SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Metrosa 0.75% Gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of gel contains 7.5 mg Metronidazole.

Excipient with known effect: propylene glycol

This medicine contains 30 mg propylene glycol in 1 g gel (which is equivalent to 50 mg per application).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gel.

A smooth clear to turbid colourless to faintly yellow gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the topical treatment of Rosacea (inflammatory papulopustules rosacea related).

4.2 Posology and method of administration

Posology

Paediatric population

Not recommended as clinical trials have not been undertaken.

Method of administration

Cutaneous use.

Apply a thin film of the gel to the affected facial areas twice daily for four weeks. Treatment may be continued for a further four weeks if necessary.

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 eye-contact should occur, wash out of the eyes carefully with warm water.

If irritation does occur the patient should be advised to use Metrosa 0.75 % Gel 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.

The recommended duration of therapy should not be exceeded. If required, the therapy could be repeated, however the interval of 6 weeks in between should be considered.

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).

Metrosa 0.75 % Gel contains propylene glycol, which may cause skin irritation.

Paediatric population

There is no adequate clinical data on efficacy and safety of Metrosa 0.75 % Gel in children; therefore Metrosa 0.75 % Gel should not be applied to children.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction with systemic medication is unlikely because absorption of metronidazole following cutaneous application of Metrosa 0.75 % Gel is low.

Nevertheless, it should be mentioned that disulfiram-like reactions have 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 Fertility, 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 concentrations 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 account the 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 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, rash, 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).

General disorders:
Common: pain

Gastrointestinal disorders:
Uncommon: nausea

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 30 g packaging Metrosa 0.75 % Gel or more than 7 tubes of the 50 g packaging of Metrosa 0.75 % Gel for an adult weighing 72 kg, and 2 tubes of the 30 g packaging of Metrosa 0.75 % Gel and more than 1 tube of the 50 g packaging for a child weighing 12 kg.

Overdosage is not to be expected with this preparation. Any excess gel may be removed by washing with warm water. Appropriate gastric emptying may be used, if considered necessary, should accidental ingestion occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Chemotherapeutics for topical use

ATC Code: D06BX01

Metronidazole is a 5-nitroimidazole derivative with activity against anerobic protozoa and bacteria, due probably to an interference with DNA by a metabolite of the metronidazole.

The precise mode of action of Metronidazole in Rosacea is not known. It has been suggested that it has an anti-inflammatory effect due to an anti-oxidant activity affecting neutrophil cell function, or that it acts as a parasiticide towards Demodex folliculorum.

5.2 Pharmacokinetic properties

The gel is applied topically for its local action.

In humans, systemic absorption of 1g gel with 7.5mg Metronidazole after topical application is low (1% of oral dose). Quantifiable serum levels are in the range 25-66 ng/ml and cmax is < 5 % of that observed after a 30 mg oral dose (41 ng/ml vs. 850 ng/ml); tmax is prolonged, 5.98 hours compared to 0.97 hours orally.

5.3 Preclinical safety data

Single dose studies in mouse and rat by oral, intraperitoneal and intravenous routes show a low order of toxicity. Repeat dose studies (oral and intravenous) in mouse, rat, dog, and monkey indicate a no-effect level of 75 mg/kg/day.

Reproductive studies showed no evidence of embryotoxicity or teratogenicity in mouse, rat and rabbit (oral and intravenous). Reversible male infertility was observed in rats treated with 400 mg/kg/day.

Metronidazole is mutagenic in bacteria and fungi, but is regarded as non-genotoxic in mammalian species.

No phototoxic or photogenotoxic effects were seen in studies in Chinese hamster lung cells.

Carcinogenicity studies in mouse and rats showed an increased incidence of tumour, but recent epidemiological studies in human showed no increased cancer risk.

No local dermal toxicity (irritation, sensitisation) was seen in guinea pigs.

6.1 List of excipients

Phenoxyethanol (Ph.Eur.)

Propylene glycol

Hypromellose (E 464)

Purified water

Due to the composition (hypromellose), the gel may flake off the skin. This does not impair the efficacy.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.
Shelf life after first opening is 3 months.

6.4 Special precautions for storage

Do not refrigerate or freeze.

6.5 Nature and contents of container

Aluminium tube, fitted with a polyethylene (HDPE) screw cap.

[To be completed nationally]

Not all pack sizes are marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

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10 DATE OF REVISION OF THE TEXT

09/05/2024