PACKAGE LEAFLET: INFORMATION FOR THE USER

Emedal®
0.75% w/w gel, Metronidazole

1. IDENTIFICATION OF THE MEDICINAL PRODUCT

1.1. Trade Name

Emedal®

1.2. Composition

Active substance: Metronidazole.
Excipients: Carbomer 940, Propylene Glycol, Methylparaben E218, Propylparaben E216, Disodium Edetate Dihydrate, Sodium Hydroxide, Water Purified.

1.3. Pharmaceutical form

Gel for cutaneous use.

1.4. Quantitative composition in active substance

0.75% w/w in Metronidazole.

1.5. Nature and contents of container

Carton box containing aluminum tube of 30 g and package leaflet.

1.6. Pharmacotherapeutic group

Chemotherapeutic for topical use

1.7. Marketing Authorization Holder

TARGET PHARMA LTD. 54 Menandrou str., 10431 Athens Greece,
Tel.: +30 210 5224830, Fax: +30 210 5224838,
E-mail: info@targetpharma.gr, www.targetpharma.gr

1.8 Παρασκευαστής – Συσκευαστής

KLEVA SA 189 Parnithos Av. Acharnai, Attica Greece.
HELP S.A. 10 Valaoritou str. Metamorfosi, Attica Greece.

2. WHAT SHOULD THE PATIENT KNOW ABOUT THIS MEDICINE

2.1. General information

Emedal® contains metronidazole that is used for the treatment of rosacea.

2.2. Indications

Treatment of acute conditions of rosacea

2.3. Contraindications

Hypersensitivity to metronidazole or any other excipients of the formulation.

2.4. Special warnings and precautions for use

2.4.1. General

Patients with blood dyscrasia should be treated with caution. These patients should be monitored about the levels of white-blood cells. It should be avoided in porphyria.
If it is needed to exceed the indicated duration of use for metronidazole, it is recommended to perform frequent blood test, especially for the number of white-blood cells and the patients should be monitored for side-effects such as peripheral neuropathy, parenthesis, ataxia, dizziness, and epileptic convulsions.
During treatment with metronidazole the color of urine may be red, due to one of metronidazole metabolite.
It is recommended that patients with severe liver dysfunction or hepatocerebral syndrome should be treated with extra caution. In patients with decompensated cirrhosis of the liver, the recommended dose should be lowered to half, due to increased risk for side effects.
It is recommended to the patients using topical pharmaceutical forms of metronidazole, to avoid or minimize exposure of treated areas in direct sun light or artificial sources of UV radiation.
Pharmaceutical form for topical use should not be applied near the eyes.

2.4.2. Elderly

Metronidazole is well tolerated to the elderly. However, due to a pharmacokinetic study, caution is advised when administered in high dosages in this patient group.

2.4.3. Pregnancy

Metronidazole should not be used during pregnancy unless your doctor considers the use essential.

2.4.4. Lactation

Metronidazole should not be used during pregnancy unless your doctor considers the use essential.

2.4.5. Children

The use in children should be limited only for the indications described in section Posology for children.

2.4.6. Effects on the ability to drive and use machines

Patients should be warned for the possibility to experience confusion, dizziness, hallucinations, convulsions or temporary sight disturbances. In such cases the patients should be advised not to drive or use machines. Interactions with disulfirame and/or alcohol should be considered also.

2.4.7. Special warnings for the excipients

There are no special warnings about any of the excipients.

2.5. Interactions with other medicines or substances

- Oral anticoagulant treatment (like warfarin): increased anticoagulant effect and increased risk for bleeding, due to the reduced liver metabolism of the substance. In cases of co-administration, prothrombin time should be monitored and during administration of metronidazole the anticoagulant treatment should be adjusted.
- Lithium: Metronidazole may increase plasma levels of lithium. Patients treated with metronidazole while they receive lithium, should be monitored for the plasma levels of lithium, creatinine and minerals (electrolytes)
- *Cyclosporin*: High risk for increased plasma levels of cyclosporine. If the co-administration is necessary, creatinine and cyclosporine plasma levels should be closely monitored.
- *Phenobarbital and phenytoin*: Both substances increase the metabolic rate of metronidazole leading to reduced plasma levels. On the other hand metronidazole may reduce phenytoin's clearance leading to elongated self-life.
- *Cimetidine*: Inhibition of metronidazole metabolism leading to high plasma levels.
- *5-fluorouracil.:* In co-administration the clearance of fluorouracil is reduced leading to increased toxicity.
- *Alcohol*: Alcohol and other medicines that contain alcohol should be avoided during treatment and for one additional day after treatment. It is possible to cause reactions like rage, vomiting, tachycardia.
- *Disulfiram*: It has been reported the systemic co-administration of metronidazole and disulfiram may lead to psychotic effects.
- *Busulfan*: Metronidazole may increase plasma levels of busulfan, leading to severe busulfan toxicity.

When metronidazole is used topically no interactions with other medicines are expected.

2.6. Posology

Apply to the affected skin a thin layer of gel twice a day, in the morning and evening. Before the administration of the treatment, the affected areas should be cleaned with a mild cleanser. The duration of the treatment should not exceed 9 weeks. Depending on the severity of the condition, your doctor will decide if you should continue the treatment beyond this time.

2.7. Overdose – Management

Overdose cases have been reported due to mistake or due to suicide attempts, in which single dose of up to 12g of metronidazole have been orally applied. When the medicine is applied topically, overdose is very unlike to happen. The related symptoms were vomiting, ataxia amd mild disorientation.

Management
In cases of overdose in topical external administration, the gel should be cleaned with excess lukewarm water.

Poison Center Athens, Tel: +30 210 7793777

2.8. Possible side effects

Like all medicines **Emedal®** can also cause side effects, not only benefits. These side effects do not appear often and not all patients have such experience. In case you have a side-effect you should tell your doctor to receive the necessary instructions.

The below mentioned side effects are listed as per organic system during systemic use:

- **Gastrointestinal disorders:** abdominal pain, nausea, vomiting, diarrhea, stomatitis, glositis, mouth mucositis, metallic taste, dysgeusia, anorexia, xerostomia, rare cases of reversible pancreatitis.
- **Hypersensitivity reactions:** rash, urticaria, burning sensation, itching, redness, fever, angioedema, rare cases of anaphylactic shock and very rare cases of blistering.
- **Nervous system disorders:** Headache, convulsions, dizziness, vertigo, ataxia, lethargy, peripheral sensory neuropathy. Very rare cases of encephalopathy have been reported (i.e. confusion) and cerebral syndrome (i.e. ataxia, dysarthria, disturbance of gait, nystagmus and tremor), where the signs disappear after discontinuation of the medicine.
- **Psychiatric disorders:** psychosis, including confusion, hallucinations. Depression.
- **Eye disorders:** transient vision disorders such as diplopia or myopia.
- **Blood disorders:** Very rare cases of agranulocytosis have been reported, neutropenia and thrombopenia and reversible leukopenia.
- **Liver disorders:** Very rare cases of reversible liver dysfunction have been reported and cholestatic hepatitis.
- **Others:** dysuria, cystitis.

When metronidazole is topically administered on the skin, the systemic absorption of the substance is minimal. The reported side effects in topical administration were: lacrimation, when the application is near to the eyes, transient redness, mild dryness, burning sensation and skin irritation.

If you get any side effects, please talk to your doctor or pharmacist or any other health care provider or directly to the National Medicines Agency (284 Mesogion Av., 15562, Cholargos, Athens, Greece www.eof.gr).

2.9. What should the patient know if fails to take a dose.

If you forgot to take a dose and you remember it soon, then you can take the missed dose and continue as planned for the next doses.
If you remember it late and it is the time for your next dose then omit the forgotten dose and continue as planned.

2.10. What should the patient know about the expiration date.

You should not use this medicine after the expiration date that appears in the labeling of the product.

2.11. Special warnings about the storage of the product

Keep out of reach of children.
Store at a temperature that does not exceed 25°C, protected from light and humidity.

2.12. Date of last revision of this leaflet

14-12-2012

3. INFORMATION FOR THE RATIONAL USE OF MEDICINES

- This medicine has been prescribed for you by your doctor only for your particular medical problem. Do not pass it on to others or use it in other medical problems without taking previously advice by your doctor.
- If any problem with the medicine occurs during the treatment contact immediately your doctor or your pharmacist.
- If you have any questions about the medicinal product that you are using, or you need additional information, do not you hesitate to ask your doctor or your pharmacist.
- To keep this medicine effective and safe for your health, you should receive it exactly as your doctor prescribed.
- For your own safety and in order to maintain your good health, it is necessary to read carefully all information concerning the prescribed medicine.
- Do not store the medicines in bathroom lockers, as high temperature and humidity may degrade this product making it harmful to your health.
- Do not store a medicine that you no longer use or a medicine that is already expired.
- Keep all medicines in a safe place out of the reach and sight of children.

4. LEGAL STATUS

This medicinal product is subject to medical prescription.