Package Insert

Zindaclin® 1% Gel

(Clindamycin Phosphate)

1. **Name of the Medicinal Product**
   ZINDACLIN 1% GEL
2. **Qualitative and quantitative composition**
   The gel contains clindamycin phosphate equivalent clindamycin 1% w/w.
   Can also be expressed as 1 g of gel contains 10 mg clindamycin (1% w/w) equivalent to 11.88 mg clindamycin phosphate
   For excipients see section 6.1
3. **Pharmaceutical form**
   Gel. A white translucent gel.
4. **Clinical particulars**

4.1 Therapeutic indications

ZINDACLIN is indicated for the treatment of mild to moderate acne vulgaris.

4.2 Posology and method of administration

Adults and adolescents

Apply a thin film of ZINDACLIN once daily to the affected area.
Patient response should be reviewed periodically.

Children

ZINDACLIN is not indicated for use in children below the age of 12 years.
Cutaneous use.
Patient response should be reviewed after 6-8 weeks of treatment and the duration of treatment should be limited to 12 weeks.

4.3 Contraindications

ZINDACLIN is contra-indicated in patients with a hypersensitivity to the active substance clindamycin or to any of the excipients in the medicinal product. Although cross-sensitization to lincomycin has not been demonstrated, it is recommended that ZINDACLIN should not be used in patients who have demonstrated lincomycin sensitivity.

4.4 Special warnings and precautions for use

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 characterized 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 ZINDACLIN is low, the potential for the development of gastrointestinal adverse effects should be taken into the account when considering treatment in patients with a previous history of antibiotic-associated colitis, enteritis, ulcerative colitis or Crohn's disease.
Cross resistance may occur with other antibiotics such as lincomycin and erythromycin. See section 4.5.
Prolonged use of clindamycin may cause resistance and/or overgrowth of the non susceptible bacteria of fungi although this is a rare occurrence.
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 bathed the affected area with copious amounts of cool water.
ZINDACLIN 1% Gel contains propylene glycol. May cause skin irritation.
The irritation potential of ZINDACLIN may be increased if the product is used under occlusion.

- Clindamycin therapy has been associated with severe colitis which may end fatally.
- It should be reserved for serious infections where less toxic antimicrobial agents are inappropriate.
- It should not be used in patients with nonbacterial infections.
- Its use in newborns are contraindicated.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions have been reported with topical clindamycin.
In vitro, antagonism has been demonstrated between erythromycin and clindamycin, synergy has been shown with metronidazole and both antagonistic and synergistic effects have been observed with aminoglycosides.

4.6 Pregnancy and lactation

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 fetus/newborn child. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal 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 ZINDACLIN. As a general rule, patients should not breastfeed while taking a drug since many drugs are excreted in human milk.

Sensitization 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.

4.7 Effects on ability to drive and use machines
None or not relevant.

4.8 Undesirable effects
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 adverse reactions* below have been reported with ZINDACLIN in clinical trials. They are listed in decreasing order of incidence.

Organ system
Skin and subcutaneous tissue disorder
Common (>1/100, <1/10)
Dry skin, erythema, skin burning, irritation around eyes, acne exacerbation, pruritis
Uncommon (>1/1000, <1/100)
Painful skin, Scaly rash

*Classified MEDDRA preferred terms.

Whilst no case of severe diarrhoea or pseudomembranous colitis has been reported in clinical trials with ZINDACLIN, 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 ZINDACLIN exists (please refer to Section 4.4.)

4.9 Overdose
No cases of overdose have been reported and it is not expected that overdose would occur in normal use.

5. Pharmacological properties

Pharmacotherapeutic group: Anti-infectives for treatment of acne.
ATC code: D10A F01

5.1 Pharmacodynamic properties
ZINDACLIN contains clindamycin phosphate which is hydrolysed in the skin to the active constituent clindamycin. Cindamycin 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.

5.2 Pharmacokinetic properties
In ZINDACLIN clindamycin phosphate binds with zinc to form a complex in a formulation which results in a reduced extent of absorption. A study with ZINDACLIN in vitro with human skin has shown the penetration of radiolabelled clindamycin phosphate from the ZINDACLIN formulation to be less than 5% of the applied dose. When applied cutaneously at 8 g/day for 5 days ie. levels well in excess of the maximum anticipated clinical dose is very small amount, (median less than 2mg/ml) of clindamycin was measured in plasma. Clindamycin phosphate is metabolized to the parent drug in the skin and clindamycin itself is primarily metabolized in the liver via N-demethylation, sulphoxidation and hydrolysis and predominantly excreted in the bile.

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

6. Pharmaceutical particulars

6.1 Lists of excipients
Propylene glycol
Purified water
Ethanol 96%
Zinc acetate dihydrate
Hydroxyethylcellulose
Sodium hydroxide 30% (w/w)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store below 30°C

6.5 Nature and contents of container
ZINDACLIN is packaged in 30 g laminate tubes with a peelable membrane laminate seal covering the orifice. The tube is fitted with a white opaque polypropylene cap.

6.6 Instructions for use and handling
No applicable.

7. Manufacturer:

Dr. August Wolff GmbH & Co. KG Arzneimittel
Sudbrackstrasse 56
33611 Bielefeld, Germany

8. Product Licence Holder

Orient EuroPharma (M) Sdn Bhd
E-08 Garden Shoppe, One City
Jalan USJ 25/1C
47650 Subang Jaya,
Selangor Malaysia
Tel: +603-8081 6637
Fax: +603-8081 8137

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