Metronidazole (topical)

Core Safety profile

4.2 Posology and method of administration

Metronidazole should be applied in a thin layer to the affected areas of the skin twice daily, morning and evening. Areas to be treated should be washed with a mild cleanser before application. Patients may use non comedogenic and non astringent cosmetics after application of metronidazole. The dosage does not need to be adjusted for elderly patients. Metronidazole is not recommended for use in children due to a lack of data on safety and efficacy. The average period of treatment varies according countries. It is usually of three to four months. The recommended duration of treatment should not be exceeded. However, if a clear benefit has been demonstrated continued therapy for a further three to four months period may be considered by the prescribing physician depending upon the severity of the condition. In clinical studies, topical metronidazole therapy for rosacea has been continued for up to 2 years. In the absence of a clear clinical improvement, therapy should be stopped.

4.3 Contraindications

Topical metronidazole therapy is contraindicated in individuals with a history of hypersensitivity to metronidazole or other ingredients of the formulation.

4.4 Special warnings and precautions for use

Contact with eyes and mucous membranes should be avoided. If irritation does occur the patient should be advised to use metronidazole less frequently or to stop temporarily and to seek medical advice if necessary. The UV exposure (sunbathing, solarium, sunlamp) should be avoided during the therapy with metronidazole. Metronidazole transforms into inactive metabolite due to UV exposure, therefore its efficacy decreases significantly. Phototoxic side-effects haven't been reported in clinical trials in relation to metronidazole.
Metronidazole is a nitro imidazole and should be used with caution in patients with an evidence of, or history of blood dyscrasia. Unnecessary and prolonged use of this medication should be avoided. Evidence suggests that metronidazole is carcinogenic in certain animal species. There is no evidence to date of a carcinogenic effect in human (see section preclinical safety data)

4.5 Interaction with other medications and other forms of interaction

Interaction with systemic medication is unlikely because absorption of metronidazole following cutaneous application is low. Nevertheless, it should be mentioned that disulfiram-like reactions has been reported in small number of patients taking metronidazole and alcohol concomitantly. Oral metronidazole has been reported to potentiate the effect of warfarin and other coumarin anticoagulants, resulting in a prolongation of prothrombin time. The effect of topical metronidazole on prothrombin time is unknown.

4.6 Pregnancy and Lactation

There has been no experience to date with the use of topical metronidazole in pregnant patients. In case of oral administration, metronidazole crosses the placental barrier and enters foetal circulation rapidly. No foetotoxicity was observed after oral metronidazole in either rats or mice. However because animal reproduction studies are not always predictive of human response and since oral metronidazole has been shown to be a carcinogen in some rodents this drug should be used in pregnancy only if clearly needed.

After oral administration metronidazole is secreted in breast milk in concentration similar to those found in plasma. Even though blood levels are significantly lower with cutaneous application of metronidazole than those achieved after oral metronidazole in nursing mothers, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Based upon the pharmacodynamic profile and clinical experience performance related to driving and using machines should not to be affected.

4.8 Undesirable effects

The following spontaneous adverse experiences have been reported, and within each system organ class, are ranked by frequency, using the following convention:
Very common (≥1/10)
Common (≥1/100, < 1/10)
Uncommon (≥ 1/ 1,000, < 1/100)
Rare (≥1/10,000, < 1/1,000)
Very rare (<1/10,000), including isolated reports

Skin and subcutaneous tissue disorders:
Common: dry skin, erythema, pruritus, skin discomfort (burning, pain of skin/stinging), skin irritation, worsening of rosacea.
Unknown frequency: contact dermatitis

Nervous System disorders:
Uncommon: hypoaesthesia, paraesthesia, dysgeusia (metallic taste)

Gastrointestinal disorders:
Uncommon: nausea

4.9 Overdose

No data exist about overdose in humans. Acute oral toxicity studies with topical gel formulation containing 0.75% w/w metronidazole in rats have shown no toxic action with doses of up to 5g of finished product per kilogram body weight, the highest dose used. This dose is equivalent to the oral intake of 12 tubes of 30g packaging Rozex gel®/Cream® or more than 7 tubes of the 50g packaging of Rozex Cutaneous Emulsion® for an adult weighing 72 kg, and 2 tubes of

Gel/Cream and more than 1 tube of Cutaneous Emulsion for a child weighing 12kg.