Nutraplus Duo 10%/5% w/w Cream
(urea, lactic acid)
PL 10590/0055

UKPAR

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(urea, lactic acid)

PL 10590/0055

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Galderma (UK) Limited a Marketing Authorisation (licence) for the medicinal product, Nutraplus Duo 10%/5% w/w Cream (PL 10590/0055), on 20th April 2011. This is a P licensed medicine, available only from pharmacies, under the supervision of a pharmacist.

This cream is used as a moisturising cream for the treatment of dry, rough, scaly skin such as eczema and similar conditions. The active substances in Nutraplus Duo 10%/5% w/w Cream are urea and lactic acid, which act as moisturisers. This helps make your skin soft and supple.

This application is considered to be identical to a previously granted licence for Calmurid 10% / 5% w/w Cream (PL 10590/0009), authorised to Galderma (UK) Limited on 9th February 1993. The proposed and reference products are identical.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of Nutraplus Duo 10%/5% w/w Cream outweigh the risk; hence a Marketing Authorisation has been granted.
Nutraplus Duo 10%/5% w/w Cream
(urea, lactic acid)
PL 10590/0055

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Galderma (UK) Limited a Marketing Authorisation for the medicinal product, Nutraplus Duo 10%/5% w/w Cream (PL 10590/0055), on 20th April 2011. The product is a P licensed medicine.

This is a simple, abridged, ‘informed consent’ application submitted according to Article 10(c) of EC Directive 2001/83 (as amended), cross-referencing the Marketing Authorisation for Calmurid 10%/5% w/w Cream (PL 10590/0009), licensed to Galderma (UK) Limited on 9th February 1993.

Nutraplus Duo 10%/5% w/w Cream is to be applied topically for the correction of hyperkeratosis and dryness in ichthyosis and allied conditions characterised by dry, rough, scaly skin.

Urea at a concentration of 10% has keratolytic, anti-microbial, anti-pruritic and hydrating effects on the skin. Lactic acid has keratolytic, hydrating and anti-microbial properties also. Treatment of ichthyotic patients shows a parallel between clinical improvement and increase in the otherwise depressed binding capacity of the horny layer.

The pharmacovigilance system as described by the Marketing Authorisation Holder (MAH) fulfils the requirements and provides adequate evidence that the MAH has the services of a Qualified Person (QP) 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.

As the application is for a product that is identical to an already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, routine pharmacovigilance activities are proposed and a risk minimisation system is not considered necessary. The reference product has been in use for many years and the safety profiles of the actives are well-established.

The MAH has provided adequate justification for the absence of an Environmental Risk Assessment (ERA). The application is submitted as an ‘informed consent’ application. The product is identical to the reference product, Calmurid 10% / 5% w/w Cream (PL 10590/0009), available on the UK market since 1993, and does not present any additional environmental risk compared to the reference product. The active substances, urea and lactic acid, both have a very high environmental exposure and it is expected that increase in their environmental exposure due to use of Nutraplus Duo 10%/5% w/w Cream will be negligible.

No new data were submitted nor was it necessary for this simple application, as the data are 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 PAR was generated for it.
PHARMACEUTICAL ASSESSMENT

1. INTRODUCTION

This is a simple abridged application, submitted under Article 10(c) of Directive 2001/83/EC (as amended) for Nutraplus Duo 10%/5% w/w Cream. The proposed Marketing Authorisation Holder (MAH) is Galderma (UK) Limited.

The reference product is Calmurid 10% / 5% w/w Cream (PL 10590/0009), authorised to Galderma (UK) Limited on 9th February 1993. The proposed and reference products are identical.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The approved name of the product is Nutraplus Duo 10%/5% w/w Cream. The product has been named in line with current requirements and the product name is acceptable.

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

Nutraplus Duo 10%/5% w/w Cream contains the active ingredients, urea 10% (100mg/g) and lactic acid 5% (50mg/g) in a homogenous, white, oil-in-water cream. The medicinal product is licensed for marketing in white polyethylene tubes, fitted with polypropylene screw-caps, which are packaged with the Patient Information Leaflet (PIL) into cardboard outer cartons in pack sizes of 15g, 20g, 30g, 50g and 100g. The medicinal product is also licensed for marketing in white polypropylene pump dispensers in pack sizes of 400g and 500g. The MAH has stated that not all pack sizes may be marketed. Full details of container closure systems are provided in the Summary of Product Characteristics (SmPC). The container closure systems and pack sizes are identical to those stated for the reference product.

The approved shelf-life (24 months) and storage conditions (‘Do not store above 25°C. Do not refrigerate or freeze’) are identical to the details registered for the cross-reference product.

2.3 Legal status

The product is a P licensed medicine available only from pharmacies, under the supervision of a pharmacist.
2.4 Marketing Authorisation Holder / Contact Persons / Company
The proposed Marketing Authorisation Holder is ‘Galderma (UK) Limited, Meridien House, 69-71 Clarendon Road, Watford, Herts. WD17 1DS, UK’.

The Qualified Person (QP) responsible for pharmacovigilance was stated and their CV 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 consistent 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
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 sourced from genetically modified organisms.

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 (homogenous, white, oil-in-water 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) / LABELLING

PIL
The patient information leaflet has been prepared in the user-tested format and in line with the details registered for the cross-reference product. The approved PIL is satisfactory.

PIL user-testing has been accepted, based on bridging to the successful user-testing of the PIL for the reference product, Calmurid 10% / 5% w/w Cream (PL 10590/0009). The text, content and layout of the proposed PIL are essentially identical to the approved PIL for the reference product. The bridging is accepted.

Labelling
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.

The MAH has committed to submitting mock-ups for currently unmarketed packs to the UK regulatory authority for approval before those packs are commercially marketed.

7. CONCLUSIONS
The grounds for this application are considered adequate. A Marketing Authorisation was therefore granted.
NON-CLINICAL ASSESSMENT

This is a simple, abridged, ‘informed consent’ application made under Article 10(c) of EC Directive 2001/83 (as amended).

No new non-clinical data have been supplied with this application and none are required for an application of this type. A non-clinical overview 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 Environmental Risk Assessment (ERA).
**CLINICAL ASSESSMENT**

This is a simple, abridged, ‘informed consent’ application made under Article 10(c) of EC Directive 2001/83 (as amended), cross-referring to the Marketing Authorisation for Calmurid 10% / 5% w/w Cream (PL 10590/0009).

No new clinical data have been supplied with the application, and none are required for applications of this type. A clinical overview has been written by a suitably qualified person and is satisfactory. The CV of the clinical expert has been supplied.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

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

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

CLINICAL
This application is considered identical to the previously granted licence for Calmurid 10% / 5% w/w Cream (PL 10590/0009, Galderma (UK) Limited).

No new or unexpected safety concerns arise from this application.

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

PIL user-testing has been accepted, based on a bridging statement provided by the applicant making reference to the successful user-testing of the PIL for the reference product, Calmurid 10% / 5% w/w Cream (PL 10590/0009). The bridging is accepted.

Mock-ups of the labelling have been provided and are satisfactory. The approved labelling 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 unmarketed packs to the UK regulatory authority for approval before those packs are commercially marketed.

BENEFIT-RISK 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 benefit: risk ratio is considered to be positive.
Nutraplus Duo 10%/5% w/w Cream

(urea, lactic acid)

PL 10590/0055

STEPS TAKEN FOR ASSESSMENT

1  The MHRA received the Marketing Authorisation application on 7th July 2010

2  Following standard checks and communication with the applicant the MHRA considered the application valid on 4th August 2010

3  Following assessment of the application the MHRA requested further information relating to the quality dossier on 20th October 2010 and 21st January 2011

4  The applicant responded to the MHRA’s requests, providing further information for the quality sections on 21st December 2010 and 22nd February 2011 respectively

5  The application was determined on 20th April 2011
Nutraplus Duo 10%/5% w/w Cream

(urea, lactic acid)

PL 10590/0055

STEPS TAKEN AFTER AUTHORISATION

Not applicable
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Nutraplus Duo 10%/5% w/w Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One gram of cream contains 100 mg of Urea and 50 mg of Lactic acid.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Cream
A homogenous, white, oil-in-water cream

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
To be applied topically for the correction of hyperkeratosis and dryness in ichthyosis and allied conditions characterised by dry, rough, scaly skin.

4.2 Posology and method of administration
For external use only.
Adults, elderly and children:
A thick layer of Nutraplus Duo is applied twice daily after washing the affected area. The cream is left on the skin for 3-5 minutes and then rubbed lightly in. Excess cream should be wiped off the skin with a tissue, not washed off. Frequency of application can be reduced as the patient progresses. In hyperkeratosis of the feet apply Nutraplus Duo as above after soaking the feet in warm water for 15 minutes and drying with a rough towel.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients

4.4 Special warnings and precautions for use
Nutraplus Duo is acidic and hypertonic and can cause smarting if applied to raw areas, fissures or mucous membranes. Where this is a barrier to therapy the use of Nutraplus Duo diluted 50% with aqueous cream B.P. for one week should result in freedom from smarting upon use of Nutraplus Duo.

4.5 Interaction with other medicinal products and other forms of interaction
Low pH of cream might affect stability of other drugs.

4.6 Pregnancy and lactation
There is no specific data available regarding the use in pregnant women and during lactation.

4.7 Effects on ability to drive and use machines
Nutraplus Duo has no or negligible influence on the ability to drive and use machines.
4.8 Undesirable effects
Nutraplus Duo is acidic and hypertonic and can cause smarting if applied to raw areas, fissures or mucous membranes.

4.9 Overdose
Unlikely. In the case of smarting, wash the cream off.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Carbamide products

ATC code: D02AE

Urea at a concentration of 10% has keratolytic, anti microbial, anti pruritic and hydrating effects on the skin. Lactic acid has keratolytic, hydrating and anti microbial properties also. Treatment of ichthyotic patients shows a parallel between clinical improvement and increase in the otherwise depressed binding capacity of the horny layer.

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 those already included in other sections of the SmPC

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Glyceryl Monostearate
Betaine Monohydrate
Diethanolamine Cetylphosphate (``Amphisol``)
Hard Fat
Cholesterol
Sodium chloride
Purified water

6.2 Incompatibilities
The low pH due to lactic acid means care in choice of other packages or other drugs admixed.

6.3 Shelf life
24 months.

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

6.5 Nature and contents of container
Tubes
White low density polyethylene tubes fitted with white polypropylene screw caps
Package sizes: 15, 20, 30, 50, 100 g.

Pump dispenser
White polypropylene bottle fitted with a white polyethylene closure and a natural polyethylene follower plate.
Package sizes: 400, 500 g.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Not relevant.

7 MARKETING AUTHORISATION HOLDER
Galderma (UK) Limited
Meridien House
69-71 Clarendon Road
Watford
Herts.
WD17 1DS
UK

8 MARKETING AUTHORISATION NUMBER(S)
PL 10590/0055

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
20/04/2011

10 DATE OF REVISION OF THE TEXT
20/04/2011
PATIENT INFORMATION LEAFLET

NutraPlus Duo
10% / 5% W/W CREAM

PACKAGE INFORMATION FOR THE USER
Nutraplus Duo 10% / 5% w/w Cream
Urea 10% w/w
Lactic Acid 5% w/w

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However, you still need to use Nutraplus Duo carefully to get the best results from it.
- Keep this leaflet. You may need to refer to it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve.
- If any of the side effects gets serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Nutraplus Duo is and what it is used for
2. Before you use Nutraplus Duo
3. How to use Nutraplus Duo
4. Possible side effects
5. How to store Nutraplus Duo
6. Further information

1. What Nutraplus Duo is and what it is used for
- Your doctor or pharmacist has recommended this cream for use as a moisturising cream for the treatment of dry, rough, scaly skin such as eczema and similar conditions.
- The active substances in Nutraplus Duo are urea and lactic acid which act as moisturisers. This helps make your skin soft and supple.

2. Before you use Nutraplus Duo
Do not use Nutraplus Duo if you are:
- Allergic (hypersensitive) to urea or lactic acid or any of the other ingredients of Nutraplus Duo. Please check by reading the list of ingredients in section 6. If you answer yes, you must inform your doctor before starting treatment.
- Please seek immediate medical attention if you experience symptoms of an allergic reaction. Signs or symptoms of a severe allergic reaction may include a rash, with or without itching, swelling of the face, eyelids or lips and difficulty in breathing.

Take special care with Nutraplus Duo
- Avoid contact with the eyes, eyelids, lips and other mucous surfaces. Upon accidental contact, rinse the affected area with clean water.
- Nutraplus Duo may cause stinging if applied to damaged skin (raw cracked areas or cracked skin) or sensitive areas of the body such as the mouth or nostrils.

Using other medicines
- This cream might affect other medicines that you apply to your skin. Tell your doctor or pharmacist if you are using other medicines in this way.
- Please tell your doctor or pharmacist if you are using or have recently used any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding
- You should not use Nutraplus Duo and tell your doctor if you are pregnant, planning to become pregnant or are breast-feeding.
- Your doctor will then decide whether you should use Nutraplus Duo.

Ask your doctor or pharmacist for advice before taking any medicine.
Please read the back of this leaflet.
3. How to use Nutraplus Duo

Always use Nutraplus Duo exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

- Nutraplus Duo Cream is for EXTERNAL USE ONLY.
- First, gently wash and dry the affected areas of your skin.
- Apply a thick layer over the affected areas. Do not rub it in.
- Leave it on your skin for 3 to 5 minutes; then rub it in gently.
- Wipe off any excess cream with a tissue (do not wash it off).
- The cream should be used in this way twice a day, or as advised by your doctor.
- If you need to use Nutraplus Duo on your feet, soak them in water for 15 minutes and then dry them with a soft towel before use.
- How long you will have to use this product will depend on how quickly your condition improves. Always seek the advice of your doctor or pharmacist.

If you use more Nutraplus Duo than you should or accidentally swallow any of the cream:
If you use too much Nutraplus Duo and stinging occurs, wash the cream off with water.
In the rare event that you accidentally swallow any of this product, seek medical advice.

If you forget to use Nutraplus Duo

Do not worry if you forget to use your cream at the right time. When you remember, start using the product again as you did before.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Nutraplus Duo can cause side effects, although not everybody gets them.

Effects on the skin
- Nutraplus Duo may cause stinging if applied to raw areas or cracks in the skin or the lips.
- Keep Nutraplus Duo away from other sensitive areas of your body.
- If stinging occurs, wash the cream off with water.
- Should stinging be a problem, you can mix it with an equal amount of Aqueous Cream BP (ask your pharmacist for this) for a week, after which it would be alright to use the cream on its own again, but you must consult your doctor or pharmacist first.

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 Nutraplus Duo

- Keep out of the reach and sight of children.
- Do not use Nutraplus Duo after the expiry date which is stated on the tube and carton. The expiry date refers to the last day of that month.
- Do not store above 25°C. Do not refrigerate or freeze.
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 Nutraplus Duo contains
- Nutraplus Duo contains the active substances urea 100mg/g and lactic acid 50mg/g.
- The other ingredients are glyceryl monostearate, betaine monohydrate, diethanolamine cetyl phosphate, hard fat, cholesterol, sodium chloride and purified water.

What Nutraplus Duo looks like and contents of the pack
Nutraplus Duo is a white cream. It is available in 15 g, 20 g, 30 g, 50g and 100 g tubes and in 400 g and 500 g pump dispensers, either on prescription from your doctor or indirectly from your pharmacist.

Not all sizes of the tube may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Galderma (UK) Limited, Mercian House, 69-71 Clarendon Road, Watford, Herts WD17 1DS, UK
Manufacturer: Laboratoires Galderma, ZI Mont-de-Liré, 74540 Alby-sur-Chêzé, France.
Marketing Authorisation Numbers: PL 10590/0055
This leaflet was last approved in 05/2010.

GALDERMA
LABELLING

30mg pack – Carton, tube label and Braille

Translation: Nutraplus Duo
500mg pack – Carton and tube label