NIDAZEA 0.75% GEL
(Metronidazole)
PL 13159/0011

UKPAR

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Medicines and Healthcare products Regulatory Agency
LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Dr August Wolff GmbH & Co a Marketing Authorisation (licence) for the medicinal product Nidazea 0.75% Gel (PL 13159/0011) on 6th March 2009. This is a prescription-only medicine (POM).

Nidazea Gel contains the active ingredient, metronidazole. Metronidazole acts against some of the fungi and other organisms that can affect the skin, and also, in patients suffering from rosacea, it can relieve the condition by acting against the inflammation which happens when the condition becomes troublesome.

Nidazea is an anti-inflammatory gel to be applied on the skin. Nidazea gel is used for the treatment of rosacea (redness in the face, sometimes together with additional pustules) when the condition suddenly gets worse, and the inflammation becomes troublesome.

This application is a duplicate of a previously granted application for Metroxx 0.75% Gel (PL 13159/0006), held by Dr August Wolff GmbH & Co, and authorised on 15th November 2004. The test and reference products are identical.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of using Nidazea 0.75% Gel outweigh the risk; hence a Marketing Authorisation has been granted.
NIDAZEA 0.75% GEL
(Metronidazole)
PL 13159/0011

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Dr August Wolff GmbH & Co a Marketing Authorisation for the medicinal product Nidazea 0.75% Gel (PL 13159/0011) on 6th March 2009. The product is a prescription-only medicine (POM).

This abridged application was submitted according to article 10a (well-established use) of Directive 2001/83/EC (as amended), cross-referring to Metroxx 0.75% Gel (PL 13159/0006, Dr August Wolff GmbH & Co), approved on 15th November 2004.

Nidazea 0.75% Gel is indicated for the treatment of acute exacerbations of acne rosacea. The gel is applied topically for its local action.

Metronidazole has been used clinically for more than 40 years. It is a 5-nitroimidazole derivative, with activity against anaerobic protozoa and bacteria, due probably to an interference with DNA by a metabolite of the metronidazole.

The precise mode of action of metronidazole in acne rosacea is not known. It has been suggested that it has an anti-inflammatory effect due to an anti-oxidant activity affecting neutrophil cell function, or that it acts as a parasiticide towards Demodex folliculorum. Orally, metronidazole is active against anaerobic protozoa such as Entamoeba histolytica, Giardia intestinalis and Trichomonas vaginalis. Most obligate anaerobes are susceptible to metronidazole.

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**

**LICENCE NUMBER:** PL 13159/0011  
**PROPRIETARY NAME:** Nidazea 0.75% Gel  
**ACTIVE INGREDIENT/S:** Metronidazole  
**COMPANY NAME:** Dr August Wolff GmbH & Co  
**E.C. ARTICLE:** Article 10a of Directive 2001/83/EC (as amended)  
**LEGAL STATUS:** POM

1. **INTRODUCTION**

This is an abridged application, submitted under Article 10a (well-established use) of Directive 2001/83/EC (as amended) for Nidazea 0.75% Gel. The proposed MA holder is ‘Dr August Wolff GmbH & Co, Sudbrackstrasse 56, 33611 Bielefeld, Germany’.

The reference product is Metroxx 0.75% Gel (PL 13159/0006), held by Dr August Wolff GmbH & Co. The test and reference products are identical.

2. **MARKETING AUTHORISATION APPLICATION FORM**

2.1 **Name(s)**

The approved name of the product is Nidazea 0.75% Gel. The product has been named in line with current requirements.

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

Nidazea 0.75% Gel is for local topical use and contains the active ingredient metronidazole 0.75%. Each 1g of gel contains 7.5 mg of metronidazole. The finished product is marketed in aluminium tubes of size 25g, 30g, 40g, and 50g, which are fitted with polyethylene (HDPE) screw caps. The tubes are packed with the Patient Information Leaflet (PIL) into cardboard outer cartons. The MAH has stated that not all pack sizes may be marketed.

The approved shelf-life is 54 months for the unopened tube, and 3 months after the first opening of the tube. The storage conditions (‘Do not store above 25°C, Do not refrigerate or freeze’) are consistent with the details registered for the cross-reference product.

2.3 **Legal status**

The product is a POM licensed medicine, available by supply through pharmacies, subject to a medical prescription.

2.4 **Marketing authorisation holder / Contact Persons / Company**

The proposed Marketing Authorisation holder is ‘Dr August Wolff GmbH & Co, Sudbrackstrasse 56, 33611 Bielefeld, Germany’.

The QP responsible for pharmacovigilance was stated and their CV included.
2.5 Manufacturers

The proposed manufacturing site is consistent with that 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

No materials of animal or human origin are included in the product.

3. EXPERT REPORTS

Satisfactory expert reports and curriculum vitae of experts were provided.

4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product name. The appearance of the product (a smooth clear to turbid colourless to faintly yellow gel) is consistent with 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 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.
Labelling

Colour 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 and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS

The grounds for this application are considered adequate. A Marketing Authorisation was, therefore, granted.
PRECLINICAL ASSESSMENT

This abridged application was submitted according to Article 10a (well-established use) 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.

Assessor’s Comments

Metronidazole, a 5-nitro-imidazole derivative, is an antimicrobial medicine with activity against anaerobic bacteria and protozoa. The pharmacology and toxicology of metronidazole are well established, and have been adequately reviewed by the Expert.

Apparently, there are no preclinical pharmacokinetic data with topically applied metronidazole. In monkeys, metronidazole (1mg/kg) applied to vagina was extensively absorbed systemically (bioavailability was 73%). However, in humans, systemic absorption of 1g metronidazole 0.75% applied to the skin was very low (approximately 1% of that seen after an oral dose) such that serum concentrations of metronidazole were in the range 25-66ng/ml and C_{max} was 20% of that observed after a 30mg oral dose (41ng/ml vs 850ng/ml).

Metronidazole is extensively metabolised by the liver. One of its two major metabolites, namely 1-(2-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole (the hydroxy metabolite) has 30-65% of the biological activity of the parent drug and a longer elimination half-life than the parent compound. It is not known whether this active hydroxy metabolite is formed following topical administration of metronidazole. However, in view of the low systemic absorption of parent drug when applied to human skin, plasma levels of the active hydroxy metabolite, if formed, are unlikely to be of safety concern.

Considering the low systemic concentrations of metronidazole anticipated with this topical formulation, the existing safety margins are unlikely to be eroded at the proposed dose regimen and there are no preclinical objections to grant a Marketing Authorisation.
CLINICAL ASSESSMENT

BACKGROUND
Metronidazole is an antimicrobial drug with high activity against anaerobic bacteria and protozoa.

INDICATIONS
Nidazea 0.75% Gel is indicated for the treatment of acute exacerbations of acne rosacea.

The indication is identical to that for the reference product and is satisfactory.

POSOLOGY AND METHOD OF ADMINISTRATION
Nidazea 0.75% Gel is for cutaneous use. For adults and the elderly, a thin film of the gel should be applied to the affected areas twice daily for four weeks. Treatment may be continued for a further four weeks if necessary.

The posology is identical to that for the reference product and is satisfactory.

TOXICOLOGY
An increased number of tumours have been reported in studies with high doses of metronidazole in rats and mice. There appears to be no evidence to date to substantiate an increased risk of cancer in humans.

CLINICAL PHARMACOLOGY
Pharmacodynamics
The precise mode of action of metronidazole in acne rosacea is not known. It has been suggested that it has an anti-inflammatory effect due to an anti-oxidant activity affecting neutrophil cell function, or that it acts as a parasiticide towards Demodex folliculorum.

Pharmacokinetics
The gel is applied topically for its local action. There is limited data on absorption using a 0.75% gel. The studies reviewed in this application show that use of 1g of gel (7.5mg metronidazole) topically results in blood levels ranging from undetectable to about 1% of the C_{max} seen from oral dosing.

EFFICACY
The applicant has submitted a critical review of thirty-two published studies and clinical trials. The findings of some of the clinical trials are summarised below.

One double-blind placebo controlled study conducted in Sweden, involving 81 patients, showed that topical metronidazole at a concentration of 1% in a cream base was effective topical therapy for rosacea. Another double-blind study comprising 51 patients, compared 1% metronidazole cream with systemic oxytetracycline; although both groups demonstrated a high degree of improvement there was no difference between the two groups.
Another double blind placebo controlled study investigated 59 subjects treated for nine weeks with metronidazole 0.75% gel or base alone. Statistically significant reductions in erythema and global improvement were seen in the metronidazole group compared with placebo. However, selective measurements of telangiectasia showed no improvements with either metronidazole or placebo.

Another double blind study consisting of 33 patients compared 0.75% metronidazole gel versus tetracycline treatment over a 9-week period. There was no statistically significant difference between the two groups. However, the study was relatively small with only 16 patients in the treatment groups and does not show clear improvement of the rosacea by both treatments.

Another double-blind randomised study had two treatment groups: (A) topical metronidazole 0.75% gel BID (plus oral placebo tetracycline) or (B) oral tetracycline 500mg (plus gel base BID). The treatment period was nine weeks with a three-week follow-up period. 74 subjects were recruited and 64 were available for per protocol analysis of efficacy. Assessments were at weeks 0, 3, 6, 9 and 12 (follow-up). The primary efficacy variable was defined as the total number of inflammatory lesions. The results of each of the two centres and the combined findings are summarised in Table 1 below.

### Table 1. Mean Total Number of Inflammatory Lesions

<table>
<thead>
<tr>
<th></th>
<th>Treatment A</th>
<th></th>
<th>Treatment B</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Cardiff</td>
<td>Gdansk</td>
<td>Combined</td>
<td>Cardiff</td>
</tr>
<tr>
<td>Week 0</td>
<td>42.05</td>
<td>75.00</td>
<td>56.30</td>
<td>38.29</td>
</tr>
<tr>
<td>Week 3</td>
<td>22.60</td>
<td>40.00</td>
<td>30.06*</td>
<td>17.13</td>
</tr>
<tr>
<td>Week 6</td>
<td>13.44</td>
<td>14.14</td>
<td>13.75*</td>
<td>8.38</td>
</tr>
<tr>
<td>Week 9</td>
<td>9.71</td>
<td>9.29</td>
<td>9.52*</td>
<td>6.50</td>
</tr>
<tr>
<td>Week 12</td>
<td>8.69</td>
<td>10.71</td>
<td>9.63*</td>
<td>4.70</td>
</tr>
</tbody>
</table>

* p<0.001 for difference from Week 0

Both treatments showed significant improvement (p <0.001), with the most rapid improvement occurring during the first three weeks, at which stage the tetracycline group was significantly better than metronidazole (p <0.05), although this difference disappears at weeks 6 and 9. At follow-up the metronidazole group remains much the same but there is continued improvement in the tetracycline group with a significant difference at twelve weeks (p <0.01).

Another study took a different approach of using topical metronidazole 0.75% gel in combination with tetracycline initially to control the rosacea, and then continuing with BID application of gel to maintain control. The study was in two parts, an open portion initially in which 113 patients were enrolled and treated with a combination of oral tetracycline plus topical metronidazole 0.75% gel. Successfully treated patients (88) were entered into the second part of the study which was randomised, double-blind, placebo controlled comparing metronidazole 0.75% gel BID with the gel base (placebo) in a long term (6 month) follow-up. The rationale was to cease oral tetracycline as soon as remission occurred to avoid the risk of systemic complications and adverse events from the use of long term systemic antibiotics. The primary
criteria for assessing efficacy were again inflammatory lesion counts. The results are summarised in Table 2 below.

Table 2  Summary of Response to Treatment with Topical Metronidazole 0.75% Gel or Placebo

<table>
<thead>
<tr>
<th></th>
<th>Metronidazole</th>
<th>Placebo</th>
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<tbody>
<tr>
<td></td>
<td>Week 12</td>
<td>Week 24</td>
</tr>
<tr>
<td>% Patients Relapsing</td>
<td>23</td>
<td>23*</td>
</tr>
<tr>
<td>% Patients free of Inflammatory Lesions</td>
<td>32</td>
<td>53</td>
</tr>
<tr>
<td>Mean No. of Inflammatory Lesions</td>
<td>3.3**</td>
<td>5.8</td>
</tr>
<tr>
<td>% Erythema rated as 0 or Mild</td>
<td>74</td>
<td>55</td>
</tr>
</tbody>
</table>

* p<0.05
** p<0.01 at both 12 and 24 weeks

The results of this maintenance treatment study showed that metronidazole 0.75% gel significantly prolonged the disease free interval and minimised recurrence.

Assessor’s Comments

The results of the studies presented show that this formulation of topical metronidazole 0.75% gel is probably as effective as oral tetracycline in the treatment of rosacea. The number of patients investigated and reviewed are adequate in terms of power calculations.

SAFETY

In general, the incidence of dermatological reactions is low. The applicant has provided a review with reference to the published clinical trials. The commonest events are erythematous rash and localised skin reactions. In reports of three studies, the irritancy and sensitisation potential of Nidazea gel was examined by the standard repeat insult technique in 102 subjects. Nidazea gel was shown to be non-irritant with a moderate potential for sensitisation. Photosensitivity potential was studied in 12 healthy volunteers using the standard technique and the results showed no evidence of phototoxicity.

Skin penetration compared with Metrogel was examined by using the skin surface biopsy (skin snipping) technique to remove five successive samples following application of Nidazea gel and Metrogel in 24 subjects. All analyses were blind. Small differences were detected indicating that Nidazea gel seemed to penetrate the stratum corneum at a greater rate.

Assessor’s Comments

It would appear that the absorption of Nidazea gel is faster than that of Metrogel preparation. However, the average dose applied to the face is less than 4mg metronidazole daily. Even if this was absorbed in total, blood levels would still be very low compared with the doses of up to 2g daily orally, where the absorption is known to approach 100%. Therefore, topical usage can be said to provide a wide therapeutic margin of safety.
EXPERT REPORT
A satisfactory clinical overview has been submitted with appropriate CV for the expert.

PRODUCT INFORMATION:
Summary of Product Characteristics
The approved SmPC is consistent with those for the reference product and is acceptable.

Patient Information Leaflet
The final PIL is in line with the approved SmPC and is satisfactory.

Labelling
Colour mock-ups of the labelling have been provided. The labelling is satisfactory and fulfils the statutory requirements for Braille.

DISCUSSION
Metronidazole has been used in clinical practice in the UK for well over thirty years. It has a recognised efficacy and acceptable safety profile. Topical metronidazole has been licensed for the treatment of rosacea for more than ten years in a number of countries including the UK, USA and France.

With regards to the current application, sufficient clinical information has been submitted. When used as indicated, Nidazea 0.75% Gel has a favourable benefit-to-risk ratio. The hazard associated with Nidazea Gel appears to be low and acceptable when considered in relation to its therapeutic benefits.

CONCLUSION
The grant of a Marketing Authorisation was recommended on medical grounds.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

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

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
Metronidazole has been used in clinical practice in the UK for well over thirty years. It has a recognised efficacy and acceptable safety profile. Topical metronidazole has been licensed for the treatment of rosacea for more than ten years in a number of countries including the UK, USA and France.

This application is identical to the previously granted application for Metroxx 0.75% Gel (PL 13159/0006, Dr August Wolff GmbH & Co).

No new or unexpected safety concerns arise from this application.

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

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The testing shows that patients/users are able to act upon the information that the leaflet contains.

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 and sufficient space has been included for a standard UK pharmacy dispensing label.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with topical metronidazole is considered to have demonstrated the therapeutic value of the active substance. The risk: benefit is, therefore, considered to be positive.
NIDAZEA 0.75% GEL
(Metronidazole)

PL 13159/0011

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the marketing authorisation application on 3\textsuperscript{rd} January 2006

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 19\textsuperscript{th} January 2006

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 28\textsuperscript{th} February 2006, 29\textsuperscript{th} September 2007, and 12\textsuperscript{th} May 2008

4 The applicant responded to the MHRA’s request, providing further information for the quality sections on 29\textsuperscript{th} August 2006, 12\textsuperscript{th} March 2008, and 14\textsuperscript{th} October 2008 respectively

5 The application was determined on 12\textsuperscript{th} January 2009 and granted on 6\textsuperscript{th} March 2009
NIDAZEA 0.75% GEL
(Metronidazole)
PL 13159/0011

STEPS TAKEN AFTER AUTHORISATION

Not applicable
SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SmPC) for Nidazea 0.75% Gel is as follows:

1 NAME OF THE MEDICINAL PRODUCT
Nidazea 0.75% Gel.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
1 g of gel contains 7.5 mg Metronidazole
Excipient: 30 mg propylene glycol / gram Gel
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Gel.
A smooth clear to turbid colourless to faintly yellow gel

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
For the treatment of acute exacerbations of acne rosacea.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
Method of administration: Cutaneous use.
Adults and the elderly: Apply a thin film of the gel to the affected areas twice daily for four weeks. Treatment may be continued for a further four weeks if necessary.
Use in children and adolescents: Not recommended as clinical trials have not been undertaken.

4.3 CONTRAINDICATIONS
Contraindicated in known hypersensitivity to metronidazole or any of the ingredients in Nidazea gel.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Avoid contact with the eyes. If contact should occur, wash out of the eyes carefully with warm water.
Nidazea gel contains propylene glycol, which may cause skin irritation.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
In the case of oral metronidazole, there have been a small number of reports of a disulfiram-like reaction if alcohol is taken concomitantly. Although the systemic absorption of metronidazole from topical presentations is slight this interaction might be seen.

4.6 PREGNANCY AND LACTATION
The product should not be used if pregnant or if breast-feeding.
4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
None known

4.8 UNDESIRABLE EFFECTS
Occasionally, dryness, peeling, or itching of the skin may occur.

4.9 OVERDOSE
Overdosage is not to be expected with this preparation. Any excess gel may be removed by washing with warm water. Appropriate gastric emptying may be used, if considered necessary, should accidental ingestion occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES
Metronidazole has been used clinically for more than 40 years. It is a 5-nitroimidazole derivative, with activity against anaerobic protozoa and bacteria, due probably to an interference with DNA by a metabolite of the metronidazole.

The precise mode of action of metronidazole in acne rosacea is not known. It has been suggested that it has an anti-inflammatory effect due to an anti-oxidant activity affecting neutrophil cell function, or that it acts as a parasiticide towards *Demodex folliculorum*.

Orally, metronidazole is active against anaerobic protozoa such as *Entamoeba histolytica*, *Giardia intestinalis* and *Trichomonas vaginalis*. Most obligate anaerobes are susceptible to metronidazole, such as *Clostridium* spp., and some facultative anaerobes, such as *Campylobacter* spp. It has also been used locally, as suppositories and pessaries.

It has been more recently used by topical application in two indications; these licensed uses in the UK are in the acute exacerbations of acne rosacea, and in the deodourisation of fungating malodorous tumours.

5.2 PHARMACOKINETIC PROPERTIES
The gel is applied topically for its local action.

5.3 PRECLINICAL SAFETY DATA
Single dose studies in mouse and rat by oral, intraperitoneal and intravenous routes show a low order of toxicity. Repeat dose studies in mouse, rat, dog and monkey indicate a minimum no-effect level of 75 mg/kg/day.

Reproductive studies showed no evidence of embryotoxicity or teratogenicity.

Metronidazole is mutagenic in bacteria and fungi, but is regarded as non-genotoxic in man.

No phototoxic or photogenotoxic effects were seen in studies in Chinese hamster lung cells.

Studies in mouse and rat showed an increased incidence of tumours, but recent epidemiological studies in man showed no increased cancer risk.

No local toxicity has been seen in animal studies.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS
Phenoxyethanol
Propylene glycol
Hypermellose
Purified water
6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

54 months. Shelf life after first opening 3 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

Aluminium tube, fitted with a polyethylene (HDPE) screw cap.
Pack sizes: 25g, 30g, 40g, or 50g.
Not all pack sizes are marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Dr August Wolff GmbH & Co
Sudbrackstrasse 56
33611 Bielefeld
Germany

8 MARKETING AUTHORISATION NUMBER(S)

PL 13159/0011

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

06/03/2009

10 DATE OF REVISION OF THE TEXT

06/03/2009
Nidazea 0.75% Gel

Metronidazole

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 Nidazea is and what it is used for
2. Before you use Nidazea
3. How to use Nidazea
4. Possible side effects
5. How to store Nidazea
6. Further Information

1. WHAT NIDAZEA IS AND WHAT IT IS USED FOR

Nidazea contains 7.5mg metronidazole as active substance. Nidazea is an anti-inflammatory gel to be applied on the skin. Nidazea is used for the treatment of rosacea (redness in the face, sometimes together with additional pustules) when the condition suddenly gets worse, and the inflammation becomes troublesome. Metronidazole acts against some of the fungi and other organisms that can affect the skin, and also, in patients suffering from rosacea, it can relieve the condition by acting against the inflammation which happens when the condition becomes troublesome.

2. BEFORE YOU USE NIDAZEA

Do not use Nidazea
If you are hypersensitive (allergic) to Metronidazole or any of the other ingredients listed below
Take special care with Nidazea
Do not let the gel come into contact with the eyes. If it does, wash the gel carefully out of the eyes with warm water.
Using Nidazea could interfere with drugs used to thin the blood (anticoagulants) such as warfarin and coumarin. Contact your doctor for advice if you are taking medicines to thin your blood, or if you suffer for any other blood disorders.
Use Nidazea with care if you suffer or suffered in the past from blood dyscrasia
Do not go out into strong sunlight, or use UV lamps while you are using this product. Avoid prolonged and unnecessary use of this medicine.

Use in children and adolescents
Nidazea should not be used in children and adolescents.

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.

Using Nidazea with food and drink
Food and meals can be consumed with only one exception: It is best not to take alcohol while using the gel, as there is a very small possibility of a reaction that might feel sick or nauseous.

Pregnancy and breast-feeding
You should not use the gel if you are pregnant or if you are breast-feeding. If you are, or think you may be, pregnant, or wish to breast-feed, please make sure your doctor knows of this immediately.

Driving and using machines
You are allowed to drive and use machines since there are no effects known on the ability to drive.

Important information about some of the ingredients of Nidazea
Propylene glycol may cause skin irritation. Should this occur, stop using the medicine and consult your doctor.
3. HOW TO USE NIDAZE

Nidaze gel is for cutaneous use only.
Unless your doctor has told you differently, apply a 2–3cm line of gel to the affected areas and rub it gently into the skin. Use the gel twice each day, for up to four weeks.
Always use Nidaze exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
If you use more Nidaze than you should
If you apply too much of the gel, simply wipe off the excess with a clean tissue. The gel is for use on the skin only. If you, or anyone else, should accidentally swallow a quantity of the gel, tell your doctor at once, or go to the nearest hospital casualty department.
If you forget to use Nidaze
If you forget to use the gel, then use it as soon as you remember, unless the next application is due within about two or three hours, in which case omit the forgotten dose.
If you stop using Nidaze
If you stop using the gel, contact your doctor or pharmacist.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Nidaze can cause side effects, although not everybody gets them.
Uncommonly (between one and ten per 1000 treated patients), you may notice
– dryness
– peeling or
– itching
after using the gel. If this should become troublesome, stop using the gel and tell your doctor.
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 NIDAZE

Keep out of the reach and sight of children.
Do not store above 25°C. Do not refrigerate or freeze the gel.
Do not use Nidaze after the expiry date which is stated on the tube. The expiry date refers to the last day of that month.
Use within 3 months of first opening.

6. FURTHER INFORMATION

What Nidaze contains
The active substance is Metronidazole.
1g of gel contains 7.5mg metronidazole
The other ingredients are phenoxyethanol, propylene glycol, hypromellose, and purified water.
What Nidaze looks like and contents of the pack
It is made available as a collapsible aluminium tube containing 25g, 30g, 40g or 50g of the gel (not all pack sizes are marketed).

Marketing Authorisation Holder and Manufacturer
Dr. August Wolff GmbH & Co. KG Arzneimittel
Sudbrackstraße 56, D-33611 Bielefeld, Germany
Phone: +49 (0)521 8808-05; Fax: +49 (0)521 8808-334
E-Mail: info@wolff-arzneimittel.de

This leaflet was last approved in 02/2008
UKPAR Nidazea 0.75% Gel  PL 13159/0011

LABELLING

25g pack
Carton

Nidazea 0.75% Gel

Metronidazole
25g

1g of gel contains 7.5 mg Metronidazole
Other ingredients: Propylene glycol, hypromellose, phenoxethanol, purified water
Contains propylene glycol - Read the package leaflet before use
Cutaneous use

Keep out of the reach and sight of children. Avoid contact with the eyes.
Do not store above 25°C. Do not refrigerate or freeze.
Use within 3 month of first opening.
Marketing authorisation number: PL 13159/0011
Dr. August Wolff GmbH & Co. KG Arzneimittel
Sudbrackstrasse 56 - 33611 Bielefeld, Germany

Tube label

Nidazea 0.75% Gel

Metronidazole
25g

1g of gel contains 7.5 mg Metronidazole
Other ingredients: Propylene glycol, hypromellose, phenoxethanol, purified water
Contains propylene glycol - Read the package leaflet before use
Cutaneous use

Keep out of the reach and sight of children. Avoid contact with the eyes.
Do not store above 25°C. Do not refrigerate or freeze.
Use within 3 month of first opening.
Marketing authorisation number: PL 13159/0011
Dr. August Wolff GmbH & Co. KG Arzneimittel
Sudbrackstrasse 56 - 33611 Bielefeld, Germany
30g pack

Carton

Tube label
UKPAR Nidazea 0.75% Gel  
PL 13159/0011

40g pack
Carton

Nidazea 0.75% Gel

DR-WOLFF

Metronidazole
40g

1g of gel contains 7.5mg Metronidazole
Other ingredients: Propylene glycol, hypromellose, phenoxethanol, purified water
Contains propylene glycol – Read the package leaflet before use
Cutaneous use

Keep out of the reach and sight of children. Avoid contact with the eyes.
Do not store above 25°C. Do not refrigerate or freeze.
Use within 3 month of first opening.
Marketing authorisation number: PL 13159/0011
Dr. August Wolff GmbH & Co. KG Arzneimittel
Sudbrackstraße 56 - 33611 Bielefeld, Germany

Tube label

Nidazea 0.75% Gel

DR-WOLFF

Metronidazole
40g

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Other ingredients: Propylene glycol, hypromellose, phenoxethanol, purified water
Contains propylene glycol – Read the package leaflet before use
Cutaneous use

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Do not store above 25°C. Do not refrigerate or freeze.
Use within 3 month of first opening.
Marketing authorisation number: PL 13159/0011
Dr. August Wolff GmbH & Co. KG Arzneimittel
Sudbrackstraße 56 - 33611 Bielefeld, Germany
UKPAR Nidzea 0.75% Gel

50g pack

Carton

Nidzea 0.75% Gel

Metronidazole

50g

1g of gel contains 7.5mg Metronidazole
Other ingredients: Propylene glycol, hypropellose, phenoxethanol, purified water
Contains propylene glycol - Read the package leaflet before use
Cutaneous use

Nidzea 0.75% Gel

Metronidazole

50g

Keep out of the reach and sight of children. Avoid contact with the eyes.
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Use within 3 month of first opening
Marketing authorisation number: PL 13159/0011
Dr. August Wolff GmbH & Co. KG Arzneimittel
Sudbrackstraße 56 · 33611 Bielefeld, Germany

Tube label

Nidzea 0.75% Gel

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