

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

Zyomet Gel

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Metronidazole 0.75% w/w

### **3 PHARMACEUTICAL FORM**

Gel for cutaneous use

### **4 CLINICAL PARTICULARS**

#### **4.1 Therapeutic indications**

Zyomet Gel is indicated for the treatment of acute inflammatory exacerbations of acne rosacea

#### **4.2 Posology and method of administration**

Adults: Apply to the affected skin of the face in a thin film twice a day for eight to nine weeks. Thereafter, further applications may be necessary depending on the severity of the condition.

Use in the elderly: As detailed for adults.

Use in Children: Not recommended

#### **4.3 Contraindications**

Patients with known hypersensitivity to any of the ingredients should not use the product.

#### **4.4 Special warnings and precautions for use**

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 and should be used with care in patients with evidence of, or history of, blood dyscrasia. Exposure of treated sites to ultraviolet or strong sunlight should be avoided during use of metronidazole. Unnecessary and prolonged use of this medication should be avoided.

*Clean copy*

Zyomet Gel has been reported to cause lacrimation of the eyes, therefore avoid contact with eyes; if eye contact does occur the gel should be washed out carefully with water. Avoid drinking alcohol while using Zyomet Gel.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

There is evidence to suggest that systemic absorption of metronidazole after topical application is negligible. A small number of patients taking oral metronidazole and alcohol concomitantly have experienced a disulfiram-like reaction.

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 is not known. However, very rare cases of modification of the INR values have been reported with concomitant use of metronidazole and coumarin anticoagulants.

#### **4.6 Pregnancy and lactation**

There is no experience to date with the use of Zyomet Gel in human 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 animals, Metronidazole was not teratogenic or embryotoxic unless administered at extremely high doses. Zyomet Gel should only be used in pregnancy where there is no safer alternative.

After oral administration, Metronidazole is excreted in breast milk in concentrations similar to those found in the plasma, Metronidazole blood levels from topical administration are significantly lower than those achieved after oral administration. A decision should be made 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**

None

#### **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 drug have not been reported with Zyomet Gel. Adverse reactions reported with Zyomet Gel have been only local and mild, and include skin discomfort (burning and stinging), erythema, pruritis, skin irritation, worsening of rosacea, nausea, metallic taste and tingling or numbness of the extremities, and watery eyes if applied too closely to this area.

## **4.9 Overdose**

No data exists about overdosage in humans. Acute oral toxicity studies with a topical gel formulation containing 0.75% w/w metronidazole in rats have shown no toxic action with doses of up to 5 g 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 Zyomet Gel for an adult weighing 72 kg, and 2 tubes of Gel for a child weighing 12 kg.

# **5 PHARMACOLOGICAL PROPERTIES**

## **5.1 Pharmacodynamic properties**

The mode of action of topical metronidazole in the treatment of rosacea is not known at present. The most likely mechanism appears to be combined immunosuppressive and anti-inflammatory activity.

## **5.2 Pharmacokinetic properties**

Percutaneous absorption from topical metronidazole gel results in negligible plasma levels of metronidazole. Human studies have shown levels of approximately 70 ng/ml, 100 times lower than levels seen with systemic treatment.

## **5.3 Preclinical safety data**

Metronidazole shows low toxicity in all animal species studied. It has been reported to be mutagenic in some bacteria but not in human lymphocytes. Micronucleus tests in mice and rats were also negative. This suggests that metronidazole is not a mammalian mutagen. Metronidazole has been used for many years and its safety in man has been demonstrated.

# **6 PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

Propylene Glycol  
Disodium Edetate  
Hydroxyethylcellulose  
Benzyl Alcohol  
Purified Water

## **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf life**

- a) For the product as packaged for sale – 3 years
- b) After first opening the container- Comply with expiry date.

### **6.4 Special precautions for storage**

The product should be stored at room temperature below 25°C. Do not refrigerate.

### **6.5 Nature and contents of container**

5g, 15g, 30g, 50g and 60g HDPE tubes

### **6.6 Special precautions for disposal**

Not applicable

## **7      MARKETING AUTHORISATION HOLDER**

Goldshield Pharmaceuticals Ltd  
NLA Tower 12-16 Addiscombe Road  
Croydon CR0 0XT  
United Kingdom

## **8      MARKETING AUTHORISATION NUMBER(S)**

PL 12762/0025

## **9      DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

30 September 1998

## **10     DATE OF REVISION OF THE TEXT**

11 May 2010