METRONIDAZOLE- metronidazole cream
Preferred Pharmaceuticals Inc.

Metronidazole Topical Cream, 0.75%
FOR TOPICAL USE ONLY
(NOT FOR OPHTHALMIC USE)

DESCRIPTION

Metronidazole topical cream contains metronidazole, USP, at a concentration of 7.5 mg per gram (0.75%) in an emollient cream consisting of benzyl alcohol, emulsifying wax, glycerin, isopropyl palmitate, purified water, sorbitol solution, lactic acid and sodium hydroxide to adjust pH.

Metronidazole is a member of the imidazole class of antibacterial agents and is classified therapeutically as an antiprotozoal and anti-bacterial agent. Chemically, metronidazole is 2-methyl-5-nitro-1*H*-imidazole-1-ethanol. The molecular formula is $C_6H_9N_3O_3$ and molecular weight is 171.15.

Metronidazole is represented by the following structural formula:

CLINICAL PHARMACOLOGY

The mechanisms by which metronidazole acts in the treatment of rosacea are unknown, but appear to include an anti-inflammatory effect.

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

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

PRECAUTIONS

General

Topical metronidazole 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 warfarin and coumarin anticoagulants, resulting in a prolongation of prothrombin time. The effect of topical metronidazole on prothrombin time is not known.

Carcinogenes is, mutagenes is, 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 mg/day to 1,200 mg/day of metronidazole for 1 months to 24 months.

However, no excess chromosomal aberrations in circulating human lymphocytes have been observed in patients treated for 8 months.

Pregnancy

Teratogenic effects

There are no adequate and well-controlled studies with the use of metronidazole topical cream in pregnant women. 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 blood levels are significantly lower with topically applied metronidazole than those achieved after oral administration of 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

In controlled clinical trials, the total incidence of adverse reactions associated with the use of metronidazole topical cream was approximately 10%. Skin discomfort (burning and stinging) was the most frequently reported event followed by erythema, skin irritation, pruritus and worsening of rosacea.

All individual events occurred in less than 3% of patients. The following additional adverse experiences have been reported with the topical use of metronidazole: dryness, transient redness, metallic taste, tingling or numbness of extremities and nausea.

To report SUSPECTED ADVERSE REACTIONS, contact Viona Pharmaceuticals Inc. at 1-888-304-5011 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION

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

Areas to be treated should be washed with a mild cleanser before application. Patients may use cosmetics after application of metronidazole topical cream.

HOW SUPPLIED

Metronidazole topical cream, 0.75% is white to off-white homogeneous cream, free from lumps, free from gritty particles and foreign matter without phase separation and is supplied as follows:

45 gram aluminum tube	NDC 68788-8552-4

Storage conditions: Store at 20°C to 25°C (68ºF to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].

Call your doctor for medical advice about side effects. You may report side effects to Viona Pharmaceuticals Inc. at 1-888-304-5011 or FDA at 1-800-FDA-1088.

SPL UNCLASSIFIED

Manufactured by:

Zydus Lifesciences Ltd.

Changodar, Ahmedabad, India

Distributed by:

Viona Pharmaceuticals Inc.

Cranford, NJ 07016

Rev.: 01/23

Relabeled By: Preferred Pharmaceuticals Inc.

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 68788-8552-4

Metronidazole Topical Cream, 0.75%

Rx only

45 g

Viona

Relabeled By: Preferred Pharmaceuticals Inc.

METRONIDAZOLE

metronidazole cream

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:68788-8552(NDC:72578-129)
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**
BENZYL ALCOHOL (UNII: LKG8494WBH)	

GLYCERIN (UNII: PDC6A3C0OX)	
ISOPROPYL PALMITATE (UNII: 8CRQ2TH63M)	
LACTIC ACID, UNSPECIFIED FORM (UNII: 33X04XA5AT)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
SORBITOL SOLUTION (UNII: 8KW3E207O2)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	WHITE (off-white)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68788-8552-4	1 in 1 CARTON	11/20/2023	
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	ANDA217128	11/20/2023	

Labeler - Preferred Pharmaceuticals Inc. (791119022)

Registrant - Preferred Pharmaceuticals Inc. (791119022)

Establishment

Name	Address	ID/FEI	Business Operations
Preferred Pharmaceuticals Inc.		791119022	RELABEL(68788-8552)

Revised: 11/2023 Preferred Pharmaceuticals Inc.