AUSTRALIAN PRODUCT INFORMATION – CLINDATECH® (CLINDAMYCIN HYDROCHLORIDE) SOLUTION

1 NAME OF THE MEDICINE

Clindamycin hydrochloride.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ClindaTech is a clear hydroalcoholic solution containing clindamycin hydrochloride 1%. Dioctyl malate, a noncomedogenic humectant, is incorporated to prevent skin dryness.

ClindaTech contains alcohol 69 % v/v. For the full list of excipients, see *Section 6.1 List of excipients*.

3 PHARMACEUTICAL FORM

ClindaTech Clindamycin hydrochloride 10 mg/mL solution bottle. A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

ClindaTech is indicated for the topical treatment of acne vulgaris, particularly forms in which comedones, papules and pustules predominate.

4.2 DOSE AND METHOD OF ADMINISTRATION

ClindaTech is for external use only and is applied directly on the skin.

Wash the entire face with mild, non-alkaline soap and warm water prior to any application. Using the Dab-O-Matic applicator provided, apply a thin film directly to each acne lesion or to areas having potential of eruption.

ClindaTech is usually applied to affected areas twice daily, once every morning and once at bedtime. The frequency of treatment will depend on the severity of acne condition as well as skin tolerance but should not be more than twice daily.

Treatment of acne vulgaris needs to be individualised according to the type of lesion predominate and the response of therapy. Application to the entire face of an average adult is equivalent to approximately 2 mL of solution or clindamycin 20 mg.

Generally, a decrease in the number of inflammatory lesions should be noticed after two or six weeks, but more than eight weeks of therapy may be required before any definite beneficial effects are observed. Therapy is usually continued until a satisfactory response is obtained. If condition does not seem to improve or worsens, modification of treatment or alternative therapy should be considered.

4.3 CONTRAINDICATIONS

ClindaTech is contraindicated in patients with known history of hypersensitivity reactions to preparations containing clindamycin, lincomycin or other ingredients in the formulation.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

FOR EXTERNAL USE ONLY

ClindaTech has an unpleasant taste. Caution should be exercised when applying the solution around the mouth to avoid any possible ingestion.

Avoid any contact with eyes, eyelids, abraded skin, nasal folds, lips or mucous membranes because of the irritating dryness caused by the alcoholic solvent. In the event of any accidental contact, bathe with copious amount of cool water.

Use with caution in the following circumstances

ClindaTech contains alcohol and may cause a burning sensation especially in those patients with sensitive skins. Sensitivity reactions including contact dermatitis and rash are rare but may occur in individuals who are hypersensitive to clindamycin, lincomycin or any ingredient of the formulation.

ClindaTech should be prescribed with caution in atopic individuals or patients with impaired hepatic or renal functions. Safety has not been established when applied to areas affected concurrently with other dermatoses or to severely inflamed skin.

The use of clindamycin may cause overgrowth of non-susceptible organisms. Although rare, gram-negative folliculitis has been reported following topical application of clindamycin. If superinfection occurs, discontinue treatment.

Use of topical clindamycin has been associated with the development of strains of *P. acnes* resistant to clindamycin in some patients. If there is evidence of the development of clinical resistance during treatment, consideration should be given to discontinuation of treatment with topical clindamycin (ClindaTech).

Check the following before use

ClindaTech is not indicated in severe and deep nodulo-cystic acne.

The drug should not be used for patients with a history of ulcerative colitis, regional enteritis or antibiotic-associated colitis.

Oral and parenteral clindamycin have been associated with severe diarrhoea and pseudomembranous colitis which may result in patient death. Use of clindamycin hydrochloride topical solution results in absorption of the antibiotic from the skin surface. Diarrhoea, bloody diarrhoea and pseudomembranous colitis have been reported with the use of topical and systemic clindamycin.

It is important to consider the diagnosis of antibiotic associated colitis in patients who develop diarrhea or colitis associated with antibiotic use. Antibiotic-associated colitis (whether pseudomembranous or not) appear to result from a toxin produced by *Clostridium difficile* in the alimentary tract. The severity of the colitis may range from mild watery diarrhoea to severe, persistent, life-threatening bloody diarrhoea. The diagnosis is usually made by recognition of the clinical symptoms. The symptoms may occur during therapy or up to several weeks after cessation of therapy. Additional confirmatory signs of antibiotic-associated colitis include pseudomembrane formation seen with colonscopy*, C. difficile* culture from the stool, or assay of the stool for *C. difficile* toxin.

Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *C. difficile* should be considered. Fluid, electrolytes and protein replacement should be provided when indicated.

Drugs which delay peristalsis, eg. opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the condition and should not be used.

Use in the elderly

No data available

Paediatric Use

No data available

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Concurrent use of topical preparations containing alcohol (eg. astringents, after shave lotion, medicated cosmetics) should be avoided because they potentiate the drying action on the skin. The solvent vehicles in some abrasive cleansers, medicated soaps or cosmetics are alcoholic. They may cause a cumulative irritant effect in patients undergoing treatment.

Topical acne preparations containing desquamative or abrasive agents (eg. benzoyl peroxide, salicylic acid, resorcinol or tretinoin) may sensitise the skin to various local reactions. Concurrent use of these agents and topical clindamycin should be treated with caution in combination therapy. Concomitant use of other anti-acne or comedogenic cosmetic products should be avoided.

Both clindamycin and erythromycin appear to compete for the same ribosomal binding site in exerting their antibacterial action. Antagonism between the two anti-infective agents has been demonstrated. Concomitant use of either antibiotic in the topical treatment of acne is not recommended.

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the actions of other neuromuscular blocking agents.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available

Use in pregnancy – Pregnancy Category A

Reproductive studies have been performed in rats and mice using oral and parenteral doses up to 300 mg/kg/day and have revealed no evidence of harm to the fetus due to clindamycin. There exist, however, no adequate and well-controlled studies to demonstrate safety of use in pregnant women.

Use in lactation

It is not known if clindamycin is excreted in human milk following use of topically administered clindamycin. However, after oral or parenteral administration clindamycin has been detected in human milk. In the absence of any adequate and well controlled studies, topical clindamycin should not be used in lactating women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The most frequent adverse effect associated with the use of topical clindamycin solution is dryness of skin. Other local reactions including erythema, peeling, oiliness, contact dermatitis, irritation, itching and burning have been reported. While the exact proportion of patients reporting skin reactions was not available in controlled clinical studies, these effects were generally mild and most skin intolerance did not cause discontinuation of treatment.

Patients very frequently (>10 %) experience a sensation of warmth, irritating, dryness and/or burning experience following application of topical clindamycin, especially during the early phase of treatment. Many of these reactions can be attributed to the dehydrating effect of the hydroalcoholic vehicle.

Diarrhoea is commonly reported (>1 %, <10 %), and infrequently, abdominal pain, bloody diarrhea (including pseudomembranous colitis) have also been reported following topical use of clindamycin hydrochloride. In one multi-centre, double-blind and placebo-controlled study comparing two formulations of 1 % topical clindamycin in acne patients, it was noted that 6 of the 120 patients (~5 %) in the clindamycin hydrochloride group, 6 of the 124 patients (~5 %) in the clindamycin phosphate group and 2 of the 113 patients (~2 %) in the placebo group reported diarrhoea during the 8-week study. The diarrhoea episode in one clindamycin-treated patient was considered by the investigator to be related to treatment. Sigmoidoscopy was performed and there was no evidence of pseudomembranous colitis. The other patients with diarrhoea continued the study and diarrhoea settled. No cause and effect relationship was established.

Reporting suspected adverse effects
Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

No information is available concerning overdosage of topical clindamycin in humans.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Clindamycin is a lincosamide antibiotic obtained as a semi-synthetic derivative from cultures of Streptomyces lincolnensis. It is active *in vitro* and *in vivo* against most aerobic gram-positive cocci and several anaerobic and micro-aerophilic gram-negative and gram-positive organisms including *Propionibacterium acnes*, a resident anaerobe found in acne-susceptible follicles.

Cross-resistance has been demonstrated between clindamycin and lincomycin. Antagonism has been demonstrated between clindamycin and erythromycin.

Clindamycin may be bacteriostatic or bactericidal in action, depending on the concentration of the drug attained at the site of infection and the susceptibility of the infecting organism. *In vitro* studies showed that the minimum inhibitory concentration of clindamycin against most wild strains *of P. acnes* (46 strains at the concentration of 108/mL) ranged from 0.05 to 0.1 µg/mL or below. The antibacterial action appears to relate to its ability in inhibiting ribosomal protein synthesis in susceptible organisms by binding to 50S ribosomal subunits.

The precise mechanism by which clindamycin reduces acne lesions has not been fully elucidated. Its therapeutic efficacy appears to act through its ability to decrease acne lesions, suppress or eliminate *P. acnes* in the sebaceous follicles, inhibit lipase activity, and reduce the levels of free fatty acids in skin surface lipids. Applied to the skin, clindamycin markedly reduces the follicular population of *P. acnes* and the concentration of skin surface free fatty acids.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Pharmacokinetic studies have not been undertaken with ClindaTech. Published results of studies which involved other clindamycin formulations are described below.

In an *in vitro* model using human skin, approximately 10 % of the dose was absorbed into the stratum corneum following topical application of a 1 % hydroalcoholic solution of radiolabelled clindamycin as the hydrochloride.

Absorption of clindamycin into comedones was assessed in an *in vivo* study in which comedones were removed from acne patients who had applied 1 % clindamycin hydrochloride twice daily for 2 weeks or longer. The whole comedonal concentration of clindamycin ranged from 0-5 µg/mg of comedonal material with a mean concentration of 0.824 µg/mg. It was stated that these antibiotic concentrations are above the minimum inhibitory concentration of clindamycin for most wild strains of *P. acnes in vitro* at 0.05-0.1 µg/mL or below.

Systemic absorption of clindamycin was assessed by measurement of serum clindamycin in another open study of 18 acne patients. No clindamycin was detected in serum from any of the subjects obtained one to nine hours after application of a 1 % clindamycin hydrochloride solution. The patients had been instructed to apply the solution with their fingertips to the affected areas 2 to 3 times daily. The duration of use ranged from 6-150 days with mean duration at 43.4 days, but the total volume of solution and surface area of application was not stated. The lower limit of quantification was 1 µg/mL.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available

Carcinogenicity

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Dioctyl malate
- Ethanol
- Purified water

6.2 INCOMPATIBILITIES

Information on the physical or chemical compatibility of topical clindamycin with other topical preparations is not available. ClindaTech should only be constituted using the base solution provided.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30 °C. Do not freeze or expose to excessive heat and direct light.

6.5 NATURE AND CONTENTS OF CONTAINER

ClindaTech is packaged in a ready-to-use pack.

The ready-to-use pack, in either 6 mL*, 10 mL*, 30 mL*, 50 mL or 100 mL, consists of a white HDPE bottle fitted with a screw-neck top and a Dab-O-Matic applicator and a polypropylene closure.

* = not marketed

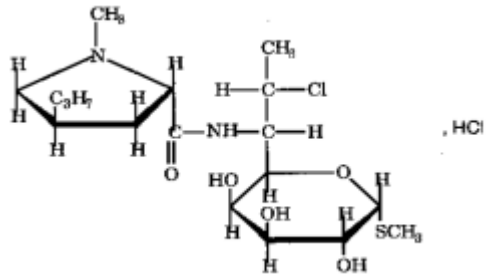
A package insert is included with the product in the carton.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure



Chemical name: methyl 6-amino-7-chloro-6,7,8-trideoxy-N-[(2S,4R)-1-methyl-4-propylprolyl]-1-thio-L-threo-α-D-galacto-octopyranoside hydrochloride.

Molecular formula is $C_{18}H_{33}ClN_2O_5S.HCl$ (molecular weight 461.5)

CAS number: 21462-39-5

1.086 g of clindamycin hydrochloride (anhydrous form) is approximately equivalent to 1 g of clindamycin.

7 MEDICINE SCHEDULE (POISONS STANDARD)

(S4) Prescription Only Medicine

8 SPONSOR

iNova Pharmaceuticals (Australia) Pty Limited

L10, 12 Help Street

Chatswood NSW 2067

Toll Free: 1800 630 056

New Zealand Toll Free: 0508 375 394

9 DATE OF FIRST APPROVAL

23 November 1998

10 DATE OF REVISION

17 July 2019

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Transfer of text from old PI format (without changes) (April 2019)
All	Reformatting of approved PI as per new TGA format (April 2019)