

METRONIDAZOLE- metronidazole gel
Cosette Pharmaceuticals, Inc.

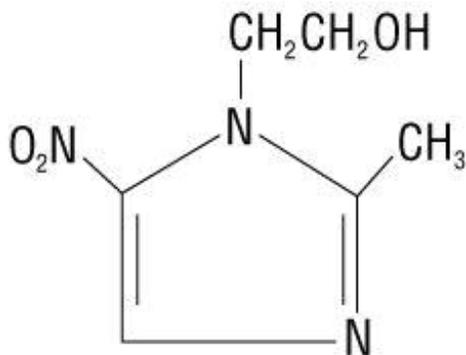
Metronidazole Gel USP, 0.75%

FOR TOPICAL USE ONLY (NOT FOR OPHTHALMIC USE)

Rx Only

DESCRIPTION:

Metronidazole Gel USP, 0.75% contains metronidazole, USP, at a concentration of 7.5 mg per gram (0.75%) in a gel consisting of carbomer homopolymer NF, 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 USP 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.

To report SUSPECTED ADVERSE REACTIONS, contact Cosette Pharmaceuticals, Inc. at 1-800-922-1038 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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 a 45 g tube
NDC 0713-0637-37

Storage conditions:

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

Distributed by:

Cosette Pharmaceuticals, Inc.
South Plainfield, NJ 07080

8-0637BFCPLNC3
Rev. 07/2022
VC7647

PRINCIPAL DISPLAY PANEL

NDC 0713-0637-37

Metronidazole Gel USP 0.75%

45 g

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NDC 0713-0637-37

Rx only

0.75%

45 g

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

KEEP OUT OF REACH OF CHILDREN.

Usual dosage: Apply a thin film to entire affected areas after washing. Use morning and evening or as directed by physician. Avoid application close to the eyes.

Each gram contains: 7.5 mg of metronidazole as the active ingredient with 0.8 mg of methylparaben and 0.2 mg of propylparaben as preservatives in a gel consisting of carbomer homopolymer NF, edetate disodium, propylene glycol, purified water, and sodium hydroxide.

See crimped end for lot number and expiration date.

Distributed by:

Cosette Pharmaceuticals, Inc.

South Plainfield, NJ 07080

VC1201 Rev. 03/2021 11-637BF37CPLNC2



0713-0637-37

FP0 J201
Read Direction

METRONIDAZOLE

metronidazole gel

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0713-0637
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
METHYLPARABEN (UNII: A2I8C7HI9T)	
PROPYLPARABEN (UNII: Z8IX2SC1OH)	
CARBOMER HOMOPOLYMER TYPE C (UNII: 4Q93RCW27E)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	

PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
WATER (UNII: 059QF0KO0R)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0713-0637-37	1 in 1 CARTON	04/01/2011	
1		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	ANDA078178	04/01/2011	

Labeler - Cosette Pharmaceuticals, Inc. (116918230)

Registrant - Cosette Pharmaceuticals, Inc. (116918230)

Establishment

Name	Address	ID/FEI	Business Operations
Cosette Pharmaceuticals NC Laboratories, LLC		079419931	analysis(0713-0637) , label(0713-0637) , manufacture(0713-0637) , pack(0713-0637)

Revised: 11/2022

Cosette Pharmaceuticals, Inc.