

New Zealand Datasheet

Name of Medicine

ROZEX gel
Metronidazole

Presentation

Metronidazole 7.5 mg/g in an aqueous gel containing methyl and propyl hydroxybenzoates, propylene glycol, carbomer 940 and disodium edetate. Metronidazole is 1- (2 hydroxyethyl)-2-methyl-5-nitroimidazole. It is a white to brownish crystalline powder that is soluble in water.

Uses

Actions

Metronidazole is an antiprotozoal (trichomoniasis, amoebiasis, giardiasis) and anaerobic antibacterial agent. However the mechanisms by which ROZEX gel acts in reducing inflammatory lesions of rosacea are unknown, but may include an antibacterial and / or anti-inflammatory effect.

Pharmacokinetics

The absorption of metronidazole following topical administration is negligible. Studies on the topical administration of 1 gram of ROZEX gel (7.5 mg of metronidazole) to the face of 10 rosacea patients showed a maximum serum concentration of 66 nanogram/mL in one patient. This concentration is approximately 100 times less than concentrations afforded by a single 250 mg tablet. The serum metronidazole concentrations were below the detectable limits of the assay at the majority of time points in all patients. Three of the patients had no detectable serum concentrations of metronidazole at any time point. The mean dose of gel applied during clinical studies was 600 mg, which represents 4.5 mg of metronidazole per application. Therefore under normal usage levels, the formulation affords minimal serum concentrations of metronidazole.

Indications

Treatment of inflammatory papules, pustules and erythema of rosacea.

Dosage and Administration

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

Elderly: The dosage recommended in the elderly is the same as that recommended in adults.

Children: Not recommended.

Areas to be treated should be cleansed before application of gel. Patients may use cosmetics after application of the product.

Significant therapeutic results should be noted within three weeks. Clinical studies have demonstrated continuing improvement over nine weeks of therapy.

Contraindications

Contraindicated in individuals with a history of hypersensitivity to metronidazole, hydroxybenzoates or other ingredients of the formulation.

Warnings and Precautions

ROZEX gel has been reported to irritate the eyes (watering) therefore contact with the eyes should be avoided, as well as with mucous membranes. If a reaction suggesting local irritation occurs, patients should be directed to use the medication less frequently, discontinue use temporarily or discontinue use until further instructions. Metronidazole is a nitroimidazole compound and should be used with care in patients with evidence or a history of blood dyscrasia.

Patients should be advised to avoid or minimize exposure of areas treated with topical metronidazole to sunlight or other sources of UV light (see section: Carcinogenicity, Mutagenicity and Impairment of Fertility). Unnecessary or prolonged use of this medication should be avoided, as the long-term safety of topical metronidazole is unknown.

Use in Pregnancy and Lactation

(Category B2)

There is no experience to date with the use of ROZEX gel in pregnancy. Metronidazole crosses the placental barrier and rapidly enters the foetal circulation. There is inadequate evidence of the safety of metronidazole in human pregnancy. In animal studies metronidazole was not teratogenic or embryotoxic unless administered at extremely high doses. Because there are no well-controlled studies of therapy with ROZEX gel in pregnant women, ROZEX gel should not be used during pregnancy.

After oral administration metronidazole is excreted in breast milk in concentrations similar to those found in the plasma. Metronidazole blood levels from topical application are significantly lower than those achieved after oral metronidazole. A decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Use in Children

ROZEX gel has not been studied in children. Rosacea is a skin disorder which principally affects adults.

Carcinogenicity, Mutagenicity and Impairment of Fertility

Animal studies with oral metronidazole showed increased incidences of tumour in the lung, liver, testes, reticulum, mammary gland and pituitary gland in certain rodent species. Evidence of photocarcinogenicity of metronidazole has also been reported in mice. Although there is no evidence to date of a carcinogenic effect in humans it is prudent to avoid unnecessary and prolonged use of ROZEX gel and to avoid or to minimise exposure of sites treated with ROZEX gel to the sun.

Metronidazole has shown evidence of mutagenic activity in several bacterial systems. In addition, a dose response increase in the frequency of micronuclei was observed in mice after intraperitoneal injection and an increase in chromosome aberrations has been found in human lymphocyte cultures. The benefit/risk ratio should therefore be carefully assessed in each case particularly in relation to the severity of the disease and the age of the patient.

Oral metronidazole caused hypospermatogenesis, infertility and abnormal spermatozoa in mice and rats with a NOEL in rats being about 200 times the estimated human metronidazole dose contained in the ROZEX gel, based on body surface area.

Adverse 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 drug have not been reported with ROZEX gel. Adverse reactions reported

with ROZEX gel include eye irritation (watering) if the gel is applied too closely to this area, transient redness, mild dryness, burning and skin irritation. None of the side effects exceeded an incidence of 2% of patients.

Post-marketing experience

The following non-serious adverse experiences have been reported since 1995: contact dermatitis/allergic reaction; local irritation, erythema, pruritis, burning, dryness, tightness, discomfort, rash; hyperpigmentation, pigmentation disorders, hypertrichosis; facial oedema; eyelid oedema; treatment failure (worsening of rosacea); watery eyes; metallic taste; tingling or numbness in the extremities; nausea; other (zoster lesion, pustules on the nose and vesicular bullous eruptions). The causal relationship with topical metronidazole has not been unequivocally established for these adverse experiences.

Interactions

Drug 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 coumarin and warfarin resulting in a prolongation of prothrombin time.

Overdosage

There is no human experience with overdosage of ROZEX gel. The acute oral toxicity of the ROZEX formulation was determined to be greater than 5g/kg (the highest dose given) in albino rats.

Pharmaceutical Precautions

Store below 25°C (room temperature)

Medicine Classification

Prescription Medicine.

Package Quantities

Gel: 15g, 30g, 50g

Further Information

Nil.

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