SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Zindaclin 1% Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The gel contains clindamycin phosphate equivalent to clindamycin 1% w/w.

3. PHARMACEUTICAL FORM

Gel
A white translucent gel.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Zindaclin 1% Gel is indicated for the treatment of mild to moderate acne vulgaris.

4.2 Posology and method of administration

Cutaneous use.

Adults and adolescents

Apply a thin film of Zindaclin 1% Gel once daily to the affected area. Patient response should be reviewed periodically.

Children

Zindaclin 1% Gel is not indicated for use in children below the age of 12 years.

4.3 Contraindications

Zindaclin 1% Gel 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-sensitisation to lincomycin has not been demonstrated, it is recommended that Zindaclin 1% Gel should not be used in patients who have demonstrated lincomycin sensitivity.

4.4 Special warnings and precautions for use

The product contains approximately 20% ethanol. Each gram contains approximately 0.2 gram alcohol.
Do not light a cigarette or come in contact with an open flame until the product has been completely dried off.

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 diarrhea 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 diarrhea and abdominal cramps. Should antibiotic associated colitis occur, appropriate diagnostic and therapeutics 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 1% 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.

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.

Prolonged use of clindamycin may cause resistance and/or overgrowth of non susceptible bacteria or fungi although this is a rare occurrence.
Zindaclin 1% Gel contains propylene glycol. May cause skin irritation.
The irritation potential of Zindaclin 1% Gel may be increased if the product is used under occlusion.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions have been reported with topical clindamycin.

4.6 Fertility, pregnancy and lactation

For clindamycin applied cutaneously, no clinical data on exposed pregnancies are available. Data on the limited number of pregnancies exposed to clindamycin administered by other routes indicate no adverse effect 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 a pregnant woman.

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 1% Gel. As a general rule, patients should not breast-feed 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.

4.7 Effects on ability to drive and use machines

None.

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 moisturiser may be of benefit.

The adverse reactions below have been reported with Zindaclin 1% Gel 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 Zindaclin 1% Gel, 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 1% Gel exists (please refer to Section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:
https://sideeffects.health.gov.il

4.9 Overdose

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

Irritant dermatitis may occur when excessive quantities of Zindaclin 1% Gel are applied. The use of a suitable moisturiser may be of benefit in these cases. In subsequent applications a thin film of Zindaclin 1% Gel should be applied in accordance with the dosage instructions (see section 4.2).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiinfective for treatment of acne.
ATC code: D10A F01

Zindaclin 1% Gel contains clindamycin phosphate which is hydrolyzed in the skin to the active constituent clindamycin. Clindamycin is a lincosamide antibiotic with primarily bacteriostataic 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 etiological factors of the disease.

As with all antibiotics, the long-term use of cutaneous clindamycin may lead to resistance.

5.2 Pharmacokinetics properties

In Zindaclin 1% Gel, clindamycin phosphate binds with zinc to form a complex in a formulation which result in a reduced extent of absorption. A study with Zindaclin 1% Gel *in vitro* with human skin has shown the penetration of radiolabelled clindamycin phosphate from the Zindaclin 1% Gel 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 the plasma.

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, genotoxicity or toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol, ethanol, hydroxyethylcellulose, zinc acetate dihydrate, sodium hydroxide, purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25ºC

6.5 Nature and content of container

Zindaclin 1% Gel is packed in 15g and 30g HDPE/LDPE tubes with polypropylene cap.

6.6 Instructions for use and handling

Do not light a cigarette or come in contact with an open flame until the product has been completely dried off.

7. MANUFACTURER

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

8. MARKETING AUTHORISATION HOLDER:

Taro International Ltd., 14 Hakitor St., Haifa Bay 2624761

9. MARKETING AUTHORIZATION NUMBER:

128.65.30648

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