

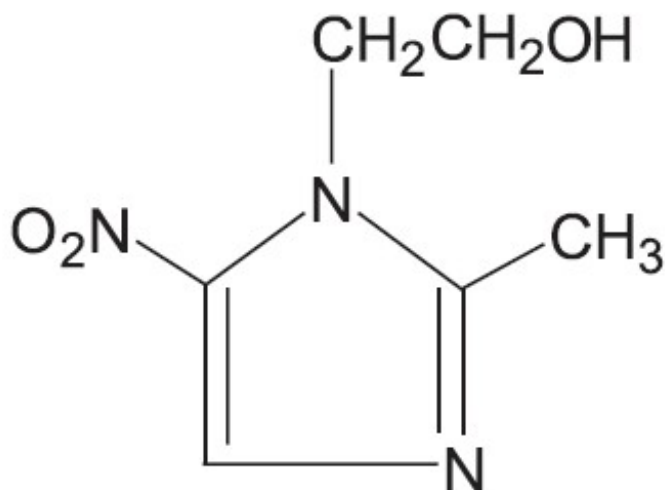
METRONIDAZOLE - metronidazole topical gel

Encube Ethicals Private Limited

Metronidazole Gel USP (Topical), 0.75%
Rx only
FOR TOPICAL USE ONLY
(NOT FOR OPHTHALMIC USE)

DESCRIPTION

Metronidazole gel USP (topical), 0.75%, contains metronidazole, at a concentration of 7.5 mg per gram (0.75%) in a gel consisting of carbopol 980, edetate disodium, methylparaben, propylene glycol, propylparaben, purified water, and sodium hydroxide. Metronidazole is classified therapeutically as an antiprotozoal and anti-bacterial agent. Chemically, metronidazole is named 2-methyl-5-nitro-1H-imidazole-1-ethanol and has the following structure:



CLINICAL PHARMACOLOGY

Bioavailability studies on the topical administration of 1 gram of metronidazole gel USP (topical), 0.75%, (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 USP (topical), 0.75%, acts in the treatment of rosacea are unknown, but appear to include an anti-inflammatory effect.

INDICATIONS AND USAGE

Metronidazole gel USP (topical), 0.75%, is indicated for topical application in the treatment of inflammatory papules and pustules of rosacea.

CONTRAINDICATIONS

Metronidazole gel USP (topical), 0.75%, is contraindicated in individuals with a history of hypersensitivity to metronidazole, parabens, or other ingredients of the formulation.

PRECAUTIONS

General

Metronidazole gel USP (topical), 0.75%, 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

Teratogenic effects: Pregnancy category B: There has been no experience to date with the use of metronidazole gel USP (topical), 0.75%, 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 USP (topical), 0.75%, 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 USP (topical), 0.75%, twice daily, morning and evening, to entire affected areas after washing. Areas to be treated should be cleansed before application of metronidazole gel USP (topical), 0.75%. Patients may use cosmetics after application of metronidazole gel USP (topical), 0.75%.

HOW SUPPLIED

Metronidazole gel USP (topical), 0.75%, is supplied as the following:
NDC 21922-070-06: 45 g aluminum tube

Storage conditions: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

To report SUSPECTED ADVERSE REACTIONS, contact Encube Ethicals Private Limited at 1-833-285 4151 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Manufactured by:

Encube Ethicals Pvt. Ltd.

Plot No. C-1, Madkaim Industrial Estate,
Madkaim, Post: Mardol, Panda,
Goa - 403 404, India.

Distributed by:

Encube Ethicals, Inc.

200 Meredith Drive,
Suite 202Durham,
NC 27713 USA

Revised: 05/2023

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Carton Label

NDC 21922-**070**-06

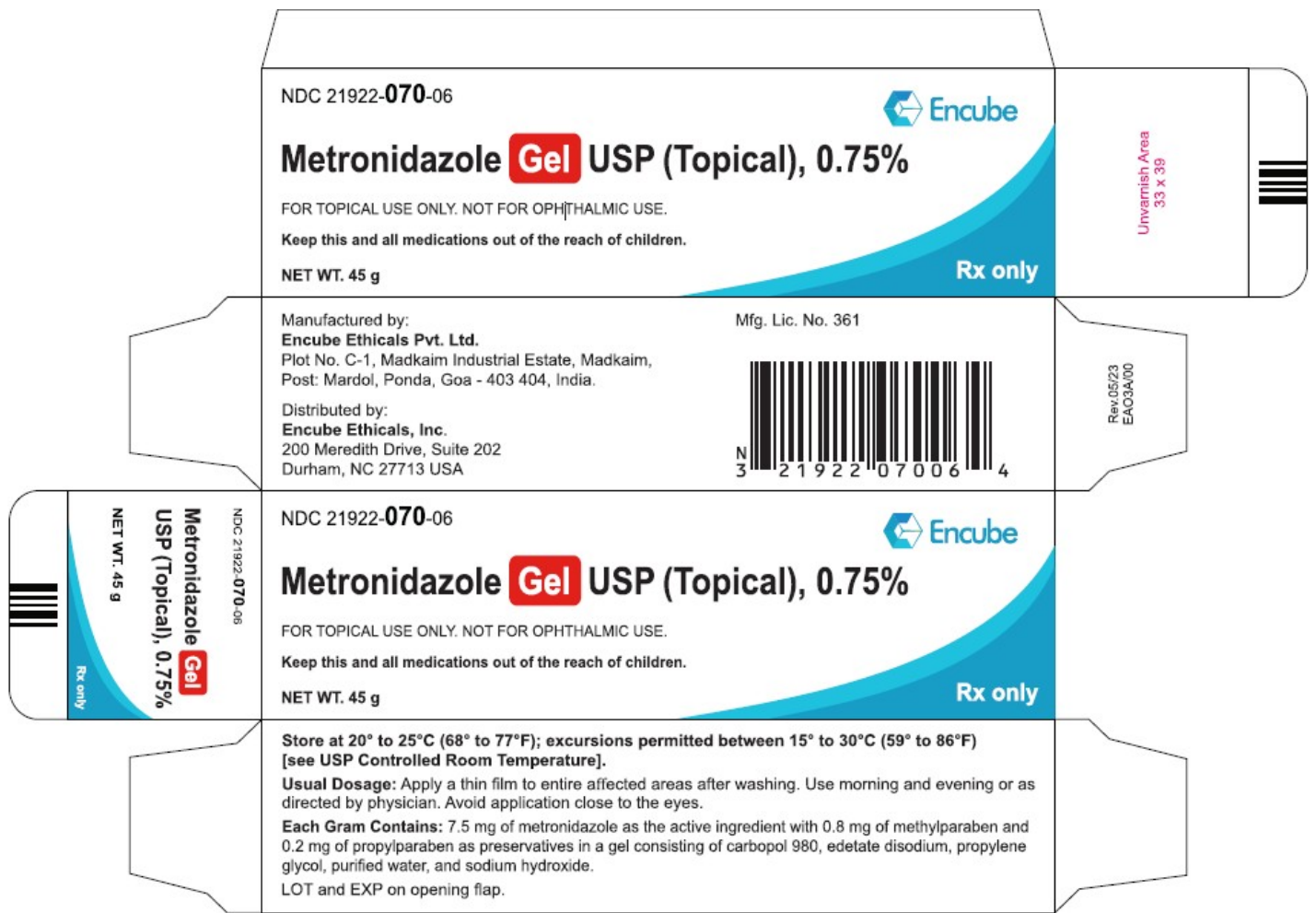
Metronidazole Gel USP (Topical), 0.75%

FOR TOPICAL USE ONLY. NOT FOR OPHTHALMIC USE.

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

NET WT.45g

Rx only



METRONIDAZOLE

metronidazole topical gel

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:21922-070
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 (ALLYL PENTAERYTHRITOL CROSSLINKED) (UNII: 4Q93RCW27E)	

PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:21922-070-06	1 in 1 CARTON	01/28/2025	
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	ANDA077547	01/28/2025	

Labeler - Encube Ethicals Private Limited (915834105)

Establishment

Name	Address	ID/FEI	Business Operations
Encube Ethicals Private Limited		725076298	ANALYSIS(21922-070) , LABEL(21922-070) , MANUFACTURE(21922-070) , PACK(21922-070)

Revised: 2/2025

Encube Ethicals Private Limited