ERYTHROMYCIN AND BENZOYL PEROXIDE- erythromycin and benzoyl peroxide Oceans ide Pharmaceuticals

Erythromycin-Benzoyl Peroxide Topical Gel

DESCRIPTION

Erythromycin-Benzoyl Peroxide Topical Gel contains erythromycin

 $[(3R^*,4S^*,5S^*,6R^*,7R^*,9R^*,11R^*,12R^*,13S^*,14R^*)-4-[(2,6-Dideoxy-3-C-methyl-3-O-methyl-\alpha-L-$ *ribo* $-hexopyranosyl)-oxy]-14-ethyl-7,12,13-trihydroxy-3,5,7,9,11,13-hexamethyl-6-[[3,4,6-trideoxy-3-(dimethylamino)-<math>\beta$ -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 C₃₇H₆₇NO₁₃. 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-Benzoyl Peroxide Topical Gel 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-Benzoyl Peroxide Topical Gel contains, as dispensed, 30 mg (3%) of erythromycin and 50 mg (5%) of benzoyl peroxide in a base of purified water USP, Carbomer Homopolymer Type C, alcohol 20%, 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-Benzoyl Peroxide Topical Gel is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS

Erythromycin-Benzoyl Peroxide Topical Gel 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-Benzoyl Peroxide Topical Gel 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 their

physician.

- 4. Patients should report to their physician any signs of local adverse reactions.
- 5. Erythromycin-Benzoyl Peroxide Topical Gel 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

Animal reproduction studies have not been conducted with Erythromycin-Benzoyl Peroxide Topical Gel 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-Benzoyl Peroxide Topical Gel. It also is not known whether Erythromycin-Benzoyl Peroxide Topical Gel can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Erythromycin-Benzoyl Peroxide Topical Gel should be given to a pregnant woman only if clearly needed.

Nursing Women:

It is not known whether Erythromycin-Benzoyl Peroxide Topical Gel 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-Benzoyl Peroxide Topical Gel 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.

To report SUSPECTED ADVERSE REACTIONS, contact Oceanside Pharmaceuticals, at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION

Erythromycin-Benzoyl Peroxide Topical Gel 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.

Size (Net Weight) NDC 68682-		Benzoyl Peroxide Gel	Active Erythromycin Powder (In Plastic Vial)	70% Ethyl Alcohol To Be Added	
23.3 grams (as dispensed)	900-23	20 grams	0.8 grams	3 mL	
46.6 grams (as dispensed)	901-46	40 grams	1.6 grams	6 mL	

How Supplied and Compounding Directions:

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 until homogeneous in appearance (1 to 1½ minutes). Erythromycin-Benzoyl Peroxide Topical Gel should then be stored under refrigeration. Do not freeze. Place a 3-month expiration date on the label.

NOTE: *Prior to reconstitution*, store at room temperature between 15° to 30°C (59° to 86°F).

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

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

Distributed by:

Oceanside Pharmaceuticals, a division of Bausch Health US, LLC Bridgewater, NJ 08807 USA

Manufactured by: Bausch Health Companies Inc. Laval, Quebec H7L 4A8, Canada

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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.**

Rev. 06/19

9437503

PRINCIPAL DISPLAY PANEL - 46.6 gram Carton

NDC 68682-901-46

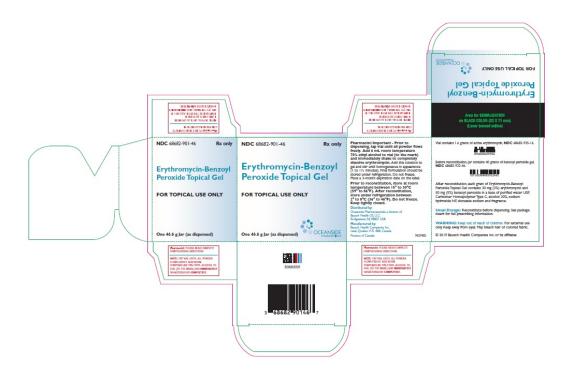
Rx only

Erythromycin-Benzoyl Peroxide Topical Gel

FOR TOPICAL USE ONLY

One 46.6 g Jar (as dispensed)

OCEANSIDE PHARMACEUTICALS



PRINCIPAL DISPLAY PANEL - 23.3 gram Carton

NDC 68682-900-23

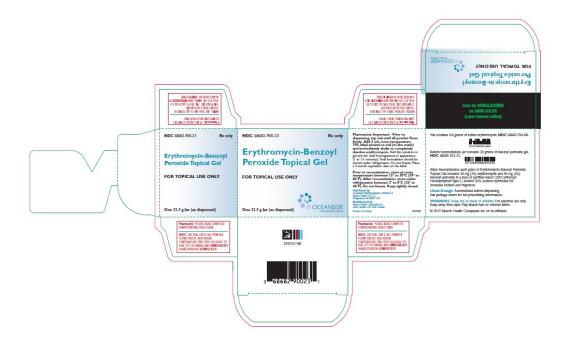
Rx only

Erythromycin-Benzoyl Peroxide Topical Gel

FOR TOPICAL USE ONLY

One 23.3 g Jar (as dispensed)

OCEANSIDE PHARMACEUTICALS



PRINCIPAL DISPLAY PANEL -

NDC 68682-924-08

Rx only

Erythromycin

Prior to dispensing, tap vial until freely. Add 3 mL room temper alcohol to vial (to the mark) and i to completely dissolve erythr solution to gel and stir until homoger (1 to 11/0 minuto) Eartheomycin Rom	rature 70% ethyl mmediately shake omycin. Add this neous in appearance zoyl Peroxide Topical
Gel (as reconstituted) should be stored Do not freeze. Place a 3-month exp label. Not for separate dispensing. See full prescribing information. WARN reach of children. For external use o eyes. Prior to reconstitution, temperature between 15° to 30°C	iration date on the e package insert for IING: Keep out of nly. Keep away from store at room
Net Wt. 0.8 grams active er	ythromycin
Dist. by: Oceanside Pharmaceuticals, a Bausch Health US, LLC Bridgewater, NJ 08807 USA	division of 9436904 20000313E
Lot :	
Exp.:	

Package/Label Display Panel

NDC 68682-923-23

Rx only

Erythromycin-Benzoyl Peroxide Topical Gel

FOR TOPICAL USE ONLY

One 23.3 g Jar (as dispensed)

 NDC 68682-923-23
 Rx only

 Erythromycin-Benzoyl Peroxide Topical Gel FOR TOPICAL USE ONLLY
 After reconstitution, each gram of Erythromycin-Benzoyl Peroxide Topical Gel contains 30 mg (3%) erythromycin and 50 mg (5%) berzoyl peroxide in a base of purfied water USP, Carbomer Homopolymer Type C, alcohol 20%, sodium hydroxide NF, docusate sodium and fragranee. Usual Dosage: Apply twice daily, morning and evening, or as directed by physician, to affected areas after skin is thronoghly washed, niar or colored fabric. Use within 3 months after mixing. Store mixed formulation under refrigeration betwith 3 months after mixing. Store mixed formulation under refrigeration betwith 3 months after mixing. Store mixed formulation under refrigeration betwith 3 months after mixing. Store mixed formulation under refrigeration betweith 3 months after mixing. Store mixed formulation under refrigeration betweith 3 months after mixing. Store mixed formulation under refrigeration betweith 3 months after mixing. Store mixed formulation under refrigeration betweith 3 months after mixing. Store mixed formulation under refrigeration betweith 40 to LLC, Bridgewater, NJ 08807 USA Mid. by: Bauch Health US, LLC, Bridgewater, NJ 08807 USA Mid. by: Bauch Health Companies Inc, Laval, Quebec H7L 4A8, Canada 9437103
 9437103
 20000321D

Package/Label Display Panel NDC 68682-925-16 Rx only Erythromycin

NDC 68682-925-16 Rx only Erythromycin	
Prior to dispensing, tap vial un freely. Add 6 mL room tem alcohol to vial (to the mark) an to completely dissolve erry solution to gel and stir until homo (1 to 1½ minutes). Erythromycin-B Gel (as reconstituted) should be sto Do not freeze. Place a 3-month label. Not for separate dispensing. full prescribing information. WA reach of children. For external use eyes. Prior to reconstitution temperature between 15° to 30	perature 70% ethyl d immediately shake thromycin. Add this ogeneous in appearance enzoyl Peroxide Topical ored under refrigeration expiration date on the See package insert for RNING: Keep out of e only. Keep away from n, store at room
Net Wt. 1.6 grams active	erythromycin
Dist. by: Oceanside Pharmaceutical	s, a division of
Bausch Health US, LLC Bridgewater, NJ 08807 USA	9437004
	20000318E
Lot :	
Lot : Exp.:	

Package/Label Display Panel

NDC 68682-922-46

Rx only

Erythromycin-Benzoyl Peroxide Topical Gel

FOR TOPICAL USE ONLY

One 46.6 g Jar (as dispensed)

(01)00368682922462

After reconstitution, each gram of Erythromycin-Benzoyl Peroxide Topical Gel contains 30 mg (3%) erythromycin and 50 mg (5%) benzoyl peroxide in a base of purified water USP, Carbomer Homopolymer Type C, alcohol 20%, sodium hydroxide NF, docusate sodium and fragrance. Usual Dosage: Apply twice daily, morning and evening, or as directed by physician, to affected areas after skin is thoroughly washed, rinsed with warm water and gently patted dry. See package insert for full prescribing information. WARNING: Keep out of reach of children. For external use only. Keep away from eyes. May bleach hair or colored fabric. Use within 3 months after mixing. Store mixed formulation under refrigeration between 2° to 8°C (36° to 46°F). Do not freeze. Keep tightly closed. NDC 68682-922-46 Rx only Area for LOT & EXP printed online Erythromycin-Benzoyl Peroxide Topical Gel FOR TOPICAL USE ONLY Dist. by: Oceanside Pharmaceuticals, a division of Bausch Health US, LLC, Bridgewater, NJ 08807 USA One 46.6 g Jar (as dispensed) 20000322D Mfd. by: Bausch Health Companies Inc., Laval, Quebec H7L 4A8, Canada 9437303

ERYTHROMYCIN AND BENZOYL PEROXIDE

erythromycin and benzoyl peroxide kit

Product Information					
Product Type HUMAN PRESCRIPTION DRUG		Item	Code (Source)	NDC:68682-900	
Pack	aging				
		Package Description			
#	Item Code	Package Description	o n	Marketing Start Date	Marketing End Date
	Item Code C:68682-900-23	Package Descriptie 1 in 1 CARTON; Type 0: Not a Combi		Marketing Start Date 10/26/1984	Marketing End Date
1 NDC				_	Marketing End Date
1 NDC	c:68682-900-23			_	
1 NDC Quan Part #	c:68682-900-23	1 in 1 CARTON; Type 0: Not a Combi Package Quantity		10/26/1984	Marketing End Date
1 NDC Quan Part # Part 1	C:68682-900-23 ntity of Parts	1 in 1 CARTON; Type 0: Not a Combi Package Quantity	nation Product	10/26/1984	
1 NDC Quan Part # Part 1	C:68682-900-23	1 in 1 CARTON; Type 0: Not a Combi Package Quantity	nation Product 0.8 g	10/26/1984	

ERYTHROM	YCIN			
erythromycin gel				
Product Informa	tion			
Item Code (Source)	1	NDC:68682-924		
Route of Administra	ation	TOPICAL		
Active Ingredien	t/Active Moi	ety		
	-	gredient Name	Basis of Str	
ERYTHROMYCIN (UI	NII: 63937KV33D) (ERYTHROMYCIN - UNII:63937KV33D)	ERYTHROMYC	IN 30 mg in 1 g
Packaging				
# Item Code		Package Description	Marketing Start Date	Marketing End Date
1 NDC:68682-924- 08	0.8 g in 1 VIAL, Product	PLASTIC; Type 0: Not a Combination		
Marketing Inf	ormation			
Marketing Catego		on Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generi	ic NDA050557	:	10/26/1984	
Part 2 of 2				
BENZOYL PI benzoyl peroxide g				
Product Informa	tion			
Item Code (Source)	1	NDC:68682-923		
Route of Administra	ation	TOPICAL		
Active Ingredien	t/Active Moi	ety		
		ngredient Name	Basis of a	
BENZOYL PEROXID	E (UNII: W9WZN9	9A0GM) (BENZOYL PEROXIDE - UNII:W9V	WZN9A0GM) BENZOYL	PEROXIDE 50 mg in 1 g
Inactive Ingredie	ents			
		Ingredient Name		Strength
ALCOHOL (UNII: 3KS	1958 V90M)			

CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED) (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:68682-923-23	20 g in 1 JAR; Type 0: Not a Combination Product					
Maylading Info						
Marketing Info	rmation					
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date			
NDA authorized generic	NDA050557	10/26/1984				
Maultating Info						
Marketing Info	rmation					
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date			
NDA authorized generic	NDA050557	10/26/1984				

_							
ERYTHROMYCIN AND BENZOYL PEROXIDE erythromycin and benzoyl peroxide kit							
F	Product Information						
Product Type HUMAN PRESCRIPTION DRUG		It	em C	Code (Source)	NDC:68682-901		
						,	
P	acka	ging					
#	Ι	tem Code	Package Descriptio	n		Marketing Start Date	Marketing End Date
1	NDC:	68682-901-46	1 in 1 CARTON; Type 0: Not a Combir	nation Produc	2t	10/26/1984	
Q	uant	tity of Parts					
P	art #		Package Quantity	Total Product Quantity			
Pa	art 1	1 VIAL, PLASTI	C	1.6 g			
Pa	art 2	1 JAR		40 g			
F	Part	1 of 2					
-							
E	ERY	THROMY	CIN				
e	rythro	omycin gel					
-							

Product Informa	tion					
Item Code (Source)		NDC:68682-925				
Route of Administra		TOPICAL				
Active Ingredien	t/Active Moi	ety				
	Ing	gredient Name		Basis of Str	ength	Strength
ERYTHROMYCIN (U	-) (ERYTHROMYCIN - UNII:63937KV33D)		RYTHROMYC	-	30 mg in 1 g
Packaging						
# Item Code		Package Description		ting Start Date		eting End Date
1 NDC:68682-925- 16	1.6 g in 1 VIAL, 1 Product	PLASTIC; Type 0: Not a Combination				
Marketing Inf	ormation					
Marketing Categor	ry Applicati	on Number or Monograph Citation	Marketing	Start Date	Marketi	ng End Dat
NDA authorized gener	ic NDA050557		10/26/1984			
BENZOYL PI benzoyl peroxide g						
Product Informa	tion					
Item Code (Source))	NDC:68682-922				
Route of Administra	ation	TOPICAL				
		10110112				
Active Ingredien		ety				
	Iı	ety ngredient Name		Basis of S		
Active Ingredien Benzoyl peroxid	Iı	ety	9 WZN9 A0 GM)			Strengtl 50 mg in 1
BENZOYL PEROXID	II E (UNII: W9WZNS	ety ngredient Name) WZN9 A0 GM)			
	II E (UNII: W9WZNS	ety ngredient Name) WZN9 A0 GM)			
BENZOYL PEROXID Inactive Ingredie	In E (UNII: W9 WZNS ents	e ty ng redient Nam e 9 A0 GM) (BENZO YL PERO XIDE - UNII:W9) WZN9 A0 GM)			E 50 mg in 1
BENZOYL PEROXID Inactive Ingredie ALCOHOL (UNII: 3KS	I1 E (UNII: W9WZNS ents 9958V90M)	e ty ng redient Name 9 A0 GM) (BENZO YL PERO XIDE - UNII:W9		BENZOYL	PEROXIDE	E 50 mg in 1
BENZOYL PEROXID Inactive Ingredic ALCOHOL (UNII: 3KS CARBOMER HOMOF	In E (UNII: W9 WZNS ents 9958 V90M) POLYMER TYPE	ety ngredient Name 9 A0 GM) (BENZO YL PERO XIDE - UNII:W9 Ingredient Name 5 C (ALLYL PENTAERYTHRITOL CROS		BENZOYL	PEROXIDE	E 50 mg in 1
BENZOYL PEROXID Inactive Ingredie ALCOHOL (UNII: 3K9 CARBOMER HOMOF SODIUM HYDROXID	In E (UNII: W9WZNS E nts 9958V90M) POLYMER TYPE E (UNII: 55X04Q6	ety ngredient Name 9 A0 GM) (BENZO YL PERO XIDE - UNII:W9 Ingredient Name 3 C (ALLYL PENTAERYTHRITOL CROS C32I)		BENZOYL	PEROXIDE	50 mg in 1
BENZOYL PEROXID Inactive Ingredie ALCOHOL (UNII: 3KS	In E (UNII: W9 WZN9 E nts 9958 V90 M) POLYMER TYPE E (UNII: 55X0 4Q I (UNII: F05Q2T2.	ety ngredient Name 9 A0 GM) (BENZO YL PERO XIDE - UNII:W9 Ingredient Name 3 C (ALLYL PENTAERYTHRITOL CROS C32I)		BENZOYL	PEROXIDE	E 50 mg in 1

Packaging					
# Item Code	Package Description	Marketing Start Date	Marketing End Date		
1 NDC:68682-922-46	40 g in 1 JAR; Type 0: Not a Combination Product				
Marketing Info	rmation				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date		
NDA authorized generic	NDA050557	10/26/1984			
Marketing Info	rmation				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date		
NDA authorized generic	NDA050557	10/26/1984			

Labeler - Oceanside Pharmaceuticals (832011691)

Establishment

Name	Address	ID/FEI	Business Operations
Bausch Health Companies Inc		245141858	MANUFACTURE(68682-900, 68682-924, 68682-923, 68682-901, 68682-925, 68682-922) , LABEL(68682-900, 68682-924, 68682-923, 68682-901, 68682-925, 68682-922) , PACK(68682- 900, 68682-924, 68682-923, 68682-901, 68682-925, 68682-922)

Revised: 6/2019

Oceanside Pharmaceuticals