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

ACNETOR AD

1. **Generic Name**

   Clindamycin & Adapalene Gel

2. **Qualitative and quantitative Composition:**

   Clindamycin Phosphate I.P.

   equivalent to Clindamycin 1.00% W/W

   Adapalene B.P. 0.1% W/W

   Preservatives

   Methyl Para-hydroxybenzoate I.P. 0.1% W/W

   Phenoxyethanol I.P. 0.25% W/W

   In gel base q.s.

   The list of excipients are Disodium Edetate, Carbopol, Sodium Hydroxide, Propylene Glycol, Methyl Paraben, Poloxamer, Phenoxy Ethanol.

3. **Dosage form and strength**

   Dosage form: Topical gel

   Strength: 15 gm gel

4. **Clinical particulars**

4.1. Therapeutic indication

ACNETOR AD is indicated for treatment of Acne vulgaris.

4.2. Posology and method of administration

Posology:

ACNETOR AD should be applied to the acne affected areas once a day before retiring and after washing. A thin film of gel should be applied, with the fingertips, avoiding the eyes and lips. Ensure that the affected areas are dry before application.

Since it is customary to alternate therapies in the treatment of acne, it is recommended that the physician assess the continued improvement of the patient after three months of treatment with ACNETOR AD Gel.

With patients for whom it is necessary to reduce the frequency of application or to temporarily discontinue treatment, frequency of application may be restored, or therapy resumed once it is judged that the patient can again tolerate the treatment.

If patients use cosmetics, these should be non-comedogenic and non-astringent.

Paediatric population: The safety and effectiveness of ACNETOR AD Gel have not been studied in children below 12 years of age. ACNETOR AD Gel should not be used in patients with severe acne.

Method of administration:

As directed by the Physician.

4.3. Contraindications

ACNETOR AD is contraindicated in:

- Individuals with a history of hypersensitivity to clindamycin, lincomycin, adapalene or to any of the excipients.
- Pregnancy.
- Women planning a pregnancy.

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 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.

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.

Adapalene

If a reaction suggesting sensitivity or severe irritation occurs, use of the medication should be discontinued. If the degree of local irritation warrants, patients should be directed to use the medication less frequently, to discontinue use temporarily until symptoms subside or to discontinue use altogether. Adapalene should not come into contact with the eyes, mouth, angles of the nose or mucous membranes.

If product enters the eye, wash immediately with warm water. The product should not be applied to either broken (cuts and abrasions), sunburnt or eczematous skin, nor should it be used in patients with severe acne, or acne involving large areas of the body.

Exposure to sunlight and artificial UV irradiation, including sunlamps, should be minimised during 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.

Methyl para-hydroxybenzoate (E218) and propyl para-hydroxybenzoate (E216) may cause allergic reactions which can possibly be delayed.

4.5. Drugs interactions

Clindamycin

No interactions have been reported with topical clindamycin.

Adapalene

There are no known interactions with other medications which might be used cutaneously and concurrently with Adapalene; however, other retinoids or drugs with a similar mode of action should not be used concurrently with adapalene.

Adapalene is essentially stable to oxygen and light and is chemically non-reactive. Whilst extensive studies in animals and man have shown neither phototoxic nor photoallergic potential for adapalene, the safety of using adapalene during repeated exposure to sunlight or UV irradiation has not been established in either animals or man. Exposure to excessive sunlight or UV irradiation should be avoided.

Absorption of adapalene through human skin is low and therefore interaction with systemic medications is unlikely. There is no evidence that the efficacy of oral drugs such as contraceptives and antibiotics is influenced by the cutaneous use of Adapalene.

Adapalene has a potential for mild local irritation, and therefore it is possible that concomitant use of peeling agents, astringents or irritant products may produce additive irritant effects. However, cutaneous antiacne treatment e.g. erythromycin (up to 4%) or clindamycin phosphate (1% as the base) solutions or benzoyl peroxide water based gels up to 10% may be used in the morning when Adapalene is used at night as there is no mutual degradation or cumulative irritation.

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 topical clindamycin is excreted in human milk following use of ACNETOR AD. 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.

Adapalene

Orally administered retinoids have been associated with congenital abnormalities. When used in accordance with the prescribing information, topically administered retinoids are generally assumed to result in low systemic exposure due to minimal dermal absorption. However, there could be individual factors (e.g. damaged skin barrier, excessive use) that contribute to an increased systemic exposure.

Pregnant women:

Adapalene is contraindicated in pregnancy, or in women planning a pregnancy.

Animal studies by the oral route have shown reproductive toxicity at high systemic exposure. Clinical experience with locally applied adapalene in pregnancy is limited but the few available data do not indicate harmful effects on pregnancy or on the health of the foetus exposed in early pregnancy. Due to the limited available data and because a very weak cutaneous passage of adapalene is possible, Adapalene should not be used during pregnancy. If the product is used during pregnancy, or if the patient becomes pregnant while taking this drug, treatment should be discontinued.

Lactating women:

No study on animal or human milk transfer was conducted after cutaneous application of Adapalene.

No effects on the suckling child are anticipated since the systemic exposure of the breast-feeding woman to Adapalene is negligible. Adapalene can be used during breastfeeding. To avoid contact exposure of the infant, application of Adapalene to the chest should be avoided when used during breast-feeding.

Paediatric population: The safety and effectiveness of ACNETOR AD gel have not been studied in children below 12 years of age. ACNETOR AD gel should not be used in patients with severe acne

4.7. Effects on ability to drive and use machines.

ACNETOR AD gel has no influence on the ability to drive and use machines.

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 topical clindamycin in clinical trials. They are listed in decreasing order of incidence.

Organ System	Common (>1/100 to <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 topical 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. Therefore, a theoretical risk of pseudomembranous colitis with topical clindamycin exists.

Adapalene

Adapalene may cause the following adverse drug reactions:

Body System (MeDRA)	**Frequency**	**Adverse Drug Reaction**
Skin and subcutaneous tissue disorders	Common (≥1/100 to <1/10)	Dry skin, skin irritation, skin burning sensation, erythema
	Uncommon (≥1/1000 to <1/100)	Dermatitis contact, skin discomfort, sunburn, pruritus, skin exfoliation, acne
	Unknown*	Dermatitis allergic (allergic contact dermatitis), pain of skin, skin swelling, application site burn**, skin hypopigmentation, skin hyperpigmentation
Eye disorders	Unknown*	Eyelid irritation, eyelid erythema, eyelid pruritus, eyelid swelling
Immune system disorders	Unknown*	Anaphylactic reaction, angioedema

*Post marketing surveillance data

** Most of the cases of "application site burn" were superficial burns but cases with second degree burn reactions have been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com

4.9. Overdose

Clindamycin

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

Irritant dermatitis may occur when excessive quantities of topical clindamycin are applied. The use of a suitable moisturiser may be of benefit in these cases. In subsequent applications a thin film of topical clindamycin should be applied in accordance with the dosage instructions.

Adapalene

Adapalene is not to be taken orally and is 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.

The acute oral dose of Adapalene required to produce toxic effects in mice is greater than 10 g/kg. Nevertheless, unless the amount accidentally ingested is small, an appropriate method of gastric emptying should be considered.

5. Pharmacological properties

5.1. Mechanism of Action

Clindamycin

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

Adapalene

The mode of action of adapalene is suggested to be a normalisation of differentiation of follicular epithelial cells resulting in decreased microcomedone formation.

5.2. Pharmacodynamic properties

Clindamycin

Pharmacotherapetic group: Anti-infectives for treatment of acne.

Clindamycin phosphate which is hydrolysed in the skin to the active constituent clindamycin.

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

Adapalene

Pharmacotherapeutic Group: D10A Anti-Acne Preparations for Topical Use

Adapalene is a retinoid-like compound which in, in vivo and in vitro models of inflammation, has been demonstrated to possess anti-inflammatory properties. Adapalene is essentially stable to oxygen and light and is chemically non-reactive. Mechanically, adapalene binds like tretinoin to specific retinoic acid nuclear receptors but, unlike tretinoin not to cytosolic receptor binding proteins.

Adapalene applied cutaneously is comedolytic in the rhino mouse model and also has effects on the abnormal processes of epidermal keratinisation and differentiation, both of which are present in the pathogenesis of acne vulgaris.

Adapalene is superior to reference retinoids in standard anti-inflammatory assays, both in vivo and in vitro. Mechanistically, it inhibits chemotactic and chemokinetic responses of human polymorphonuclear leucocytes and also the metabolism by lipoxidation of arachidonic acid to pro-inflammatory mediators. This profile suggests that the cell mediated inflammatory component of acne may be modified by adapalene. Studies in human patients provide clinical evidence that cutaneous adapalene is effective in reducing the inflammatory components of acne (papules and pustules).

5.3. 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 topical clindamycin in vitro with human skin has shown penetration of radio labelled clindamycin phosphate from the topical clindamycin 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.

Adapalene

Absorption of adapalene through human skin is low, in clinical trials measurable plasma adapalene levels were not found following chronic cutaneous application to large areas of acneic skin with an analytical sensitivity of 0.15 ng/ml. After administration of [^{14}C]-adapalene in rats (IV, IP, oral and cutaneous), rabbits (IV, oral and cutaneous) and dogs (IV and oral), radioactivity was distributed in several tissues, the highest levels being found in liver, spleen, adrenals and ovaries. Metabolism in animals has been tentatively identified as being mainly

by O-demethylation, hydroxylation and conjugation, and excretion is primarily by the biliary route.

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.

Adapalene

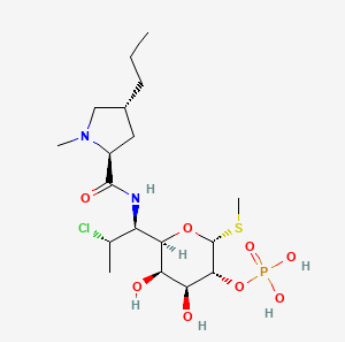
In animal studies, adapalene was well tolerated on cutaneous application for periods of up to six months in rabbits and for up to two years in mice. The major symptoms of toxicity found in all animal species by the oral route were related to an hypervitaminosis A syndrome, and included bone dissolution, elevated alkaline phosphatase and a slight anaemia. Large oral doses of adapalene produced no adverse neurological, cardiovascular or respiratory effects in animals. Adapalene is not mutagenic. Lifetime studies with adapalene have been completed in mice at cutaneous doses of 0.6, 2 and 6 mg/kg/day and in rats at oral doses of 0.15, 0.5 and 1.5 mg/kg/day. The only significant finding was a statistically significant increase of benign phaeochromocytomas of the adrenal medulla among male rats receiving adapalene at 1.5 mg/kg/day. These changes are unlikely to be of relevance to the cutaneous use of adapalene.

Adapalene produces teratogenic effects by the oral route in rats and rabbits. At cutaneous doses up to 200 fold the therapeutic dose, producing circulating plasma levels of adapalene at least 35 to 120 times higher than plasma levels demonstrated in therapeutic use, adapalene increased the incidence of additional ribs in rats and rabbits, without increasing the incidence of major malformations. It is not known whether adapalene is secreted in animal or human milk. In animal studies, infant rats suckled by mother with circulating levels of adapalene at least 300 times those demonstrated in clinical use developed normally.

7. Description

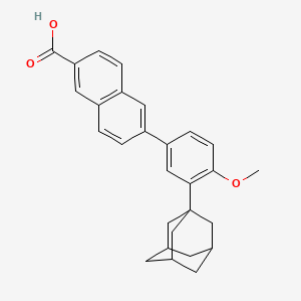
Clindamycin:

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-octopyranoside2-(dihydrogen phosphate). The empirical formula is $C_{18}H_{34}ClN_2O_8PS$ and its molecular weight is 505.0 g/mol. The chemical structural formula is:



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 & Adapalene Gel

Clindamycin & Adapalene Gel is white colour smooth gel free from lumps. The list of excipients is Disodium Edetate, Carbopol, Sodium Hydroxide, Propylene Glycol, Methyl Paraben, Poloxamer, Phenoxy Ethanol.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than date of expiry.

8.3. Packaging information

ACNETOR AD GEL is available in pack of 15 gm.

8.4. Storage and handing instructions

Store at a Temperature not exceeding 25^0C.

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
- Have kidney or liver problems
- 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

Helios Pharmaceuticals (Div. of P.K.T.P. Pvt. Ltd.)

Village Malpur, P.O. Bhud, Tehsil Nalagarh,

Baddi, Dist. Solan, (H.P.)- 173205

11. Details of permission or licence number with date

Mfg. Licence No.: MB/05/281. Issued on 26.03.2021.

12. Date of revision

Feb 2026

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/ACNETOR AD gel/Feb-2026/02/PI