METRONIDAZOLE- metronidazole gel
Taro Pharmaceuticals U.S.A., Inc.

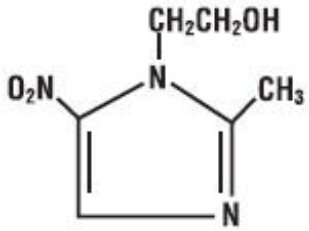
Metronidazole
Gel USP, 0.75%

Rx Only

FOR TOPICAL USE ONLY
NOT FOR OPHTHALMIC USE

DESCRIPTION

Metronidazole gel contains metronidazole, USP, at a concentration of 7.5 mg per gram (0.75%) in a gel consisting of carbomer 940, edetate disodium, methylparaben, propylene glycol, propylparaben, purified water, and sodium hydroxide. Metronidazole is classified therapeutically as an antiprotozoal and antibacterial agent. Chemically, metronidazole is named 2-methyl-5-nitro-1*H*-imidazole-1-ethanol and has the following structure:



CLINICAL PHARMACOLOGY

Bioavailability studies on the topical administration of 1 gram of metronidazole gel (7.5 mg of metronidazole) to the face of 10 rosacea patients showed a maximum serum concentration of 66 nanograms per milliliter in one patient. This concentration is approximately 100 times less than concentrations afforded by a single 250 mg oral 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. The mechanisms by which metronidazole gel acts in the treatment of rosacea are unknown, but appear to include an anti-inflammatory effect.

INDICATIONS AND USAGE

Metronidazole gel is indicated for topical application in the treatment of inflammatory papules and pustules of rosacea.

CONTRAINDICATIONS

Metronidazole gel is contraindicated in individuals with a history of hypersensitivity to metronidazole, parabens, or other ingredients of the formulation.

PRECAUTIONS

General

Metronidazole gel has been reported to cause tearing of the eyes. Therefore, contact with the eyes should be avoided. If a reaction suggesting local irritation occurs, patients should be directed to use the medication less frequently or discontinue use.

Metronidazole is a nitroimidazole and should be used with care in patients with evidence of, or history of blood dyscrasia.

Information for patients

This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.

Drug interactions

Oral metronidazole has been reported to potentiate the anticoagulant effect of coumarin and warfarin resulting in a prolongation of prothrombin time. The effect of topical metronidazole on prothrombin time is not known.

Carcinogenesis, mutagenesis, impairment of fertility

Metronidazole has shown evidence of carcinogenic activity in a number of studies involving chronic, oral administration in mice and rats but not in studies involving hamsters.

Metronidazole has shown evidence of mutagenic activity in several *in vitro* bacterial assay systems. In addition, a dose-response increase in the frequency of micronuclei was observed in mice after intraperitoneal injections and an increase in chromosome aberrations have been reported in patients with Crohn's disease who were treated with 200-1200 mg/day of metronidazole for 1 to 24 months. However, no excess chromosomal aberrations in circulating human lymphocytes have been observed in patients treated for 8 months.

Pregnancy

Teratogenic effects

Pregnancy category B

There has been no experience to date with the use of metronidazole gel in pregnant patients. Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. No fetotoxicity was observed after oral metronidazole in 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 during pregnancy only if clearly needed.

Nursing mothers

After oral administration, metronidazole is secreted in breast milk in concentrations similar to those found in the plasma. Even though metronidazole gel blood levels are significantly lower than those achieved after oral metronidazole, 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.

Pediatric use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

The following adverse experiences have been reported with the topical use of metronidazole: burning, skin irritation, dryness, transient redness, metallic taste, tingling or numbness of extremities and nausea.

DOSAGE AND ADMINISTRATION

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

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

HOW SUPPLIED

Metronidazole Gel USP, 0.75% is supplied in aluminum tubes containing:

5 g NDC 51672-4116-5 (physician sample, tube only)
30 g NDC 51672-4116-2
45 g NDC 51672-4116-6

Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].

Mfd. by:
Taro Pharmaceutical Industries Ltd.
Haifa Bay, Israel 26110

Dist. by:
Taro Pharmaceuticals U.S.A., Inc.
Hawthorne, NY 10532

Revised: February, 2011

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449

PRINCIPAL DISPLAY PANEL - 30 g Tube Carton

NDC 51672-4116-2

Metronidazole
Gel USP, 0.75%

FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC USE.

Keep this and all medications out of the reach of children.

30 g

Rx only

TARO

METRONIDAZOLE

metronidazole gel

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51672-4116
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
metronidazole (UNII: 140QMO216E) (metronidazole - UNII:140QMO216E)	metronidazole	7.5 mg in 1 g

Inactive Ingredients	
Ingredient Name	**Strength**
carbomer homopolymer type c (allyl pentaerythritol crosslinked) (UNII: 4Q93RCW27E)	
edetate disodium (UNII: 7FLD91C86K)	
methylparaben (UNII: A2I8C7HI9T)	
propylene glycol (UNII: 6DC9Q167V3)	
propylparaben (UNII: Z8IX2SC1OH)	
water (UNII: 059QF0KO0R)	
sodium hydroxide (UNII: 55X04QC32I)	

Product Characteristics

Color	YELLOW (Colorless to Pale Yellow)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51672-4116-5	5 g in 1 TUBE; Type 0: Not a Combination Product	07/18/2006	
2	NDC:51672-4116-2	1 in 1 CARTON	07/18/2006	
2		30 g in 1 TUBE; Type 0: Not a Combination Product		
3	NDC:51672-4116-6	1 in 1 CARTON	07/18/2006	
3		45 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA077819	07/18/2006	

Labeler - Taro Pharmaceuticals U.S.A., Inc. (145186370)

Establishment

Name	Address	ID/FEI	Business Operations
Taro Pharmaceutical Industries Ltd.		600072078	MANUFACTURE(51672-4116)

Revised: 3/2017 Taro Pharmaceuticals U.S.A., Inc.