mild to moderate eczema (inflammation of the skin)

These applications are considered to be identical to a previously granted licence for Hydrocortisone Cream 1% (PL 13606/0022) on 9th October 1996 to the same Marketing Authorisation Holder.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of Hydrocortisone Cream 1% (PL 13606/0181-2 and PL 13606/0191) outweigh the risks; hence Marketing Authorisations have 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 MHRA granted Co-pharma Limited, Marketing Authorisations for the medicinal products, Hydrocortisone Cream 1% (PL 13606/0181) and its duplicate licences (PL 13606/0182 and PL 13606/0191), on 13th Septemeber 2011. The product is a P licensed medicine.

These are simple, abridged, 'informed consent' applications submitted according to Article 10(c) of EC Directive 2001/83 (as amended), cross-referencing the Marketing Authorisaion for Hydrocortisone Cream 1% (PL 13606/0022), licensed to Co-pharma Limited on 9th October 1996. The reference product has been authorised in the EEA for over 10 years.

Hydrocortisone Cream 1% is to be applied topically in the treatment of irritant dermatitis, contact allergic dermatitis, insect bite reactions and mild to moderate eczema.

No new data were submitted nor were they necessary for these simple applications, as the data is identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) has been generated for it.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 13606/0181-2 & PL 13606/0191
PROPRIETARY NAME: Hydrocortisone Cream 1%
ACTIVE: Hydrocortisone 1%
COMPANY NAME: Co-pharma Ltd
E.C. ARTICLE: Article 10c of Directive 2001/83/EC
LEGAL STATUS: P

1. INTRODUCTION

This is a simple, informed consent application forHydrocortisone Cream 1% submitted under Article 10c of Directive 2001/83/EC. The proposed Marketing Authorisation Holder is Co-pharma Ltd, Unit 4, Metro Centre, Tolpits Lane, Watford, Hertfordshire, WD18 9SS, UK.

The application cross-refers to Hydrocortisone Cream 1% (PL 13606/0022) authorised to the same Marketing Authorisation Holder on 9th October 1996. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name

The proposed name of the product is for Hydrocortisone Cream 1%. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Hydrocortisone Cream 1% contains the active ingredient, micronised hydrocortisone 1% w/w in a white cream. The medicinal product is licensed for marketing in collapsible aluminium tubes, with a membrane seal at the nozzle and a white plastic cap for re-closure after piercing membrane. The tubes are packaged with the Patient Information Leaflet (PIL) into cardboard outer cartons in pack sizes of 10 g and 15 g. The MAH has stated tha not all pack sizes may be marketed.

The approved shelf-life (60 months) and storage conditions (Do not store above 25°C) are identical to the details registered for the cross-reference product.

2.3 Legal status

This product is a P licensed meidine available only from pharmacies, under the supervision of a pharmacist.

2.4 Marketing authorisation holder/Contact Persons/Company

The proposed Marketing Authorisation Holder is Co-pharma Ltd., Unit 4, Metro Centre, Tolpits Lane, Watford, Hertfordshire, WD18 9SS, UK.

The Quality Person (QP) responsible for pharmacovigilance is stated and their curriculum vita has been included.

2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specification is in-line with the details registered for the cross-reference product.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance
The applicant has provided a declaration confirming that there are no materials of human or animal origin contained in or used in the manufacturing process for the proposed product. None of the excipients are soureced from genticially modified organisms.
This is consistent with the cross-reference product.

3. EXPERT REPORT
A satisfactory quality overall summary has been prepared by an appropriately qualified expert. The CV of the expert was provided.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product (white cream) is identical to that of the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)
The approved SmPC is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET (PIL)/CARTON
PIL
The PIL is satisfactory and in line with the approved SmPC and has been prepared in the user-tested format.

The package leaflet for the product, Hydrocortisone Cream 1% (PL 13606/0181), has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

Carton and label
Mock-ups of the labelling have been provided and are satisfactory. The approved artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has included the name of the product in Braille on the outer packaging.

7. CONCLUSIONS

The data submitted with these applications are acceptable. Marketing Authorisations were, therefore, granted.

NON-CLINICAL ASSESSMENT

These are simple, abridged, 'informed consent' applications made under Article 10c of EC Directive 2001/83 (as amended). These applications are identical to the reference product Hydrocortisone Cream 1% (PL 13606/0022) authorised to the same Marketing Authorisation Holder, therefore, no new non-clinical data has been supplied with this application and none are required. A non-clinical overview report has been written by a suitably qualified person and is satisfactory. The CV of the non-clinical expert has been supplied.

The marketing authorisation holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As this application is identical to an already authorised reference product, it is not expected that the environmental exposure to hydrocortisone will increase following the marketing approval of the proposed product.

CLINICAL ASSESSMENT

These are simple, abridged, 'informed consent' application made under Article 10(c) of EC Directive 2001/83 (as amended), cross-referring to Hydrocortisone Cream 1% (PL 13606/0022) authorised to the same Marketing Authorisation Holder.

No new clinical data has been supplied with this application and none are required. A clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the clinical expert has been supplied.

The marketing authorisation holder (MAH) has provided adequate justification for not submitting a Risk Management Plan (RMP). As this application is identical to an already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference product has been in use for many years and the safety profile of the active is well-established.

The MAH has provided a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the MAH has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for these applications are consistent with those previously assessed for the cross-reference product and as such has been judged to be satisfactory.

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

EFFICACY
These applications are considered identical to the previously granted licence for Hydrocortison Cream 1% (PL 13606/0022) authorised to the same Marketing Authorisation Holder.

No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE
The approved SmPC, PIL and labelling are satisfactory, and consistent with those for the cross-reference product.

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. This application is identical to the reference product. The language used for the purpose of user testing the PIL was English. The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

Mock-ups of the labeling have been provided and are satisfactory. The approved labeling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging. The MAH has committed to submitting mock-ups for currently mock-ups for currently unmarketed packs to the UK regulatory authority for approval before those packs are commercially marketed.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. The risk benefit is, therefore, considered to be positive.

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PL 13606/0191

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 7 September 2010.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 24 September 2010.
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 30 November 2010, 14 February 2011, and 24 May 2011.
4	The applicant responded to the MHRA's requests, providing further information on 24 January 2011, 13 April 2011 and 1 July 2011.
5	The application was determined on 13 September 2011.

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STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

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PL 13606/0181-2
PL 13606/0191

SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SmPC) for Hydrocotisone Cream 1% (PL 13606/0181-2 and PL 13606/0191) is as follows:

1 NAME OF THE MEDICINAL PRODUCT
Hydrocortisone Cream 1%

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Cream containing 1% micronised hydrocortisone

For excipients, see 6.1

3 PHARMACEUTICAL FORM
Cream

White Cream

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Hydrocortisone has topical anti-inflammatory activity of value in the treatment of irritant dermatitis, contact allergic dermatitis, insect bite reactions and mild to moderate eczema.

4.2 Posology and method of administration
Use sparingly over a small area once/twice a day for a maximum period of 1 week.
Wash hands after application unless these are the intended site of treatment.
If the condition is not improved, consult your doctor.

4.3 Contraindications
Hypersensitivity to any of the ingredients.
Use on the eyes, face or ano-genital region
Use on broken or infected skin, including skin lesions caused by infections with viruses (e.g. herpes infections such as cold sores, chicken pox), fungi (e.g. athlete's foot, ringworm, thrush) or bacteria (e.g. impetigo)
Acne

The product is not recommended for use on children under 10 years of age without medical supervision.

4.4 Special warnings and precautions for use
Do not use under an occlusive dressing or napkin because of the potential for increased absorption of hydrocortisone and subsequent risk of adrenal suppression.

In infants and children, long-term continuous topical therapy with hydrocortisone should be avoided where possible, as adrenal suppression can occur even without occlusion. Treatment should be limited to a maximum of 7 days.

Care should be taken to avoid transfer of product to the eye or periorbital region. Increased intraocular pressure or glaucoma has been reported following use of topical steroids around the eye.

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

4.6 Pregnancy and lactation

There is inadequate evidence of safety in human pregnancy. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-growth retardation. There may therefore be a very small risk of such effects in the human foetus.

There is no evidence against use in lactating women. However, caution should be exercised when hydrocortisone ointment is administered to nursing mothers. In this event, the product should not be applied to the chest area.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Hydrocortisone preparations are usually well tolerated, but if any signs of hypersensitivity including allergic contact dermatitis or worsening of the original condition appear, treatment should be stopped immediately.

Epidermal thinning, telangiectasia and striae may occur in areas of high absorption such as skin folds. Skin pigmentation changes and hypertrichosis may occur after application of topical steroids.

Although less likely than with other more potent topical corticosteroids, prolonged use of large amounts or treatment of extensive areas can result in sufficient systemic absorption to produce suppression of the hypothalamic-pituitary-adrenal axis and the clinical features of Cushing's syndrome (see section 4.4). These effects are more likely to occur in infants and children, and if occlusive dressings are used. In infants the napkin may act as an occlusive dressing.

Striae may occur in intertriginous areas.

4.9 Overdose

Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse the features or hypercorticism may appear and in this situation topical steroids should be discontinued.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Hydrocortisone is an anti-inflammatory steroid. Its anti-inflammatory action is due to reduction of the vascular component of the inflammatory response and reduction of the formation of inflammatory fluid and cellular exudates. The granulation reaction is also decreased due to the inhibition effect of hydrocortisone on connective tissue. Stabilisation of most cell granules and lysomal membranes decreases the mediators involved in inflammatory response and reduces release of enzymes involved in prostaglandin synthesis. The vasoconstrictor action of hydrocortisone may also contribute to its anti-inflammatory activity.

5.2 Pharmacokinetic properties

Absorption: Topically applied steroids are absorbed to a significant extent only if applied to broken skin, to very large areas or under occlusive dressings.

Distribution: Corticosteroids are rapidly distributed to all body tissues. They cross the placenta and may be excreted in small amounts in breast milk.
Metabolism: Hydrocortisone is metabolised mainly in the liver, but also the kidney, to various degraded and hydrogenated forms such as tetrahydrocortisone.
Elimination: Hydrocortisone is excreted in the urine, mostly conjugated as glucuronides. Only very small amounts of unchanged hydrocortisone are excreted.

5.3 Preclinical safety data

Adverse effects of hydrocortisone are due to its effects on electrolyte balance, metabolism and particularly adrenal suppression. Topical use of hydrocortisone has only rarely been associated with systemic side effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetomacrogol Emulsifying Wax
Chlorocresol
Liquid Paraffin
Macrogol 300
White Soft Paraffin
Purified Water

6.2 Incompatibilities

None known

6.3 Shelf life

60 Months

6.4 Special precautions for storage

Do not Store above 25^0 C

6.5 Nature and contents of container

A collapsible aluminium tube, with a membrane seal at the nozzle, internal epoxy lacquer, latex endseal band in the crimp seal area and a white plastic cap for re closure after piercing membrane.

Pack Sizes are 10 and 15g. Not all pack sizes are marketed

6.6 Special precautions for disposal

No special precautions are required

7 MARKETING AUTHORISATION HOLDER

Co-pharma Ltd
Unit 4, Metro Centre
Tolpits Lane
Watford
Hertfordshire
WD18 9SS

8 MARKETING AUTHORISATION NUMBER(S)

PL 13606/0181
PL 13606/0182
PL 13606/0191

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/09/2011

10 DATE OF REVISION OF THE TEXT

13/09/2011

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PATIENT INFORMATION LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

HYDROCORTISONE CREAM 1%

{Hydrocortisone}

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others.
- It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT HYDROCORTISONE CREAM IS AND WHAT IT IS USED FOR

Hydrocortisone cream is a topical anti-inflammatory used in the treatment of
- irritant dermatitis (inflammation of the skin)
- contact allergic dermatitis
- insect bite reactions
- mild to moderate eczema (inflammation of the skin)

2. BEFORE YOU USE HYDROCORTISONE CREAM

Do not use Hydrocortisone Cream
- if you are allergic (hypersensitive) to hydrocortisone or any of the other ingredients of Hydrocortisone Cream (See section 6, Further information)
- if you are a child under 10 years old without medical supervision
- on cut or infected skin such as cold sores, herpes, impetigo (bacterial skin infection), athlete's foot, chicken pox, ringworm or thrush.
- on the eyes and face or ano-genital area
- if you have acne
- under a water or air tight dressing as this may increase the absorption of hydrocortisone through the skin

Take special care with Hydrocortisone Cream
- treatment of children should be restricted to no more than 7 days

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

Should not be used in pregnancy and breastfeeding without medical advice.

3. HOW TO USE HYDROCORTISONE CREAM

Always use Hydrocortisone cream exactly as your doctor has told you.
You should check with your doctor or pharmacist if you are not sure.
For cutaneous (external) use only. Wash your hands after use unless the hands are the area being treated.
Use sparingly over a small area once or twice a day for a maximum period of one week.
If the condition is not improved after this time, consult your doctor

If you use too much cream
If you use too much cream or if you or someone else accidently swallows some cream, contact your doctor or go to your nearest hospital emergency department immediately, take the cream with you so the doctor knows what you have taken.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Hydrocortisone Cream can cause side effects, although not everybody gets them.

Hydrocortisone preparations are usually well tolerated, but if any signs of hypersensitivity appear, application should stop immediately; this may include allergic contact dermatitis (rash which may be red, itchy and burning) or worsening of your condition.

Prolonged use of large amounts or treatment of extensive areas can result in features of Cushing's syndrome (symptoms include increased fat on the body, fragile or discoloured skin, weakening of bones, excessive hair growth, changes in periods in women, altered sexual function in men, increased thirst and urination, tiredness, irritability, anxiety or depression). If you experience these symptoms or are worried contact your doctor.

Other side effects:
- Stretch marks may occur in areas where the skin may rub, for example at the joints and at folds in the skin.
- Thinning of the skin, changes in skin pigmentation (colour) and hair growth.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE HYDROCORTISONE CREAM

Keep out of the reach and sight of children.
Do not use Hydrocortisone Cream after the expiry date stated on the carton. The expiry date refers to the last day of that month.
Medicines should not be disposed of via wastewater or household waste.
Ask your pharmacist how to dispose of medicines no longer required.
These measures will help to protect the environment.

6. FURTHER INFORMATION

What Hydrocortisone Cream contains
The active substance is micronised hydrocortisone
The other ingredients are Cetomacrogol emulsifying wax, Chlorocresol,
Liquid paraffin, Macrogol 300, White soft paraffin, Purified water

What Hydrocortisone Cream looks like and contents of the pack
A collapsible aluminium tube, with a membrane seal at the nozzle, internal epoxy lacquer, latex endseal band in the crimp seal area and a white plastic cap for reclosure after piercing membrane.

Hydrocortisone Cream is provided in a 15 g tube.

Marketing Authorisation Holder and Manufacturer
Co-Pharma Ltd
Unit 4 Metro Centre, Tolpits Lane, Watford, Hertfordshire, WD18 9SS

This medicinal product is authorised in the Member States of the EEA under the following names: Not applicable

This leaflet was last approved in {08/2011}.

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LABELLING

PLEASE NOTE THAT THE LABELLING FOR PL 13606/0182 & 0191 ARE IDENTICAL TO THAT SHOWN BELOW EXCEPT FOR THE PL NUMBER