ERYTHROMYCIN AND BENZOYL PEROXIDE- erythromycin and benzoyl peroxide
Sandoz Inc.

Erythromycin and Benzoyl Peroxide Topical Gel, USP
Topical gel: erythromycin (3%), benzoyl peroxide (5%)

Rx only

PLEASE READ COMPLETE COMPOUNDING DIRECTIONS
NOTE: TAP VIAL UNTIL ALL POWDER FLOWS FREELY. ADD ROOM TEMPERATURE 70% ETHYL ALCOHOL TO VIAL (TO THE MARK) AND **IMMEDIATELY** SHAKE/DISSOLVE **COMPLETELY.**

For Dermatological Use Only – Not for Ophthalmic Use

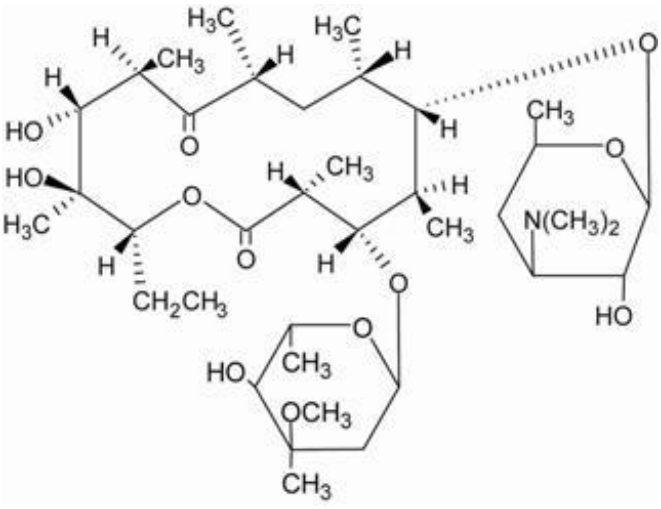
Reconstitute Before Dispensing

DESCRIPTION

Erythromycin and benzoyl peroxide topical gel USP, 3%;5% contains erythromycin [(3R*, 4S*, 5S*, 6R*, 7R*, 9R*, 11R*, 12R*, 13S*, 14R*)-4-[(2,6-Dideoxy-3-*C*-methyl-3-*O*-methyl-α-L-*ribo*-hexopyranosyl)-oxy]-14-ethyl-7,12,13-trihydroxy-3,5,7,9,11,13-hexamethyl-6-[[3,4,6-trideoxy-3-(dimethylamino)-ß-D-*xylo*-hexopyranosyl]oxy]oxacyclotetradecane-2,10-dione].

Erythromycin is a macrolide antibiotic produced from a strain of *Saccharopolyspora erythraea* (formerly *Streptomyces erythreus*). It is a base and readily forms salts with acids.

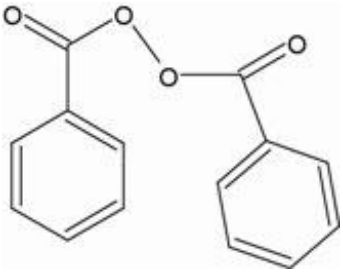
Chemically, erythromycin is ($C_{37}H_{67}NO_{13}$). It has the following structural formula:



Erythromycin has the molecular weight of 733.94. It is a white crystalline powder and has a solubility of approximately 1 mg/mL in water and is soluble in alcohol at 25°C.

Erythromycin and benzoyl peroxide topical gel USP, 3%;5% also contains benzoyl peroxide for topical use. Benzoyl peroxide is an antibacterial and keratolytic agent.

Chemically, benzoyl peroxide is ($C_{14}H_{10}O_4$). It has the following structural formula:



Benzoyl peroxide has the molecular weight of 242.23. It is a white granular powder and is sparingly soluble in water and alcohol and soluble in acetone, chloroform and ether.

Each gram of erythromycin and benzoyl peroxide topical gel USP, 3%;5% contains, as dispensed, 30 mg (3%) of erythromycin, USP and 50 mg (5%) of benzoyl peroxide, USP in a gel of purified water, USP, alcohol 20%, carbomer homopolymer type C, NF, sodium hydroxide, NF, docusate sodium and fragrance.

CLINICAL PHARMACOLOGY

The exact mechanism by which erythromycin reduces lesions of acne vulgaris is not fully known; however, the effect appears to be due in part to the antibacterial activity of the drug.

Benzoyl peroxide has a keratolytic and desquamative effect which may also contribute to its efficacy. Benzoyl peroxide has been shown to be absorbed by the skin where it is converted to benzoic acid.

MICROBIOLOGY: Erythromycin acts by inhibition of protein synthesis in susceptible organisms by reversibly binding to 50 ***S*** ribosomal subunits, thereby inhibiting translocation of aminoacyl transfer–RNA and inhibiting polypeptide synthesis. Antagonism has been demonstrated *in vitro* between erythromycin, lincomycin, chloramphenicol and clindamycin.

Benzoyl peroxide is an antibacterial agent which has been shown to be effective against *Propionibacterium acnes*, an anaerobe found in sebaceous follicles and comedones. The antibacterial action of benzoyl peroxide is believed to be due to the release of active oxygen.

INDICATIONS AND USAGE

Erythromycin and benzoyl peroxide topical gel USP, 3%;5% is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS

Erythromycin and benzoyl peroxide topical gel USP, 3%;5% is contraindicated in those individuals who have shown hypersensitivity to any of its components.

WARNINGS

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including erythromycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of “antibiotic-associated colitis.”

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be

initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

PRECAUTIONS

General

For topical use only; not for ophthalmic use. Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating or abrasive agents. If severe irritation develops, discontinue use and institute appropriate therapy.

The use of antibiotic agents may be associated with the overgrowth of nonsusceptible organisms including fungi. If this occurs, discontinue use and take appropriate measures.

Avoid contact with eyes and all mucous membranes.

Information for Patients

Patients using erythromycin and benzoyl peroxide topical gel USP, 3%;5% should receive the following information and instructions.

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes, nose, mouth, and all mucous membranes.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. Patients should not use any other topical acne preparation unless otherwise directed by physician.
4. Patients should report to their physician any signs of local adverse reactions.
5. Erythromycin and benzoyl peroxide topical gel USP, 3%;5% may bleach hair or colored fabric.
6. Keep product refrigerated and discard after 3 months.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Data from a study using mice known to be highly susceptible to cancer suggests that benzoyl peroxide acts as a tumor promoter. The clinical significance of this is unknown.

No animal studies have been performed to evaluate the carcinogenic and mutagenic potential or effects on fertility of topical erythromycin. However, long-term (2-year) oral studies in rats with erythromycin ethylsuccinate and erythromycin base did not provide evidence of tumorigenicity. There was no apparent effect on male or female fertility in rats fed erythromycin (base) at levels up to 0.25% of diet.

Pregnancy

Teratogenic Effects

Pregnancy CATEGORY C: Animal reproduction studies have not been conducted with erythromycin and benzoyl peroxide topical gel USP, 3%;5% or benzoyl peroxide.

There was no evidence of teratogenicity or any other adverse effect on reproduction in female rats fed erythromycin base (up to 0.25% diet) prior to and during mating, during gestation and through weaning of two successive litters.

There are no well-controlled trials in pregnant women with erythromycin and benzoyl peroxide topical gel USP, 3%;5%. It also is not known whether erythromycin and benzoyl peroxide topical gel USP, 3%;5% can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Erythromycin and benzoyl peroxide topical gel USP, 3%;5% should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether erythromycin and benzoyl peroxide topical gel USP, 3%;5% is excreted in human milk after topical application. However, erythromycin is excreted in human milk following oral and parenteral erythromycin administration. Therefore, caution should be exercised when erythromycin is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of this product in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS

In controlled clinical trials, the incidence of adverse reactions associated with the use of erythromycin and benzoyl peroxide topical gel USP, 3%;5% was approximately 3%. These were dryness and urticarial reaction.

The following additional local adverse reactions have been reported occasionally: irritation of the skin including peeling, itching, burning sensation, erythema, inflammation of the face, eyes and nose, and irritation of the eyes. Skin discoloration, oiliness and tenderness of the skin have also been reported.

DOSAGE AND ADMINISTRATION

Erythromycin and benzoyl peroxide topical gel USP, 3%;5% should be applied twice daily, morning and evening, or as directed by a physician, to affected areas after the skin is thoroughly washed, rinsed with warm water and gently patted dry.

HOW SUPPLIED[/S]

Compounding Directions[/TC]				
Size(Net Weight)	NDC 0781-	Benzoyl Peroxide Gel	Active Erythromycin Powder (In Plastic Vial)	70% Ethyl Alcohol To Be Added
23.3 grams(as dispensed)	7054-49	20 grams	0.8 grams	3 mL
46.6 grams(as dispensed)	7094-59	40 grams	1.6 grams	6 mL

TO THE PHARMACIST: IMPORTANT – Prior to dispensing, tap vial until all powder flows freely. Add indicated amount of room temperature 70% ethyl alcohol to vial (to the mark) and immediately shake to completely dissolve erythromycin. Add this solution to gel and stir with supplied spatula until homogeneous in appearance (1 to 1 ½ minutes). Erythromycin and benzoyl peroxide topical gel USP, 3%;5% should then be stored under refrigeration. Do not freeze. Place a 3-month expiration date on the label.

NOTE: Prior to reconstitution, store at 20° to 25°C (68° – 77°F). [See USP Controlled Room Temperature].

After reconstitution, store under refrigeration between 2° and 8°C (36° – 46°F).

Do not freeze. Keep tightly closed. Keep out of the reach of children.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Manufactured by
TOLMAR Inc.
Fort Collins, CO 80526 for
Sandoz Inc.
Princeton, NJ 08540

04275 Rev. 6 04/11

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

0.8g vial

1.6g vial

23.3g jar

46.6g jar

ERYTHROMYCIN AND BENZOYL PEROXIDE

erythromycin and benzoyl peroxide kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0781-7054

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0781-7054-49	1 in 1 CARTON; Type 0: Not a Combination Product	03/29/2004	

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL, PLASTIC	0.8 g
Part 2	1 JAR	20 g

Part 1 of 2

ERYTHROMYCIN

erythromycin gel

Product Information	
Item Code (Source)	NDC:0781-8054
Route of Administration	TOPICAL

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ERYTHROMYCIN (UNII: 63937KV33D) (ERYTHROMYCIN - UNII:63937KV33D)	ERYTHROMYCIN	30 mg in 1 g

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**

1	NDC:0781-8054-01	0.8 g in 1 VIAL, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065112		

Part 2 of 2

BENZOYL PEROXIDE

benzoyl peroxide gel

Product Information

Item Code (Source)	NDC:0781-9054
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
BENZOYL PEROXIDE (UNII: W9WZN9A0GM) (BENZOYL PEROXIDE - UNII:W9WZN9A0GM)	BENZOYL PEROXIDE	50 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
CARBOMER HOMOPOLYMER TYPE C (UNII: 4Q93RCW27E)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
DOCUSATE SODIUM (UNII: F05Q2T2JA0)	
WATER (UNII: 059QF0KO0R)	
LIMONENE, (+)- (UNII: GFD7C86Q1W)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-9054-22	20 g in 1 JAR; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065112		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065112	03/29/2004	

ERYTHROMYCIN AND BENZOYL PEROXIDE

erythromycin and benzoyl peroxide kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0781-7094

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-7094-59	1 in 1 CARTON; Type 0: Not a Combination Product	03/29/2004	

Quantity of Parts		
Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, PLASTIC	1.6 g
Part 2	1 JAR	40 g

Part 1 of 2

ERYTHROMYCIN

erythromycin gel

Product Information	
Item Code (Source)	NDC:0781-8094
Route of Administration	TOPICAL

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
ERYTHROMYCIN (UNII: 63937KV33D) (ERYTHROMYCIN - UNII:63937KV33D)	ERYTHROMYCIN	30 mg in 1 g

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-8094-02	1.6 g in 1 VIAL, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065112		

Part 2 of 2

BENZOYL PEROXIDE

benzoyl peroxide gel

Product Information

Item Code (Source)	NDC:0781-9094
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
BENZOYL PEROXIDE (UNII: W9WZN9A0GM) (BENZOYL PEROXIDE - UNII:W9WZN9A0GM)	BENZOYL PEROXIDE	50 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
ALCOHOL (UNII: 3K9958V90M)	
CARBOMER HOMOPOLYMER TYPE C (UNII: 4Q93RCW27E)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
DOCUSATE SODIUM (UNII: F05Q2T2JA0)	
WATER (UNII: 059QF0KO0R)	
LIMONENE, (+)- (UNII: GFD7C86Q1W)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-9094-44	40 g in 1 JAR; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065112		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA065112	03/29/2004	

Labeler - Sandoz Inc. (005387188)

Establishment

Name	Address	ID/FEI	Business Operations
TOLMAR Inc.		791156578	ANALYSIS(0781-7054, 0781-8054, 0781-9054, 0781-7094, 0781-8094, 0781-9094) , LABEL(0781-7054, 0781-8054, 0781-9054, 0781-7094, 0781-8094, 0781-9094) , MANUFACTURE(0781-7054, 0781-8054, 0781-9054, 0781-7094, 0781-8094, 0781-9094) , PACK(0781-7054, 0781-8054, 0781-9054, 0781-7094, 0781-8094, 0781-9094)

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