PROFESSIONAL INFORMATION

NUBAN OINTMENT

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

NUBAN OINTMENT 2 % (*m/m*)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of NUBAN OINTMENT contains mupirocin 20 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ointment.

A white colour ointment, free of foreign particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NUBAN OINTMENT is indicated for the topical treatment of primary and secondary bacterial skin infections caused by *Staphylococcus aureus* and other susceptible organisms.

Primary skin infections:

Impetigo, folliculitis, furunculosis and ecthyma.

Secondary infections:

Infected dermatoses e.g. infected eczema. Infected traumatic lesions e.g. abrasions, insect bites, minor (not requiring hospitalisation) wounds and burns.

Prophylaxis:

NUBAN OINTMENT may be used to avoid bacterial contamination of small wounds, incisions and other clean lesions, and to prevent infection of abrasions and small cuts and wounds.

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

4.2 Posology and method of administration

Posology

Adults, elderly and children (older than 2 months):

2 - 3 times a day for up to 10 days, depending on the response.

Special populations

Patients with hepatic impairment

As above

Patients with renal impairment

Refer to section 4.4

Method of administration

Cutaneous use.

Before applying, wash affected areas and dry thoroughly.

Apply a small quantity of NUBAN OINTMENT to cover the affected area.

The treated area(s) may be covered with a gauze dressing if desired.

Complete the full course of treatment.

Any product remaining at the end of treatment should be discarded.

Do not mix with other preparations as there is a risk of dilution, resulting in a reduction in the antibacterial activity and potential loss of stability of the mupirocin in the ointment.

4.3 Contraindications

- hypersensitivity to mupirocin or to any of the ingredients of NUBAN OINTMENT listed in section 6.1
- treatment of skin lesions infected with *Pseudomonas aeruginosa.*

4.4 Special warnings and precautions for use

NUBAN OINTMENT formulation is not suitable for:

- intranasal use
- use in conjunction with cannulae
- use at the site of central venous cannulation
- ophthalmic use.

Avoid contact with eyes. If accidental contact occurs, wash the eyes thoroughly with water until all traces of the ointment have been removed.

Treatment with NUBAN OINTMENT should be discontinued in the event of a sensitisation reaction or severe local irritation occurring. NUBAN OINTMENT should be rinsed off and alternative therapy for the infection should be prescribed.

Irregular or prolonged use is not recommended as this may result in overgrowth of non-susceptible strains of *S. aureus* and other organisms.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is less likely to occur with topically applied mupirocin, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately, and the patient investigated further.

Renal impairment

No restrictions, unless the condition being treated could lead to absorption of polyethylene glycol and there is evidence of moderate to severe renal impairment. Polyethylene glycol can be absorbed from open wounds, burns and damaged skin and is excreted by the kidneys.

NUBAN OINTMENT should not be used in conditions where absorption of large quantities of polyethylene glycol is possible, especially if there is evidence of moderate or severe renal impairment. The excretion of polyethylene glycol may be impaired and could lead to nephrotoxicity and severe metabolic disturbances.

4.5 Interaction with other medicines and other forms of interaction

Do not mix with other preparations. Mixing may result in a decrease in antibacterial activity and a loss of stability of NUBAN OINTMENT.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established.

Pregnancy

Adequate human data on use during pregnancy are not available.

Studies in animals do not indicate reproductive toxicity (see section 5.3).

Breastfeeding

Adequate human and animal data on use during lactation are not available.

Fertility

There are no data on the effects of mupirocin on human fertility. Studies in rats showed no effects on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

No adverse effects on the ability to drive or operate machinery have been identified.

NUBAN OINTMENT will most likely not affect the patients' ability to drive or operate machinery.

4.8 Undesirable effects

Tabulated list of adverse effects

System Organ Class	Frequency	Side effects
Infections and Infestations	Less frequent	Secondary wound infection
Immune system disorders	Less frequent	Hypersensitivity reactions Systemic allergic reactions including anaphylaxis, generalised rash, urticaria and angioedema

Nervous system disorders	Less frequent	Dizziness
Skin and subcutaneous tissue disorders	Frequent Less frequent	Burning localised to the area of application Dry skin, skin burning, itching, pain, rash, erythema, stinging or swelling, cutaneous sensitisation reactions to mupirocin or the ointment base
General disorders and administrative site conditions	Less frequent	Headache

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the online service for adverse drug reaction reporting by using either of the following links: https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/ or https://www.sahpra.org.za/Publications/Index/8.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

There is currently limited experience with overdosage of NUBAN OINTMENT.

See Undesirable effects (section 4.8) and Special warnings and precautions for use (section 4.4).

Management of overdose:

Treatment is symptomatic and supportive. There is no specific treatment for an overdose of mupirocin, as in NUBAN OINTMENT. Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Dermatologicals

ATC code: D06AX09

Pharmacological classification: A 20.1.6 Topical antibiotics

Mechanism of action:

Mupirocin is an antibiotic produced by *Pseudomonas fluorescens* that inhibits bacterial protein synthesis by binding to bacterial isoleucyl transfer RNA synthetase.

It is primarily bacteriostatic at minimum inhibitory concentrations and bactericidal in the higher concentrations achieved by topical application to the skin.

Mechanism of resistance:

Low-level resistance in *staphylococci* is thought to result from point mutations within the usual staphylococcal chromosomal gene (ileS) for the target isoleucyl tRNA synthetase enzyme. High-level resistance in *staphylococci* has been shown to be due to a distinct, plasmid encoded isoleucyl tRNA synthetase enzyme. Intrinsic resistance in Gram negative organisms such as the Enterobacteriaceae could be due to poor penetration of the outer membrane of the Gram-negative bacterial cell wall.

Due to its particular mode of action, and its unique chemical structure, mupirocin does not show any cross-resistance with other clinically available antibiotics.

Microbiological susceptibility:

The prevalence of acquired resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infection is questionable.

Commonly susceptible species
*Staphylococcus aureus**
*Streptococcus pyogenes**
Streptococcus spp. (β-haemolytic, other than S. pyogenes)
Species for which acquired resistance may be a problem
Staphylococcus spp., coagulase negative
Inherently resistant organisms
Corynebacterium spp.
Micrococcus spp.

* Activity has been satisfactorily demonstrated in clinical studies

5.2 Pharmacokinetic properties

Absorption:

Absorption of mupirocin through intact human skin is poor (less than 0,24 %). Mupirocin is however metabolised to the microbiologically inactive metabolite monic acid and rapidly excreted after absorption, when absorbed through broken or diseased skin or after systemic administration.

Elimination:

After metabolism to its inactive metabolite monic acid, mupirocin is rapidly eliminated from the body, excreted mainly (90 %) by the kidneys.

Pharmacokinetics in special patient groups

Elderly patients:

No restrictions unless there is evidence of moderate or severe renal impairment (see section 4.4).

5.3 Preclinical safety data

Carcinogenesis/mutagenesis

Carcinogenesis

Carcinogenicity studies with mupirocin have not been conducted.

Genotoxicity

Mupirocin was not mutagenic in *Salmonella typhimurium* or *Escherichia coli* (Ames assay). In a Yahagi assay, small increases in *Salmonella typhimurium TA98* were observed at highly cytotoxic concentrations. In an *in vitro* mammalian gene mutation assay (MLA), no increase in mutation frequency was observed in the absence of metabolic activation. In the presence of metabolic activation, small increases in mutation frequency were observed at highly cytotoxic concentrations. However, no effects were observed in, yeast cell assays for gene conversion/mutation, an *in vitro* human lymphocyte assay or in an *in vitro* unscheduled DNA synthesis (UDS) assay. Furthermore, an *in vivo* mouse micronucleus assay (chromosome damage) and a rat Comet assay (DNA strand breakage) were negative, indicating the small increases observed at highly cytotoxic concentrations *in vitro* do not translate to the *in vivo* situation.

Reproductive Toxicology:

Fertility

Mupirocin administered subcutaneously to male rats 10 weeks prior to mating and to female rats 15 days prior to mating until 20 days post coitum, at doses up to 100 mg/kg/day, had no effect on fertility.

Pregnancy

In embryo-foetal development studies in rats there was no evidence of developmental toxicity at subcutaneous doses up to 375 mg/kg/day.

In an embryo-foetal development study in rabbits at subcutaneous doses up to 160 mg/kg/day, maternal toxicity (impaired weight gain and severe injection site irritation) at the high dose resulted in abortion or poor litter performance. However, there was no evidence of developmental toxicity in foetuses of rabbits maintaining pregnancy to term.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol 400

Polyethylene glycol 3350.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C. Do not refrigerate or freeze.

Replace cap after use.

NUBAN OINTMENT can be used for up to 6 months after first opening the tube.

6.5 Nature and contents of container

15 g or 30 g* aluminium tubes internally coated with gold epoxy- phenolic lacquer, externally coated with white enamel and closed with white HDPE caps. One tube is packed in an outer carton.

*Not all pack sizes are marketed.

6.6 Special precautions for disposal and other handling

Any product remaining at the end of treatment should be discarded.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Wash your hands after application.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor, Grapevine House, Steenberg Office Park

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South Africa

8. REGISTRATION NUMBER

A44/20.1.6/0971

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