Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

Decentralised Procedure

Mupirocin 20 mg/g Ointment (mupirocin)

MR number: UK/H/6776/001/DC

UK Licence Number: PL 15011/0024

Infectopharm Arzneimittel und Consilium GmbH

LAY SUMMARY

Mupirocin 20 mg/g Ointment
(mupirocin)

This is a summary of the Public Assessment Report (PAR) for Mupirocin 20 mg/g Ointment (PL 15011/0024; UK/H/6776/001/DC). It explains how this medicine was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use Mupirocin 20 mg/g Ointment.

The product will be referred to as Mupirocin Ointment throughout the lay summary

For practical information about using Mupirocin 20 mg/g Ointment, patients should read the package leaflet or contact their doctor or pharmacist.

What is Mupirocin 20 mg/g Ointment and what is it used for?
Mupirocin 20 mg/g Ointment is a 'hybrid medicine'. Assessment of the application concluded that the ointment is similar to a reference medicine containing the same active substance, mupirocin, in the same dose.

The reference medicine for Mupirocin 20 mg/g Ointment is Bactroban 2% Ointment (PL 00038/0319; Beecham Group PLC)

Mupirocin 20 mg/g Ointment can be used in adults, adolescents, children and infants aged 4 weeks and older to treat infections on the skin such as:

- infected hair follicles which form pimples containing pus ("folliculitis"),
- an infectious skin infection with blistering and crusting known as "impetigo" or
- recurring boils ("furunculosis").

How does Mupirocin 20 mg/g Ointment work?
The active substance in this medicine is called mupirocin, mupirocin is an antibiotic ointment for external use on the skin only.

How is Mupirocin 20 mg/g Ointment used?
The pharmaceutical form of this medicine is an ointment and the route of administration is cutaneous use (on the skin only).

Using this medicine
Mupirocin Ointment should usually be applied on the skin 2 to 3 times a day. Mupirocin Ointment must not be mixed with any other external cream or ointment medicines on the infected area of the skin, as this may reduce the effectiveness of Mupirocin Ointment.

Mupirocin Ointment should be used for as long as the patient's doctor has told their patient. If the patient is not sure, they should ask their doctor or pharmacist. The bacteria are normally cleared from the skin within 10 days of starting treatment. This medicine should not be used for more than 10 days. Any product remaining at the end of treatment course should be discarded. If the skin condition does not improve within 3 to 5 days, a doctor should be seen.

Please read section 3 of the package leaflet for detailed dosing recommendations, the route of administration, and the duration of treatment.

For further information on how Mupirocin 20 mg/g Ointment is used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

What benefits of Mupirocin 20 mg/g Ointment been shown in studies?
Because Mupirocin is considered to be therapeutically equivalent, to the reference product Bactroban 2% Ointment, its benefits and risks are taken as being the same as those of the reference medicine.

What are the possible side effects of Mupirocin 20 mg/g Ointment?
Like all medicines, this medicine can cause side effects, although not everybody gets them.

The common side effect with Mupirocin 20 mg/g Ointment (which may affect up to 1 in 10 people) is burning where the ointment is applied.

For the full list of restrictions, see the package leaflet.

For the full list of all side effects reported with Mupirocin 20 mg/g Ointment, see section 4 of the package leaflet available on the MHRA website.

Why was Mupirocin 20 mg/g Ointment approved?
The MHRA decided that Mupirocin 20 mg/g Ointment's benefits are greater than its risks and recommended that it be approved for use.

What measures are being taken to ensure the safe and effective use of Mupirocin 20 mg/g Ointment?
A risk management plan (RMP) has been developed to ensure that Mupirocin 20 mg/g Ointment is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics (SmPC) and the package leaflet for Mupirocin 20 mg/g Ointment including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Mupirocin 20 mg/g Ointment
The UK, Austria, Czech Republic, Spain, Hungary, Portugal, and Slovakia agreed to grant a Marketing Authorisation for Mupirocin 20 mg/g Ointment on 4 December 2018. A Marketing Authorisation was granted in the UK on 28 December 2018.

The full PAR for Mupirocin 20 mg/g Ointment follows this summary.

For more information about treatment with Mupirocin 20 mg/g Ointment read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in February 2019.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Reference Member States (RMS) and Concerned Member States (CMSs) considered that the application for Mupirocin 20 mg/g Ointment (PL 15011/0024; UK/H/6776/001/DC) could be approved. The product is a prescription-only medicine (POM).

Mupirocin 20 mg/g Ointment is indicated for the treatment of skin infections, e.g. impetigo, folliculitis, furunculosis in adults, adolescents, children and infants aged 4 weeks and older.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

For data on the antimicrobial spectrum and the microbial susceptibility against mupirocin please refer to section 5.1 of the SmPC, available on the MHRA website.

The application was submitted under Article 10(3) of Directive 2001/83/EC, as amended, as a hybrid medicinal product. The reference medicinal product for the application is Bactroban Ointment 2 % (PL 00038/0319) which was first authorised in the UK on 26 March 1985. As this reference product has been authorised in the EEA for at least 10 years the legal basis of these applications is acceptable.

Mupirocin is a novel antibiotic produced through fermentation by Pseudomonas fluorescens. Mupirocin inhibits isoleucyl transfer-RNA synthetase, thereby arresting bacterial protein synthesis.

Mupirocin has bacteriostatic properties at minimum inhibitory concentrations and bactericidal properties at the higher concentrations reached when applied locally.

No new non-clinical studies were conducted, which is acceptable given that this is a hybrid application cross-referring to a product that has been licensed for over 10 years.

To support the application, the Marketing Authorisation Holder (MAH) submitted a therapeutic equivalence study to compare the test product of the same formulation as Mupirocin 20 mg/g Ointment (Infectopharm Arzneimittel und Consilium GmbH) versus the reference product Bactroban Ointment 2 % (Beecham group Plc). The study was carried out in accordance with Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product type at all sites responsible for the manufacture and assembly of this product.

No new or unexpected safety concerns were identified during the review of information provided by the Marketing Authorisation Holder and it was, therefore, judged that, similarly to the reference product, the benefits of taking Mupirocin 20 mg/g Ointment outweigh the risks and Marketing Authorisations were granted.

II QUALITY ASPECTS

II.1 Introduction

The product is an ointment containing 20 mg/g mupirocin as the active ingredient.

The other ingredients are polyethylene glycol 400, and polyethylene glycol 3350 (with butylated hydroxytoluene ([E 321]).

Mupirocin 20 mg/g Ointment is packaged in an aluminium tube. This medicinal product is available in pack sizes of 5g or 15g. Not all pack sizes may be marketed.

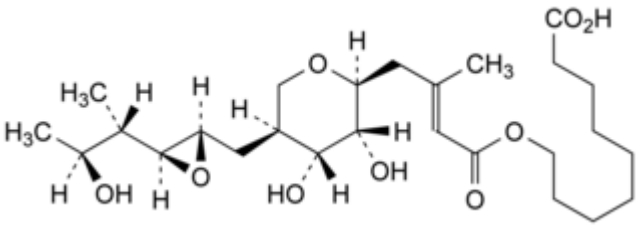
Satisfactory specifications and Certificates of Analysis have been provided for all packaging components.

II.2 Drug Substance

INN: Mupirocin

Chemical name: 9-[[(2E)-4-[(2S,3R,4R,5S)-3,4-Dihydroxy-5-[[(2S,3S)-3-[(1S,2S)-2-hydroxy-1-methylpropyl]oxiranyl]methyl]tetrahydro-2H-pyran-2-yl]-3-methylbut-2-enoyl]oxy]nonanoic acid

Structure:



Molecular formula: $C_{26}H_{44}O_9$

Molecular weight: 500.6

Appearance: White or almost white powder.

Solubility: Slightly soluble in water, freely soluble in acetone, in anhydrous ethanol and in methylene chloride.

Appropriate stability data have been generated to support a suitable retest period when stored in the proposed packaging.

Mupirocin is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance, mupirocin, are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3. Medicinal Product

Pharmaceutical Development

The objective of the development programme was to a produce a stable topical preparation (ointment) that is comparable in performance to the reference product Bactroban 2% Ointment (PL 00038/0319).

A satisfactory account of the pharmaceutical development has been provided.

All excipients comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients. Suitable batch analysis data have been provided for each excipient.

There are no materials of human or animal origin used in the manufacture of the products. The products do not contain or consist of genetically modified organisms (GMO).

Manufacture of the product

Satisfactory batch formula have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and the results were satisfactory.

Finished Product Specification

The finished product specification proposed is acceptable. Test methods have been described that have been adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Stability of the Product

Finished product stability studies were performed in accordance with current guidelines on batches of the finished product in the packaging proposed for marketing. The data from these studies support a shelf-life of 2 years with the storage condition “Store below 25 °C”, after first opening, the contents can be used for 10 days.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

Therapeutic Equivalence
Bioequivalence studies i.e. the demonstration of systemic equivalence, is not necessary to support applications for locally applied products intended to act without systemic absorption, instead pharmacodynamics or comparative clinical studies are required. The pivotal study provided to establish therapeutic equivalence between the proposed product and the reference product is discussed in the clinical section IV of this report. An in vitro skin permeation study was also provided, the study evaluated the proposed Mupirocin Test Formulation against the Bactroban Reference Product in terms of comparative penetration and diffusion across excised human skin (Franz cell technique). Comparison of the permeation and penetration findings showed no statistically significant difference between test and reference products (by t-test for independent samples at the 0.05 significance level).

II.4 Discussion on chemical, pharmaceutical and biological aspects
There are no objections to the approval of this application from a pharmaceutical viewpoint.

III NON-CLINICAL ASPECTS
III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of mupirocin are well-known, no new non-clinical studies are required and none have been provided. An overview based on the literature review is, thus, appropriate.

The applicant's non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

III.2 Pharmacology
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.3 Pharmacokinetics
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.4 Toxicology
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.5 Ecotoxicity/environmental risk assessment (ERA)
Since Mupirocin 20 mg/g Ointment is intended for generic substitution, this will not lead to an increased exposure of the environment. An environmental risk assessment is therefore not deemed necessary**.**

III.6 Discussion on the non-clinical aspects
There are no objections to the approval of this application from a non-clinical viewpoint.

IV CLINICAL ASPECTS
IV.1 Introduction
The clinical pharmacology of mupirocin is well-known. With the exception of data from the therapeutic equivalence study detailed below, no new clinical data are provided or are required for this application.

Based on the data provided, Mupirocin 20 mg/g Ointment can be considered therapeutically equivalent to Bactroban 2% Ointment (Beecham group Plc).

IV.2 Pharmacokinetics
Systemic pharmacokinetics (PK) are not-relevant to this product because of negligible systemic absorption, furthermore, any mupirocin reaching the circulation would be rapidly metabolised to the inactive metabolite monic acid.

IV.3 Pharmacodynamics
No new pharmacodynamic data were submitted and none were required for applications of this type.

IV.4 Clinical efficacy

In support of the application, the applicant has submitted the following therapeutic equivalence study.

A multicentre, prospective, double-blind, two-armed phase III study comparing Mupirocin test product (formulation identical to Mupirocin 20 mg/g Ointment) versus the reference product, Bactroban 2% Ointment (Beecham group Plc) in the efficacy and safety of topical impetigo therapy.

Objectives

Primary

To prove that the Mupirocin Test Formulation was statistically equivalent to the Bactroban 2% Ointment with respect to the proportion of patients who are clinically cured at the final visit (Day 14 i.e. 7 days after the end of a 7-day treatment period).

Secondary

The investigation of additional aspects of efficacy (e.g. microbiological cure) and safety.

The proposed objectives are appropriate and consistent with a therapeutic equivalence study

Design

Phase III, randomised, double-blind, two-arm, parallel group efficacy and safety study in infants and children, aged 28 days to 15 years, presenting with clinically confirmed impetigo which was culture positive for *Staphylococcus aureus* and/or *Streptococcus pyogenes* plus a SIRS (Skin Infection Rating Scale) of at least 3 for the five signs/symptom categories, at baseline. Impetigo is an appropriate model of skin infection for this product. In the absence of specific EU guidelines for topical mupirocin, the study was based on the Draft FDA Guidance, rather than general EU statistical guidelines.

The study duration was 14 days (comprising a 7-day treatment period followed by 7 days' follow-up). An interim, 'control', visit was scheduled after 3 days. The study ointment was to be applied as a thin layer to the affected parts of the skin. Evaluation of compliance was based on patient diaries.

Patients were randomised (1:1 ratio) to receive 7 days' thrice daily application of either: Mupirocin Test Formulation or Bactroban Reference Formulation (Bactroban 2% Ointment).

A placebo (vehicle) arm was not incorporated into the study, although recommended in both the specific FDA and general EU guidelines for 'assay sensitivity'. The absence of a placebo (vehicle) arm is accepted and is not considered to have compromised the robustness of the study, based on the following:

- by giving inactive treatment to a paediatric population with proven active infection, when standard therapy is available, would pose ethical difficulties and,

- a high cure rate (≥ 90%) has been consistently reported with topical 2%, mupirocin compared to a placebo (vehicle) rate of 25-50% (supported by literature references provided by the applicant). Consequently, based on the anticipated cure rates, the study would have had >99% power to show superiority over placebo (vehicle) with the planned sample size. The results of the IMUP study confirm the expected high clinical cure ≥95% with concomitant evidence of microbiological eradication, demonstrating a convincing treatment effect which is consistent with the published reports.

Summary of therapeutic equivalence study results

Treatment arm	# Enrolled / completed	Primary Endpoint (Clinical cure on Day 14, PP pop.)	Statistical test / result	Secondary Endpoints (mITT population)				
				Microbiol. cure on Day 14	Clinical cure on Day 7	Microbiol. cure on Day 7	Premature discontinuation on Day 3 due to lack of efficacy	Mean SIRS total score on Day 0, Day 7, and Day 14
Mupirocin Infectopharm 20 mg/g Ointment; Bactroban® Ointment 2 %	153 (75/78) (enrolled) 150 (75/75) (SE pop.) 119 (56/63) (mITT pop.) 115 (55/60) (PP pop.)	100 % (Mupirocin Infectopharm 20 mg/g Ointment) 95.0 % (Bactroban® Ointment 2 %)	Test for therapeutic equivalence according to the method of Westlake; 90 % CI of the difference in cure rates [-0.01 ; +0.11] lies entirely within the interval [-0.20 ; +0.20]; Mupirocin Infectopharm 20 mg/g Ointment and Bactroban® Ointment 2 % are therapeutically equivalent	100.0 % (Mupirocin Infectopharm 20 mg/g Ointment) 98.4 % (Bactroban® Ointment 2 %) 95 % CI of the difference in rates [-0.03 ; +0.06]	73.2 % (Mupirocin Infectopharm 20 mg/g Ointment) 69.8 % (Bactroban® Ointment 2 %) 95 % CI of the difference in rates [-0.15 ; +0.21]	85.7 % (Mupirocin Infectopharm 20 mg/g Ointment) 91.9 % (Bactroban® Ointment 2 %) 95 % CI of the difference in rates [-0.19 ; +0.07]	0 % (Mupirocin Infectopharm 20 mg/g Ointment) 1.6 % (Bactroban® Ointment 2 %) 95 % CI of the difference in rates [-0.06 ; +0.03]	8.7 (Day 0) 1.5 (Day 7) 0.3 (Day 14) (Mupirocin Infectopharm 20 mg/g Ointment) 8.7 (Day 0) 1.7 (Day 7) 0.7 (Day 14) (Bactroban® Ointment 2 %)

For the primary (PP) analysis of 'clinical cure rate' at Day 14, 90% confidence intervals (CIs) of the difference in both cure rates [-0.01; +0.11] were contained well within the pre-specified [-0.20; +0.20] interval required. The modified intention to treat (mITT) analysis was consistent with this as were microbiological cure rates at the Day 14 primary timepoint. Nor did other secondary efficacy endpoints indicate any treatment differences. The FDA guidance on which this study was based is not entirely consistent with the general EU statistical approach to establishing therapeutic equivalence on clinical, as opposed to pharmacokinetic, endpoints. As stated in CPMP/EWP/239/95final 'The [CI] limits between which a product is […] defined as being "equivalent" depend on the compound to be studied and the parameters used, so a reference to the bioequivalence guideline, where a variation of 20% is found acceptable [and which is recommended in the FDA Guideline] in most cases, is not acceptable as such'. However, in the study, the large effect size (≥95% primary clinical cure rate and consistent secondary endpoints, including bacterial eradication), which are consistent with published trials of topical 2% mupirocin in the treatment of impetigo, and which is much greater than an anticipated placebo (vehicle) effect from the literature, supports the validity of the trial findings in relation to equivalence between the mupirocin test formulation and the reference product Bactroban 2% Ointment. Furthermore, although not pre-specified, 95% CIs have been provided.

The study can, therefore, be considered to have satisfactorily established therapeutic equivalence between the Mupirocin Test Formulation and Bactroban Reference product, and therefore supports the authorisation of Mupirocin 20 mg/g Ointment, particularly given the additional support from the pharmaceutical and in vitro equivalence data, see the therapeutic equivalence section on page 7 of this report.

IV.5 Clinical safety

Apart from the study above, there was no apparent difference in the safety profile of the proposed Mupirocin Test formulation compared to the Bactroban Reference product. There were no serious adverse events (SAEs) and no drop-outs due to adverse events (AEs). Furthermore, no new safety concerns have arisen from post-marketing data for this formulation which was first approved under previous DCP procedure UK/H/4991/001/DC.

IV.6 Risk Management Plan (RMP) and Pharmacovigilance System

The applicant has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended.

There are no differences from the reference product in terms of proposed uses, maximum pack size / strength or pharmaceutical form / formulation that would have any implications for safety.

In line with the reference product, the applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns (labelling in the SmPC and the PIL). This is agreed.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures

IV.7 Discussion on the clinical aspects

The grant of a marketing authorisation is recommended for this application from a clinical viewpoint.

V User consultation

A user consultation with target patient groups on the PIL has been performed on the PIL of Mupirocin Infectopharm 20 mg/g Ointment (PL 15011/0016), this PIL is for all intents and purposes identical to the PIL for Mupirocin 20 mg/g Ointment. The user consultation was deemed acceptable in line with the requirements set out in Council Directive 2004/27/EC, Article 59 (3), in line with the requirements set out in Council Directive 2004/27/EC, Article 59 (3).

VI Overall conclusion, benefit/risk assessment and recommendation

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with mupirocin is considered to have demonstrated the therapeutic value of the compound. The benefit-risk balance is, therefore, considered positive.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for this medicine is presented below:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

Mupirocin 20 mg/g Ointment
mupirocin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of ointment contains 20 mg mupirocin.

3. LIST OF EXCIPIENTS

Other ingredients: polyethylene glycol 400 and polyethylene glycol 3350 (with butylated hydroxytoluene (E 321)).

Contains butylated hydroxytoluene. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

5 g
15 g

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For cutaneous use only.
Apply to the affected area as prescribed by your doctor.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Avoid contact with the eyes.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.
After first opening of the tube the contents can be used for up to 10 days.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

INFECTOPHARM Arzneimittel und Consilium GmbH
Von-Humboldt-Str. 1
64646 Heppenheim
Germany

12. MARKETING AUTHORISATION NUMBER(S)

PL 15011/0024

13. BATCH NUMBER

LOT

14. GENERAL CLASSIFICATION FOR SUPPLY

POM
Medical sample – not for sale

15. INSTRUCTIONS ON USE

Optional: pictogram of the pharmaceutical form or the route of administration.

16. INFORMATION IN BRAILLE

mupirocin 20 mg/g

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC: <to be completed nationally>
SN: <to be completed nationally>
NN: <to be completed nationally>

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

TUBE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Mupirocin 20 mg/g Ointment
mupirocin

2. METHOD OF ADMINISTRATION

For cutaneous use only.

3. EXPIRY DATE

Lot/EXP see tube fold

4. BATCH NUMBER

Lot/EXP see tube fold

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 g

6. OTHER

PL 15011/0024

INFECTOPHARM

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

Mupirocin 20 mg/g Ointment

mupirocin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of ointment contains 20 mg mupirocin.

3. LIST OF EXCIPIENTS

Other ingredients: polyethylene glycol 400 and polyethylene glycol 3350 (with butylated hydroxytoluene (E 321)).

Contains butylated hydroxytoluene. Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

15 g

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For cutaneous use only.
Apply to the affected area as prescribed by your doctor.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Avoid contact with the eyes.

8. EXPIRY DATE

Lot/EXP see tube fold

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.
Use up within 10 days after first opening.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

INFECTOPHARM Arzneimittel und Consilium GmbH
Von-Humboldt-Str. 1
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Table of content of the PAR update for MRP and DCP

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

Scope	Procedure number	Product information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached Y/N (version)