***For the Use of a Registered Medical Practitioner Only***

## 1. GENERIC NAME AND BRAND NAME

Ozenoxacin 1% cream
**OZEWID™**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ozenoxacin…… 1.0% w/w
Preservative:
Benzoic acid I.P…. 0.1% w/w
In a cream base……q.s.

## 3. DOSAGE FORM AND STRENGTH

Refer section 1 & 2

## 4. CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATION

Ozenoxacin is indicated for the topical treatment of impetigo due to Staphylococcus aureus or Streptococcus pyogenes in adult and pediatric patients 2 months of age and older.

### 4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Apply a thin layer of OZEWID topically to the affected area twice daily for five days. Affected area may be up to 100 $cm^2$ in adult and pediatric patients 12 years of age and older or 2% of the total body surface area and not exceeding 100 $cm^2$ in pediatric patients less than 12 years of age.

Patients not showing a clinical response within three days should be re-evaluated and alternative therapy should be considered

- Wash hands after applying OZEWID cream.
- OZEWID cream is for topical use only.
- Not for oral, ophthalmic, intranasal, or intravaginal use.
- The treated area may be covered with a sterile bandage or gauze dressing.

### 4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

### 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

**Potential for Microbial Overgrowth**

The prolonged use may result in overgrowth of non-susceptible bacteria and fungi. If such infections occur during therapy, discontinue use and institute appropriate supportive measures.

**Sensitization or severe local irritation**
In the event of a sensitization or severe local irritation from the use of ozenoxacin cream, treatment should be discontinued, the cream carefully wiped off, and appropriate alternative therapy for the infection instituted.
Caution should be exercised when used on patients with increased skin sensitivity, e.g. rosacea or seborrheic dermatitis, since deterioration of already present skin conditions have been observed.

**Eyes and mucous membranes**
Ozenoxacin cream must be kept away from the eyes and mucous membranes.

**Ingestion**
Care must be taken to avoid ingestion which is especially important in children who has lesions around the mouth.
OZEWID contains propylene glycol which may cause skin irritation.
OZEWID contains stearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).
OZEWID contains benzoic acid which may be irritant to the skin, eyes and mucous membranes and may increase the jaundice in pre-term and full-term jaundiced neonates because of its absorption through the skin.

## 4.5 DRUGS INTERACTIONS

The effect of concurrent application of ozenoxacin and other topical medicinal products to the same area of skin has not been studied, and it is not recommended.
In human liver microsomes, ozenoxacin showed to cause mild direct competitive inhibition of CYP3A4 at high concentrations (100µM), and possibly cause very mild time-dependent inhibition of CYP2C9 at high concentrations (200µM). However, since systemic exposure to ozenoxacin was not observed following topical application of 10 mg/g cream in adult and paediatric patients aged 6 months and older, it is not expected that concurrent systemic administration of CYP3A4 or CYP2C9 substrates will result in clinically important inhibition of their metabolism by Ozenoxacin.

Ozenoxacin does not induce cytochrome P450 enzymes in vitro. In vitro data very strongly suggest that the use of ozenoxacin in combination with commonly used antimicrobial agents should not represent a risk to clinical outcome.

## 4.6 USE IN SPECIAL POPULATIONS (SUCH AS PREGNANT WOMEN, LACTATING WOMEN, PAEDIATRIC PATIENTS, GERIATRIC PATIENTS ETC.)

**Pregnancy**
There are no available data on the use of OZEWID in pregnant women to inform a drug associated risk. Systemic absorption of Ozenoxacin in humans is negligible following topical administration of Ozenoxacin (up to twice the concentration of the

marketed formulation). Due to the negligible systemic exposure, it is not expected that maternal use of Ozenoxacin will result in fetal exposure to the drug.

Animal reproduction studies were not conducted with Ozenoxacin. However, toxicity studies conducted in pregnant rats and rabbits administered the oral form of ozenoxacin showed no significant adverse developmental effects (at >10,000 times the maximum human plasma concentration seen with dermal application of ozenoxacin).

The estimated background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

**Lactation**

No data are available regarding the presence of ozenoxacin in human milk, and the effects of ozenoxacin on the breastfed infant or on milk production. However, breastfeeding is not expected to result in exposure of the child to ozenoxacin due to the negligible systemic absorption of ozenoxacin in humans following topical administration of Ozenoxacin. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Ozenoxacin and any potential adverse effects on the breast-fed child from Ozenoxacin or from the underlying maternal condition.

**Fertility**

There are no data on the effects of ozenoxacin on human fertility. No treatment-related effects on male or female fertility have been shown in animal studies

**Pediatric Use**

The safety and effectiveness of Ozenoxacin in the treatment of impetigo have been established in pediatric patients 2 months to 17 years of age. Use of OZENOXACIN in pediatric patients (2 months to 17 years of age) is supported by evidence from adequate and well-controlled studies of OZENOXACIN in which 251 pediatric patients received at least one dose of OZENOXACIN. The median age of the patients enrolled in the clinical trials was 10 years; 3 % of patients were 2 months to less than 2 years of age, 55 % of patients were 2 to less than 12 years of age, 11 % of patients were 12 to less than 18 years of age, and 31 % of patients were 18 years of age or older. In these studies, the maximum dose applied was approximately 0.5 g of OZENOXACIN applied twice daily for up to 5 days (i.e., up to 10 applications total.

The safety profile of OZENOXACIN in pediatric patients 2 months and older was similar to that of adults.

The safety and effectiveness of OZENOXACIN in pediatric patients younger than 2 months of age have not been established.

**Geriatric Use**

Clinical studies of OZENOXACIN did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Ozenoxacin has no or negligible influence on the ability to drive and use machines.

## 4.8 UNDESIRABLE EFFECTS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety profile of OZENOXACIN was assessed in two clinical trials (Trial 1 and Trial 2) in 362 adult and pediatric patients two months of age and older with impetigo. The patients used at least one dose from a 5-day, twice a day regimen of OZENOXACIN. Control groups included 361 patients who used placebo and 152 patients who used retapamulin ointment. The median age of the patients enrolled in the clinical trials was 10 years; 3 % of patients were 2 months to less than 2 years of age, 55 % of patients were 2 to less than 12 years of age, 11 % of patients were 12 to less than 18 years of age, and 31 % of patients were 18 years of age or older.
Adverse reactions (rosacea and seborrheic dermatitis) were reported in 1 adult patient treated with OZENOXACIN.

In clinical studies in which 559 patients with superficial skin infections applied ozenoxacin cream, the most commonly reported adverse reaction was application site irritation, which affected less than 1% of patients.
No significant safety issues were reported during the clinical studies.

**Pediatric Population**

During the clinical development program no adverse drug reactions were reported in the paediatric population. Frequency, type and severity of adverse reactions in the pediatric population are expected to be the same as in adults.

## 4.9 OVERDOSE

Any sign or symptom of overdose, either topically or by accidental ingestion, should be treated symptomatically. No specific antidote is known.

# 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibiotics and chemotherapeutics for dermatological use, Antibiotics for topical use.
OZEWID contains ozenoxacin, a quinolone antimicrobial. It is intended for topical use only.

The chemical name of ozenoxacin is 1-Cyclopropyl-8-methyl-7-(5-methyl-6-methylamino-pyridin-3-yl)-4-oxo1,4-dihydro-quinoline-3-carboxylic acid. Ozenoxacin, a white to pale-yellow crystalline solid, has a molecular formula of C21H21N3O3, and a molecular weight of 363.41

## 5.1 MECHANISM OF ACTION

Ozenoxacin is a quinolone antimicrobial drug. The mechanism of action involves the inhibition of bacterial DNA replication enzymes, DNA gyrase A and topoisomerase IV. Ozenoxacin has been shown to be bactericidal against S. aureus and S. pyogenes organisms.

### Resistance

**Mechanism of resistance**
The development of quinolone resistance is caused by point mutations in discrete regions of the DNA gyrase (gyrA) and topoisomerase IV (grlA) genes called the Quinolone Resistance-Determining Regions (QRDR).

Ozenoxacin shows a dual target of action, inhibiting DNA gyrase and topoisomerase IV, showing an ability to inhibit both enzymes. As a result of this inhibitory target activity and bactericidal property, ozenoxacin shows a low frequency of selection of spontaneous resistant mutants.

Against Gram-positive organisms Ozenoxacin has shown no cross-resistance with other families of commercial antibacterial and retains activities below the breakpoints for mutants resistant to other marketed quinolones.

It is worth noting that ozenoxacin shows the same activity against methicillin-sensitive and methicillin-resistant strains of all studied bacterial species**.**

**Interaction with Other Antimicrobials**
Ozenoxacin has been tested in combination with 17 other commonly used antimicrobial agents against S. aureus and S.pyogenes. Antagonism interactions with ozenoxacin were observed with ciprofloxacin against S. aureus.

**Antimicrobial Activity**
Ozenoxacin is characterized by its potency and bactericidal activity against clinical bacterial isolates involved in skin infections, including S. aureus and S. pyogenes. The proposed epidemiological cut off (ECOFF) values for S. aureus and S. pyogenes, are of 0.008 and 0.06 µg/ml, respectively**.**

**Gram-positive bacteria**
Staphylococcus aureus (including methicillin-resistant isolates)
Streptococcus pyogenes.

## 5.2 PHARMACODYNAMICPROPERTIES

**Exposure-Response Relationship**
The exposure response relationship for ozenoxacin following topical application has not been studied, however; a relationship is unlikely because systemic exposure following topical application is negligible.

## 5.3 PHARMACOKINETIC PROPERTIES

**Absorption**
Four pharmacokinetic studies were conducted in 110 patients utilizing varying strengths of ozenoxacin cream, up to 2% (twice the concentration of the marketed formulation). Three of these studies assessed systemic absorption in healthy subjects and in subjects with impetigo. These studies were conducted with either single or repeated application of up to 1 g ozenoxacin cream to intact or abraded skin (up to 200 cm2 surface area). No systemic absorption was observed in 84 of 86 subjects, and negligible systemic absorption was observed at the level of detection (0.489 ng/mL) in 2 subjects.

**Distribution**
Plasma protein binding of [14C]-ozenoxacin was moderate (~80 to 85%) and did not appear to be dependent on concentration. Since negligible systemic absorption was observed in clinical studies, tissue distribution has not been investigated in humans.

**Elimination Metabolism**
Ozenoxacin was not metabolized in the presence of fresh human skin discs and was minimally metabolized in human hepatocytes.

**Excretion**
Studies have not been investigated in humans due to the negligible systemic absorption observed in clinical studies.

**Special populations**
No pharmacokinetic data are available in patients with renal or hepatic impairment. However, due to the undetectable systemic plasma levels that have been observed, no safety problems are foreseen.

# 6. NONCLINICAL PROPERTIES

## 6.1 ANIMAL TOXICOLOGY OR PHARMACOLOGY

**Carcinogenesis, Mutagenesis, Impairment of Fertility**
Long-term studies in animals to evaluate carcinogenic potential have not been conducted with ozenoxacin.

Ozenoxacin demonstrated no genotoxicity when evaluated in vitro for gene mutation and/or chromosomal effects in the Ames test, mouse lymphoma cell assay, or when evaluated in vivo in a rat micronucleus test with demonstrated systemic exposure.

Oral doses of Ozenoxacin did not affect mating and fertility in male and female rats treated up to 500 mg/kg/day (about 8500 and 16,000 times respectively, the maximum human plasma concentration seen with dermal application of ozenoxacin 1% cream).

**Repeated dose studies**
Topically administered, Ozenoxacin was well tolerated. Plasma levels of Ozenoxacin after single dermal administration were below LOQ while only low systemic exposure was detected after 28-day dermal administration.

Ozenoxacin was also well tolerated in both intact and abraded skin in minipigs after dermal administration during 28 consecutive days.

**Juvenile animals**
In the 2-weeks repeated oral toxicity study in juvenile dogs, where adequate systemic exposure was achieved, the NOAEL was 100 mg/kg/day.
There was no evidence of articular toxicity.

**Local tolerance**
Adverse effects usually related to quinolones, such as phototoxicity, photo allergenic and sensitizer potential have not been observed with ozenoxacin in the non-clinical studies conducted.

## 7. DESCRIPTION

OZEWID is supplied for external application, as a cream dosage form. Each pack of OZEWID cream contains Ozenoxacin 1%.

## 8. PHARMACEUTICAL PARTICULARS

### 8.1 INCOMPATIBILITIES
Not Applicable

### 8.2 SHELF-LIFE
Refer Pack

### 8.3 PACKAGING INFORMATION
Refer Pack

### 8.4 STORAGE CONDITION AND HANDING INSTRUCTIONS
Refer Pack

## 9. PATIENT COUNSELLING INFORMATION

Advise patients (and/or their caregivers or guardians) using OZEWID of the following information and instructions:

- Use OZEWID as directed by the healthcare practitioner. As with any topical medication, patients and caregivers should wash their hands after application if the hands are not the area for treatment.
- OZEWID is for external use only. Do not swallow OZEWID or use it in the eyes, on the mouth or lips, inside the nose, or inside the female genital area.
- The treated area may be covered by a sterile bandage or gauze dressing.
- Not for oral, ophthalmic, intranasal, or intravaginal use.
- The treated area may be covered with a sterile bandage or gauze dressing.

## 10. DETAILS OF MANUFACTURER

Refer Pack for manufacturer details.

Marketed By:
**Abbott Healthcare Pvt. Ltd.**
Angel Space, Bldg. D-4, Gala No. 1 to 3 &
11 to 13 Ground Floor, 101 to 106 & 111 to
116 First Floor, 201 to 206 & 211 to 216
2nd Floor, Pimplas, Dist. Thane,
Bhiwandi - 421 302, Maharashtra,
India.

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## 11. DETAILS OF PERMISSION OR LICENCE NUMBER

Refer Pack for Permission/License details

## 12. DATE OF REVISION

Version 3.0, dated 02-Jan-26

For Product Complaints/Adverse events or Queries please write to
**webmasterindia@abbott.com**