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

CLINMISKIN AD GEL

1. **Generic Name**

   Adapalene & Clindamycin Phosphate Gel

2. **Qualitative and quantitative composition**

   Composition:

   Adapalene BP……..…0.1% w/w

   Clindamycin Phosphate IP

   equivalent to Clindamycin ……..…...1.0% w/w

   Aloe – Allantoin Gel Base ……..….q.s.

   Preservatives:

   Methyl Paraben IP……..0.1% w/w

   Phenoxyethanol BP…….25% w/w

   The Excipients used are Carbomer, Collodial Silicon Dioxide, Disodium Edetate, Aloe Vera Gel, Sodium Hydoxide, Propylene Glycol, Butylated Hydroxytoluene, Caproylo Caproyl Macrogol Glycerides, Polyethylene Glycol and Glycerin.

3. **Dosage form and strength**

   Dosage form: Gel

   Strength: Adapalene 0.1 % w/w and Clindamycin Phosphate 1.0 % w/w

4. **Clinical particulars**

4.1 Therapeutic indication

It is indicated for the treatment of acene vulgaris.

4.2 Method of administration.

Clinmiskin® Ad Gel should be applied once a day to affected areas after washing in the evening before retiring. A thin film of the Gel should be applied, avoiding eyes, lips, and mucous membranes. During the early weeks of therapy, an apparent exacerbation of acne may occur. This is due to the action of the medication on previously unseen lesions and should not be considered a reason to discontinue therapy. Therapeutic results should be noticed after eight to twelve weeks of treatment.

4.3 Contraindications

Clinmiskin® Ad Gel should not be administered to Individuals who are hypersensitive to Adapalene, Clindamycin, Lincomycin or any of the components in the Gel base. In individuals with a history of regional enteritis or ulcerative colitis, or a history of antibiotic associated colitis.

4.4 Special warnings and precautions for use

WARNINGS

Use of Clinmiskin® Ad Gel should be discontinued if hypersensitivity to any of the

ingredients is noted. Patients with sunburn should be advised not to use the product until fully recovered.

PRECAUTIONS

If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued. Exposure to sunlight, including sunlamps, should be minimized during the use of Adapalene. Patients who normally experience high levels of sun exposure, and those with inherent sensitivity to sun, should be warned to exercise caution. Use of sunscreen products and protective clothing over treated areas is recommended when exposure cannot be avoided.

Weather extremes, such as wind or cold, also may be irritating to patients under treatment with Adapalene.

Avoid contact with the eyes, lips, angles of the nose, and mucous membranes.

The product should not be applied to cuts, abrasions, eczematous skin, or sunburned skin.

Certain cutaneous signs and symptoms such as erythema, dryness, scaling, burning or pruritus may be experienced during treatment. These are most likely to occur during the first two to four weeks and will usually lessen with continued use of the medication. Depending upon the severity of adverse events, patients should be instructed to reduce the frequency of application or discontinue use.

Diarrhoea and colitis including pseudomembranous colitis have been reported infrequently with topical Clindamycin. Symptoms can occur after a few days, weeks or months following initiation of Clindamycin therapy. They have also been observed to begin up to several weeks after cessation of therapy with Clindamycin. Therefore, the Physician should be alert to the possible development of antibiotic-associated diarrhoea or colitis. If significant or prolonged diarrhoea occurs, the product should be discontinued. Studies indicate that a toxin produced by C. difficile is the major cause of antibiotic-associated colitis which is characterized by sever persistent diarrhoea, severe abdominal cramps and in some cases with passage of blood and mucus in stool. Endoscopic examination may reveal pseudomembranous colitis. Stool culture for C. difficile and assay for C. difficile toxin may be helpful diagnostically. Mild cases of colitis may respond to simple drug discontinuance and to Vancomycin. Cholestyramine has been effective in the treatment of some mild cases of antibiotic-associated colitis. Cholestyramine resins have been shown to bind Vancomycin; therefore, when both Cholestyramine and Vancomycin are used concurrently, their administration should be separated by at least 2 hours. Anticholinergics and antiperistaltic agents may worsen colitis.

4.5 Drugs interactions

As Clinmiskin® Ad Gel has the potential to produce local irritation in some patients, concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices or lime) should be approached with caution. Particular caution should be exercised in using preparations containing Sulfur, Resorcinol, or Salicylic Acid in combination with Clinmiskin® Ad Gel. If these preparations have been used, it is advisable not to start therapy with Clinmiskin® Ad Gel until the effects of such preparations in the skin have subsided. No photo carcinogenicity studies were conducted. Animal studies have shown an increased tumorigenic risk with the use of pharmacologically similar drugs (e.g. Retinoids) when exposed to UV

irradiation in the Laboratory or to sunlight. Although the significance of these studies to human use is not clear, patients should be advised to avoid or minimize exposure to either sunlight or artificial UV irradiation sources

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

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Clinmiskin® Ad Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether the drugs in the combination are excreted in human milk. Since many drugs are excreted in human milk, caution should be exercised when Clinmiskin® Ad Gel is administered to a nursing woman.

Paediatric Use

Safety and effectiveness in paediatric patients below the age of 12 have not been established.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects:

Some adverse effects such as erythema, scaling, dryness, pruritus, and burning will occur in 10-40% of patients. These are most commonly seen during the first month of therapy and decreases in frequency and severity thereafter. Most of the adverse effects with us of Clinmiskin® Ad Gel are reversible upon discontinuation of therapy. Other adverse effects reported with Clindamycin include: oily skin, contact dermatitis, stinging of the eye, Gastrointestinal disturbances like abdominal pain, gram-negative folliculitis.

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

4.9 Overdose

Clinmiskin® Ad Gel is intended for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and marked redness, peeling, or discomfort may occur.

5. Pharmacological properties

5.1 Mechanism of Action

5.2 Pharmacodynamic properties

Adapalene is a chemically stable, retinoid-like compound. Biochemical and pharmacological profile studies have demonstrated that Adapalene is a modulator of cellular differentiation, keratinization and inflammatory processes, all of which represent important features in the pathology of acne vulgaris. Mechanistically, Adapalene binds to specific retinoid acid nuclear receptors but does not bind to the Cytosolic Receptor Protein.

Although the exact mode of action of Adapalene is unknown, it is suggested that topical Adapalene may normalize the differentiation of follicular epithelial cells resulting in decreased microcomedone formation. Clindamycin have been shown to have in vitro activity against *propionibacterium acnes* - an organism which has been associated with acne vulgaris.

5.3 Pharmacokinetic properties

Absorption of Adapalene through human skin is low. Only trace amounts (<0.25 ng/ml) of parent substance have been found in the plasma of acne patients following chronic topical application of Adapalene in controlled clinical trials. Excretion appears to be primarily by the biliary route. Systemic bioavailability of topical Clindamycin is suggested to be less than 1%. The mean concentration of antibiotic activity in extracted comedones after application of Clindamycin topical application for 4 weeks was 597mg/g of comedonal material (range 60 to1490). Free fatty acids on the skin surface have been decreased from approximately 14% to 2% following application of Clindamycin.

6 Nonclinical properties

Not applicable

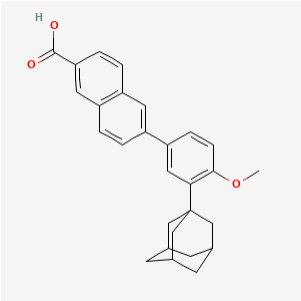
6.1 Animal Toxicology or Pharmacology

Not applicable

7 Description

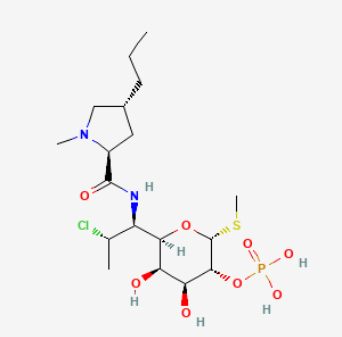
Adapalene:

Adapalene is 6-[3-(1-adamantyl)-4-methoxyphenyl]naphthalene-2-carboxylic acid. The empirical formula is $C_{28}H_{28}O_3$ and its molecular weight is 412.5 g/mol The chemical structural formula is



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-thero-α-D-galacto-octopyranoside 2-(dihydrogen phosphate). The empirical formula is $C_{18}H_{34}CIN_2O_8PS$ and its molecular weight is 505.0 g/mol. The chemical structural formula is:



CLINMISKIN AD GEL:

Adapalene & Clindamycin Phosphate Gel is white coloured homogenous. The Excipients used are Carbomer, Collodial Silicon Dioxide, Disodium Edetate, Aloe Vera Gel, Sodium Hydoxide, Propylene Glycol, Butylated Hydroxytoluene, Caproylo Caproyl Macrogol Glycerides, Polyethylene Glycol and Glycerin.

8 Pharmaceutical particulars

8.1 Incompatibilities

None known.

8.2 Shelf-life

Do not use later than date of expiry

8.3 Packaging information

CLINMISKIN AD GEL is available in pack of 5 gm and 20 gm.

8.4 Storage and handing instructions

Do not store above 30^0C. Store in a dry place, protectedfrom 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

CLINMISKIN AD GEL

(Adapalene & Clindamycin Phosphate Gel)

Read all of this leaflet carefully before you start taking this medicine because it contains Important information for you.

· Keep this leaflet. You may need to read it again.

· If you have any further questions, ask your doctor or pharmacist.

· This medicine has been prescribed for you only. Do not pass it on to others; it may harm them, even if their signs of illness are the same as yours.

· If you get any side effects, talk to your doctor or pharmacist. This includes any

possible side Effects not listed in this leaflet.

What is in this leaflet?

9.1 What CLINMISKIN AD GEL is and what it is used for

CLINMISKIN AD GEL contain Adapalene & Clindamycin Phosphate.

9.2 How to apply CLINMISKIN AD GEL

Wash the affected area with water. Apply a small amount of Clinmiskin AD Gel as a thin layer and gently rub on the clean and dry affected area of the skin.

9.3 Possible side effects

Possible side effects are as erythema, scaling, dryness, pruritus, burning, oily skin, contact dermatitis, stinging of the eye, Gastrointestinal disturbances like abdominal pain, gram-negative folliculitis.

Reporting of Adverse reaction

If you get any side effects, talk to your doctor or pharmacist. 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: http://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.

9.4 How to store CLINMISKIN AD GEL.

Do not store above 30^0C. Store in a dry place, protectedfrom direct sunlight. Do not freeze.

9.5 Contents of the pack and other information

CLINMISKIN AD GEL consists of Adapalene BP and Clindamycin Phosphate IP As active ingredients of 0.1% w/w and 1.0% w/w Respectively.

The Excipients used are Carbomer, Collodial Silicon Dioxide, Disodium Edetate, Aloe Vera Gel, Sodium Hydoxide, Propylene Glycol, Butylated Hydroxytoluene, Caproylo Caproyl Macrogol Glycerides, Polyethylene Glycol and Glycerin.

CLINMISKIN AD GEL is available in pack of 5 gm and 20 gm.

10 Details of manufacturer

Sankalp Healthcare and Allied Products Private

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

Dist. Satara – 415 109, Maharashta, India.,

11 Details of permission or licence number with date

Mfg. Licence No. : PD/89 Issued on: 16.03.2021

12 Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/ CLINMISKIN AD GEL 5 gm and 20 gm/NOV-23/01/PI