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

IMPINOZ CREAM

1. Generic Name

Ozenoxacin Cream 1% w/w

2. Qualitative and quantitative Composition:

Composition:

Ozenoxacin…….1.0% w/w

Preservative:

Benzoic Acid I.P,……..…..0.1% w/w

In a Cream Base…….....q.s.

The Excipients is Cetostearyl alcohol, Cetyl alcohol, Oleoyl polyoxyl-6 glycerides, PEG-6 Stearate and Glycol stearate and PEG-32 stearate, Benzoic acid, Glyceryl Stearate (and) PEG 100 Stearate, Propylene Glycol, Carbopol, Benzyl alcohol, Octyldodecanol.

3. Dosage form and strength

Dosage form: Cream

Strength: Ozenoxacin 1.0% w/w

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

Posology

Apply a thin layer of Ozenoxacin 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 100Cm^2 in pediatric patients less than 12 years of age.

Method of administration

- Wash hands after applying Ozenoxacin Cream.
- Ozenoxacin Cream is for topical use only.
- Not for Oral, Ophthalmic, Intranasal, or lntravaginal use.
- The treated area may be covered with a Sterile Bandage or Gauze Dressing.

4.3 Contraindications

It is contraindicated with patients having a hypersensitivity to the drug product.

4.4 Special warnings and precautions for use

Potential for Microbial Overgrowth

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

4.5 Drugs interactions

No studies on the interaction with other medicinal products and other forms of interaction have been performed.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

Risk Summary

There are no available data on the use of Ozenoxacin in pregnant women to inform a drug associated risk. Systemic absorption of Ozenoxacin in humans is negligible following topical administration of Ozenoxacin due to the negligible systemic exposure, it is not expected that maternal use of Ozenoxacm will result in foetal exposure to the drug.

The estimated background risk of major birth defects and miscarriage for the indicated populatlon 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

Risk Summary

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.

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 251pediatric 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 than12 years of age, 11%of patients were 12 to less than 18years of age, and31% 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 to10 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 2months 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

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Summary of the safety profile

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.

As per data from Ozenoxacin global innovator; 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 361patients 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 than2years of age,55%of patients were 2toless than 12 years of age,11%of patients were 12 to less than 18years of age,and31%of patients were18 years of age or older.

Adverse reactions (Rosacea and Seborrheic Dermatitis) were reported in 1 adult patient treated with Ozenoxacin.

Reporting of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting by reporting side effects, you can help provide more information on the safety of this medicine.

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

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

The mechanism of Quinolone resistance can arise through mutations of one or more of the genes that encode DNA Gyrase or topoisomerase IV. Resistant organisms will typically carry a combination of mutations within gyrA and parC subunits. Overall the frequency of resistant mutants selected by Ozenoxacinis: $\leq 10^{-10}$.

Interaction with Other Antimicrobials

Ozenoxacin has been tested in combination with 17 other commonly used antimicrobial agents against S.*aureusand S.pyogenes.* Antagonism interactions with Ozenoxacin were observed with Ciprolloxacin against S.*aureus.*

Antimicrobial Activity

Ozenoxacin has been shown to be active against most isolates of the following microorganisms, both in Vitro and in clinical infections: Gram-positive bacteria *Staphylococcus aureus* (including Methicillm- resistant isolates),*Streptococcus pyogenes.*

5.2 Pharmacodynamic properties

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 in110 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 1gOzenoxacin Cream to intact or abraded skin (up to 200 Cm^2 sur1ace 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 [^{14}C]-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.

Metabolism

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

Excretion

Ozenoxacin have not been investigated in humans due to the negligible systemic absorption observed.

6 Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Long-term studies in animals to evaluate carcinogenic potential have not been conducted with Ozenoxacin.

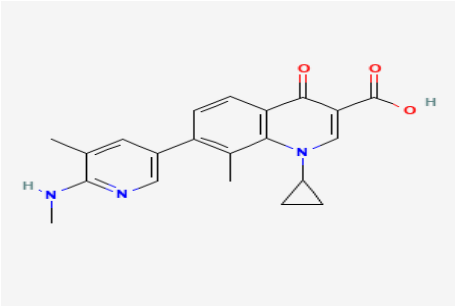
Ozenoxacin demonstrated no genotoxicity when evaluated in vitro for gene mutation and/or Chromosomal effects in the Ames test, Mouse Lymphoma Cell assay, or when evaluated in vivo in a rat micronucleus test with demonstrated systemic exposure.

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).

7 Description

Ozenoxacin:

Ozenoxacin 1-cyclopropyl-8-methyl-7-[5-methyl-6-(methylamino)pyridin-3-yl]-4-oxoquinoline-3-carboxylic acid The empirical formula is $C_{21}H_{21}N_3O_3$ and its molecular weight is 363.4g/mol. The chemical structural formula is:



IMPINOZ CREAM

Ozenoxacin cream are off white to pale yellow cream. The Excipients is Cetostearyl alcohol, Cetyl alcohol, Oleoyl polyoxyl-6 glycerides, PEG-6 Stearate and Glycol stearate and PEG-32 stearate, Benzoic acid, Glyceryl Stearate (and) PEG 100 Stearate, Propylene Glycol, Carbopol, Benzyl alcohol, Octyldodecanol.

8 Pharmaceutical particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Do not use later than date of expiry

8.3 Packaging information

IMPINOZ CREAM is available in pack of 10 gm

8.4 Storage and handing instructions

Store at a temperature not exceeding 25°C.

Do not freeze.

Protect from light and moisture.

Keep out of reach of children.

Avoid contact with eyes.

For external use only.

Replace the cap tightly closed after each use.

9 Patient Counselling Information

Package leaflet: Information for the user

IMPINOZ CREAM

(Ozenoxacin Cream 1% w/w)

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

9.1 What IMPINOZ CREAM is and what it is used for

IMPINOZ CREAM is Ozenoxacin Cream 1% w/w.

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.

9.2 What you need to know before you take IMPINOZ CREAM

Do not take IMPINOZ

It is contraindicated with patients having a hypersensitivity to the drug product.

Warnings and precautions

Potential for Microbial Overgrowth

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

Pregnancy, breast-feeding and fertility

Pregnancy

Risk Summary

There are no available data on the use of Ozenoxacin in pregnant women to inform a drug associated risk. Systemic absorption of Ozenoxacin in humans is negligible following topical administration of Ozenoxacin due to the negligible systemic exposure, it is not expected that maternal use of Ozenoxacm will result in foetal exposure to the drug.

The estimated background risk of major birth defects and miscarriage for the indicated populatlon 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%to20%, respectively.

Lactation

Risk Summary

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.

9.3 How to apply IMPINOZ CREAM

- Wash hands after applying Ozenoxacin Cream.
- Ozenoxacin Cream is for topical use only.
- Not for Oral, Ophthalmic, Intranasal, or lntravaginal use.
- The treated area may be covered with a Sterile Bandage or Gauze Dressing.

9.4 Possible side 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.

As per data from Ozenoxacin global innovator; 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 361patients 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 than2years of age,55%of patients were 2toless than 12 years of age,11%of patients were 12 to less than 18years of age,and31%of patients were18 years of age or older.

Adverse reactions (Rosacea and Seborrheic Dermatitis) were reported in 1 adult patient treated with Ozenoxacin.

Reporting of adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting by reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store IMPINOZ CREAM

Store at a temperature not exceeding 25°C.

Do not freeze.

Protect from light and moisture..

9.6 Contents of the pack and other information

IMPINOZ CREAM content of Ozenoxacin as Active ingredirnts.

The Excipients is Cetostearyl alcohol, Cetyl alcohol, Oleoyl polyoxyl-6 glycerides, PEG-6 Stearate and Glycol stearate and PEG-32 stearate, Benzoic acid, Glyceryl Stearate (and) PEG 100 Stearate, Propylene Glycol, Carbopol, Benzyl alcohol, Octyldodecanol,

IMPINOZ CREAM is available in pack of 10 gm

10 Details of manufacturer

Om Sai Pharma Pack

(A WHO GMP Certified Company)

Plot No. 38& 39,

Sector-11, I.I.E., SIDCUL, Haridwar,

Uttarakhand-249403, (India).

11 Details of permission or licence number with date

Mfg. Licence. No.: 58/UA/2018 Issued on.:11.05.2021

12. Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

IN/IMPINOZ CREAM 10 gm/NOV 2023/01/PI