

Applicant:	GALDERMA LABORATORIES SOUTH AFRICA (PTY) LTD.
Proprietary name:	ROZEX GEL
Dosage form and strength:	Gel (7,5 mg per g)
Registration Number	29/13.4.2/0771

PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S3

1. NAME OF THE MEDICINE

ROZEX 0.75 % w/w GEL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

ROZEX GEL contains metronidazole 7,5 mg per g.

ROZEX GEL excipients with a known effect: propylene glycol 30 mg/g, methyl parahydroxybenzoate (E218) 0.8 mg/g, propyl parahydroxybenzoate (E216) 0.2 mg/g.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

A clear, colourless to light yellow, viscous gel which may turn slightly brown over time.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ROZEX GEL is indicated for the treatment of inflammatory papules, pustules and erythema of rosacea.

4.2 Posology and method of administration

Posology

For topical administration only.

Adults: Apply and rub a thin film of ROZEX GEL twice daily, morning and evening, to entire affected areas after washing.

The average period of treatment is usually of three to four months. The recommended duration of treatment should not be exceeded.

Paediatric population: Not recommended due to the lack of data on safety and efficacy.

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4.3 Contraindications:

Hypersensitivity to metronidazole, parabens or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

ROZEX GEL contains:

- Propylene glycol that can be irritating to the skin.
- Methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

ROZEX GEL has been reported to cause tearing of the eyes, therefore, contact with the eyes and mucous membranes should be avoided. If a reaction suggesting local irritation occurs, patients should be directed to use the medication less frequently, discontinue use temporarily or discontinue use completely and to seek medical advice if necessary.

Metronidazole is a nitroimidazole and should be used with care in patients with evidence of, or history of, blood dyscrasia.

Exposure of metronidazole treated sites to excessive sunlight or artificial sources of ultraviolet irradiation such as sun beds should be avoided.

Unnecessary and prolonged use of this medication should be avoided.

4.5 INTERACTIONS with other medicines and other forms of interaction

Medicine interactions are less likely with topical administration but should be kept in mind when ROZEX GEL is prescribed for patients who are receiving anticoagulant treatment. Oral metronidazole has been reported to potentiate the anticoagulant effect of warfarin and other coumarin anticoagulants resulting in a prolongation of prothrombin time (INR).

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Disulfiram-like reaction has been reported in a small number of patients taking oral metronidazole and alcohol concomitantly.

4.6 Fertility, pregnancy and lactation:

Pregnancy

Safety and efficacy of ROZEX GEL during pregnancy have not been established.

Metronidazole crosses the placental barrier and rapidly enters the foetal circulation.

ROZEX GEL should not be used in pregnancy.

Lactation

Mothers on treatment with ROZEX GEL should not breastfeed their infants.

4.7 Effects on ability to drive and the use of machines

ROZEX GEL has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Because of the minimal absorption of metronidazole and consequently its insignificant plasma concentration after topical administration, the adverse experiences reported with the oral form of the agent have not been reported with ROZEX topical gel. Adverse reactions reported with ROZEX GEL include watery (tearing) eyes if the gel is applied too closely to this area, transient redness and mild dryness, burning and skin irritation.

The following spontaneous adverse experiences have been reported, and within each system organ class, are ranked by frequency, using the following convention:

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1\ 000$ to $< 1/100$)

Rare ($\geq 1/10\ 000$ to $< 1/1\ 000$)

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Very rare (<1/10 000), including isolated reports

Unknown (frequency not assessable based on the available data)

They are presented in the table below:

Table 1: Adverse reactions reported in clinical trials:

System Organ Class	Incidence	Preferred Terms
Skin and subcutaneous tissue disorders	Common ($\geq 1/10$)	Dry skin Erythema Pruritus Skin discomfort (burning, pain of skin/stinging) Skin irritation Worsening of rosacea
	Unknown frequency	Contact dermatitis Skin exfoliation
Nervous System Disorders	Uncommon ($\geq 1/1000 < 1/100$)	Hypoesthesia Paraesthesia Dysgeusia (metallic taste)
Gastrointestinal Disorders	Uncommon ($\geq 1/1000 < 1/100$)	Nausea

Swelling face has been reported during post-marketing surveillance, with unknown frequency.

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 providers are asked to report any suspected adverse reactions to SAHPRA via the **“6.04 Adverse Drug Reactions**

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Reporting Form,” found online under SAHPRA’s publications:

<https://www.sahpra.org.za/Publications/Index/8>.

4.9 Overdose

In the event of accidental ingestion, treatment should be symptomatic and supportive.

In overdose, side effects (see section 4.8) can be precipitated and/or be of increased severity.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A.13.4.2. Dermatologicals – Other

Metronidazole is an antiprotozoal and antibacterial agent which is active against a wide range of pathogenic micro-organisms. The mechanism of action in rosacea is unknown, but available evidence suggests that the effects may be antibacterial and/or anti-inflammatory.

5.2 Pharmacokinetic properties

Metronidazole is absorbed after oral administration. The agent is not significantly bound to serum proteins and distributes well to all body compartments with the lowest concentration found in the fat. Metronidazole is excreted primarily in the urine as parent agent, oxidative metabolites and conjugates. Bioavailability studies with ROZEX GEL in rosacea patients treated with 7,5 mg metronidazole applied topically to the face resulted in maximum serum concentrations of 66 nanograms per ml which is approximately 100 times less than those attained after a single oral dose of 250 mg. In most patients at most time points after ROZEX GEL application, serum concentrations of metronidazole were below the detectable limits of the assay (25 ng/ml)

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Carbomer 940 (Carbopol 980)

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Disodium Edetate

Methyl Parahydroxybenzoate (E218)

Propyl Parahydroxybenzoate (E216)

Propylene Glycol

Sodium Hydroxide (for pH adjustment)

Purified Water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at room temperature, at or below 25 °C, away from direct heat.

Avoid exposure to temperatures below 4 °C.

KEEP OUT OF REACH OF CHILDREN.

FOR EXTERNAL USE ONLY.

6.5 Nature and contents of container

ROZEX GEL is packed in lined aluminium tubes containing 30 g gel.

6.6 Special precautions for disposal

No special requirements for disposal.

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

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7. HOLDER OF CERTIFICATE OF REGISTRATION:

Galderma Laboratories South Africa (Pty) Ltd

Nicol Main Office Park,

Block C, First Floor,

FutureSpace,

2 Bruton Road,

Bryanston,

2191

8. REGISTRATION NUMBER

29/13.4.2/0771

9. DATE OF FIRST AUTHORISATION

06 February 1996

10. DATE OF REVISION OF THE TEXT

19 April 2022