For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

CLINMISKIN GEL

1. Generic Name

Clindamycin Phosphate & Nicotinamide Gel

(In Aloe- Allantoin gel base)

2. Qualitative and quantitative Composition:

Clindamycin Phosphate IP

equivalent to Clindamycin ……1.0% w/v

Nicotinamide IP……..…..4.0 %w/v

Aloe - Allantoin Gel Base……...……q.s.

The Excipient used are Allantoin, Aloe Vera Extract, Carbomer, Sodium Methyl Paraben, Sodium Propyl Paraben, Disodium Edetate, Sodium Hydroxide, Polyoxyl, Hyrogenated Castor Oil, Propylene Glycol, Polyethylene Glycol, and Butylated Hydroxytoluene.

3. Dosage form and strength

Dosage form: Gel

Strength: Clindamycin (1.0% w/v) & Nicotinamide (4.0% w/v)

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for the topical treatment of mild to moderate inflammatory acne vulgaris.

4.2 Posology and method of administration

Posology

As directed by physician

Method of administration

Apply a thin film of gel to the affected area.

4.3 Contraindications

It is contraindicated in persons who have shown hypersensitivity to Clindamycin, Nicotinamide or any of its ingredients. Although Clindamycin cross-sensitisation to lincomycin has not been demonstrated, it is recommended that it should not be used in patients who have demonstrated lincomycin sensitivity.

4.4 Special warnings and precautions for use

Clindamycin

Oral and parenteral clindamycin, as well as most other antibiotics, have been associated with severe pseudomembranous colitis. Topical clindamycin has very rarely been associated with pseudomembranous colitis; however if diarrhoea occurs the product should be discontinued immediately.

Studies indicate a toxin(s) produced by Clostridium difficile is the major cause of antibiotic-associated colitis. Colitis is usually characterised by severe persistent diarrhoea and abdominal cramps. Should antibiotic associated colitis occur appropriate diagnostic and therapeutic measures (such as vancomycin treatment) should be taken immediately. Responses may not be seen for 4-6 weeks.

Although the risk of systemic absorption following the administration of clindamycin gel is low, the potential for the development of gastrointestinal adverse effects should be taken into account when considering treatment in patients with a previous history of antibiotic-associated colitis, enteritis, ulcerative colitis or Crohn's disease.

Prolonged use of clindamycin may cause resistance and/or overgrowth of non susceptible bacteria or fungi although this is a rare occurrence. Cross resistance may occur with other antibiotics such as lincomycin and erythromycin.

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Nicotinamide

Nicotinamide is not suitable for patients with severe acne, who should be encouraged to seek treatment advice from a doctor or pharmacist.

Contact with the eyes or the mucous membranes of the nose and mouth should be avoided. In the event of accidental contact with the eyes or mucous membranes bathe the affected area with copious amounts of cool water. If excessive dryness, irritation or peeling occurs reduce the dosage to one application per day or every other day.

4.5 Drugs interactions

No data available.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Clindamycin

For clindamycin applied cutaneously no clinical data on exposed pregnancies are available. Data on a limited number of pregnancies exposed to clindamycin administered by other routes indicate no adverse effects on pregnancy or on the health of the foetus/newborn child. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women.

Orally and parenterally administered clindamycin has been reported to appear in breast milk. It is not known whether clindamycin is excreted in human milk following use of gel. As a general rule, patients should not breastfeed while taking a drug since many drugs are excreted in human milk. Sensitisation and diarrhoea cannot be ruled out in nursed infants.

For use during pregnancy and lactation, benefit and possible risks have to be weighed carefully against each other.

Nicotinamide

Vitamin B derivative requirements such as nicotinamide, are increased during pregnancy and infancy. Nicotinamide is excreted in breast milk. As with all medicines, care should be exercised during the first trimester of pregnancy.

4.7 Effects on ability to drive and use machines

NA

4.8 Undesirable effects

Clindamycin

Approximately 10% of patients can be expected to experience an adverse reaction. These reactions are typical of irritant dermatitis. The incidence of these is likely to increase if an excess of gel is used. Should irritation occur, the use of a moisturiser may be of benefit.

The table below shows all adverse reactions reported with Clindamycin in clinical trials. They are listed in decreasing order of incidence.

Organ System	Common (>1/100, <1/10)	Uncommon (>1/1000, <1/100)
Skin and Subcutaneous tissue disorder	Dry skin Erythema Skin burning Irritation around eyes Acne exacerbation Pruritis	Painful skin Scaly rash

Whilst no case of severe diarrhoea or pseudomembranous colitis has been reported in clinical trials with clindamycin, and only a small amount of clindamycin is absorbed percutaneously, pseudomembranous colitis has very rarely been reported with the use of other topical clindamycin products.

Nicotinamide

The most frequently encountered adverse effect reported is dryness of the skin. Other less frequent adverse effects include pruritus, erythema, burning sensation and irritation.

Reporting of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

It is not expected that overdose would occur in normal use.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Clindamycin

Clindamycin is a lincosamide antibiotic with primarily bacteriostatic action against Gram positive aerobes and wide range of anaerobic bacteria.

When clindamycin phosphate is applied cutaneously, clindamycin is found in comedone samples at sufficient levels to be active against most strains of Propionibacterium (P. acnes). It thus reduces the number of surface and follicular P.acnes, one of the aetiological factors of the disease. As with all antibiotics, the long-term use of cutaneous clindamycin may lead to resistance.

Nicotinamide

Niacin (nicotinic acid) is an essential B complex Vitamin (B3), whose deficiency results in the clinical syndrome known as pellagra. Nicotinic acid is converted in the body to nicotinamide

adenine dinucleotide (NAD) or nicotinamide adenine dinucleotide phosphate (NADP), which function as coenzymes for a wide variety of vital oxidation-reduction reactions. Nicotinamide (niacinamide), the active ingredient, is the physiologically active form of niacin and is the chemical form of Vitamin B3 found in virtually all multivitamin products. Though nicotinic acid and nicotinamide are so closely related chemically, they differ somewhat in pharmacological properties.

5.2 Pharmacokinetic properties

Clindamycin

Clindamycin phosphate binds with zinc to form a complex in a formulation which results in a reduced extent of absorption. A study with clindamycin in vitro with human skin has shown penetration of radiolabelled clindamycin phosphate from the formulation to be less than 5% of the applied dose. When applied topically to patients with acne at the maximum anticipated clinical dose a very small amount, (median less than 2ng/ml) of clindamycin was measured in plasma.

Nicotinamide

Percutaneous absorption levels of nicotinamide, even following application to broken and inflamed acne skin, are very low compared to the oral doses routinely used in multi vitamin products . Following oral administration, nicotinamide is readily absorbed from the gastrointestinal tract and widely distributed in the body tissues. The main route of metabolism is the conversion to N -methylnicotinamide and the 2-pyridone and 4-pyridone derivatives; nicotinuric acid is also formed. Small amounts of nicotinamide are excreted unchanged in the urine; this amount increases with larger doses.

6 Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Clindamycin

Preclinical data for clindamycin reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or toxicity to reproduction.

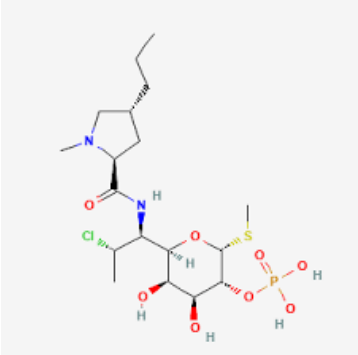
Nicotinamide

Nicotinic acid amide (nicotinamide) has been recognised since 1937 as an essential B complex vitamin whose deficiency results in the clinical syndrome known as pellagra. It is widely available, in tablets and in sterile solution in water for intravenous administration, for the prophylaxis and treatment of pellagra and nutritional deficiency. In the United States, nicotinamide is included in the Food and Drug Administration's listing of nutritional agents which are Generally Recognised As Safe (GRAS).

7 Description

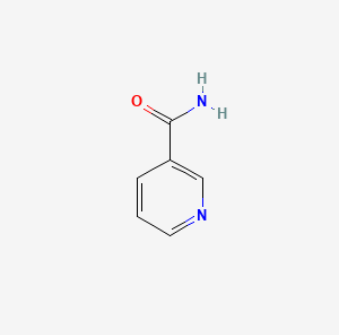
Clindamycin Phosphate:

Clindamycin Phosphate is methyl 7-chloro-6,7,8-trideoxy-6-[[[(2S,4R)-1 –methyl-4-propylpyrrolidin-2-yl]carbonyl]amino]-1-thio-L-threo-α-D-galacto-octopyranoside 2-(dihydrogen phosphate). The empirical formula is $C_{18}H_{34}CLN_2O_8PS$ and its molecular weight is 505.0 g/mol. The structural formula is:



Nicotinamide:

Nicotinamide is pyridine-3-carboxamide. The empirical formula is $C_6H_6N_2O$ and its molecular weight is 122.12 g/mol. The structural formula is



CLINMISKIN GEL:

Clindamycin Phosphate & Nicotinamide are Clear, Colourless transparent Gel. The Excipient used are Allantoin, Aloe Vera Extract, Carbomer, Sodium Methyl Paraben, Sodium Propyl Paraben, Disodium Edetate, Sodium Hydroxide, Polyoxyl, Hyrogenated Castor Oil, Propylene Glycol, Polyethylene Glycol, and Butylated Hydroxytoluene.

8 Pharmaceutical particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

CLINMISKIN GEL is available in pack of 20 gm.

8.4 Storage and handing instructions

Do not store above 30°C. Store in a dry place, protected from direct sunlight.

Do not freeze

For External Use Only.

Avoid contact with eyes.

Keep out of reach of children.

Replace the cap tightly after use.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10 Details of manufacturer

Sankalp Healthcare and Allied Products

Privated Limited,

Plot No. A-16, M.I.D.C., Tasavade,

Karad, Dist., Satara – 415 109

Maharashtra, India

11 Details of permission or licence number with date

Mfg. Licence. No.: PD/89 Issued on: 16.07.2018

12. Date of revision

NA

MARKETED BY

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