Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT

ZOCON (Fluconazole Eye Drops 0.3% w/v)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Fluconazole ……..…. ..0.3% w/v
Benzalkonium Chloride ……..….. 0.01% w/v
(as preservative)
Aqueous buffered vehicle …….q.s.

3. PHARMACEUTICAL FORM

Ophthalmic solution

Description

Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

ZOCON Eye Drops is indicated in adults for the treatment fungal corneal ulcers (also called as fungal keratitis).

4.2 Posology and Method of Administration

Adults

Instil 1 to 2 drops in the eye at every 4 hour interval. In severe cases, the frequency may be 1 hourly in initial days of therapy. The frequency may be decreased to 4 to 5 times a day after few days depending on response to treatment. Therapy should be continued for 21 days or until complete resolution of the ulcer or keratitis.
Or, as directed by the Physician.

Paediatric Population

Data is not available on use of this product in children.

Method of Administration

- This product is for topical ocular use only.
- Not for injection.
- Patients should remove contact lenses, if any, and wash their hands before using this eye drops.
- If eye irritation occurs, discontinue the use and consult the Physician.
- After opening the vial, to avoid microbial contamination, dropper/vial tip should not be touched by hands or the tip should not be contacted with any other surface/substance.
- If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 to 15 minutes apart; eye ointments should be administered last.
- Use the solution within 1 month after opening the vial. Discard the unused portion of eye drop, if any, after one month of first opening the vial (even though expiry date is longer).
- Follow the directions mentioned on the container label.

4.3 Contraindications

ZOCON Eye Drops is contraindicated in the following:

- Hypersensitivity to fluconazole or to any of the excipients listed in section 6.1.
- Soft contact lenses.

4.4 Special Warnings and Precautions for Use

Failure of improvement of fungal keratitis following 7 to 10 days of administration of drug suggests that the infection may be caused by an organism not susceptible to fluconazole. Continuation of therapy should be based on clinical re-evaluation and additional laboratory studies on fungal sensitivity.

Preservative - Benzalkonium Chloride (BKC): Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

Contact Lenses: Remove contact lenses before using this product. ZOCON Eye Drops contains benzalkonium chloride which may cause irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses. In case patients are allowed to wear contact lenses they should be instructed to remove them prior to application of drops and wait at least 15 minutes before reinsertion.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Specific drug interaction studies have not been conducted with fluconazole eye drops. Given the low systemic concentration of fluconazole following topical ocular administration, drug interactions are unlikely to occur.

4.6 Fertility, Pregnancy and Lactation

Pregnancy

There are no adequate and well controlled studies available on use of fluconazole ophthalmic solution in pregnant women. Oral formulation of fluconazole was found to be harmful to the foetus when given to the pregnant women during first trimester. Therefore, ZOCON Eye Drops should not be used during pregnancy unless potential benefits of the medicine justify the possible risk to the foetus.

Lactation

It is not known whether topical ocular administration of fluconazole is excreted in human milk; however, it is known that orally administered fluconazole is excreted in the human breast milk. Thus, caution should be exercised when ZOCON Eye Drops are administered to a nursing mother.

Fertility

In animal studies, fluconazole did not affect the fertility of male or female rats. Human data is not available.

4.7 Effects on Ability to Drive and Use Machines

ZOCON Eye Drops has no or negligible influence on the ability to drive or use machines. Temporarily blurred vision or other visual disturbances may affect the ability to drive or use

machines. If transient blurred vision occurs upon instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable Effects

No adverse effects have been reported with the topical application of fluconazole eye drops. However, transient irritation, burning and ocular discomfort may occur as seen with other eye drop preparations.

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation 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 via the national reporting system.

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4.9 Overdose

A topical overdose of fluconazole ophthalmic solution may be rinsed out from the eye(s) with lukewarm tap water. Toxic effects are not expected with an ocular overdose. There is no data available on the accidental ingestion of this product.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic Group: Ophthalmologicals; antimycotics, triazole derivatives.
ATC Code: J02AC01.

Mechanism of Action

Fluconazole is a highly selective inhibitor of fungal cytochrome P450 dependent enzyme lanosterol 14-α-demethylase. This enzyme functions to convert lanosterol to ergosterol. The subsequent loss of normal sterols correlates with the accumulation of 14-α-methyl sterols in fungi and may be responsible for the fungistatic activity of fluconazole.

Pharmacodynamic Effects / Microbiology

In vitro, fluconazole displays antifungal activity against clinically common Candida species (including *C. albicans, C. parapsilosis, C. tropicalis*). *C. glabrata* shows reduced susceptibility to fluconazole while *C. krusei* and *C. auris* are resistant to fluconazole.
Fluconazole also exhibits *in vitro* activity against *Cryptococcus neoformans* and *Cryptococcus gattii* as well as the endemic moulds *Blastomyces dermatiditis*, *Coccidioides immitis*, *Histoplasma capsulatum* and *Paracoccidioides brasiliensis*.

5.2 Pharmacokinetic Properties

Pharmacokinetics of topical fluconazole 0.2% upon single and multiple drop applications have been studied in one of the trial involving 49 patients.
After single and loading dose applications peak aqueous levels were achieved at 15 min (3.35 +/- 0.64 and 7.13 +/- 0.79 mcg/ml, respectively). Both had a steady decrease in concentration at 30, 45 and 60

min down to 4.06 +/- 0.37 mcg/ml with loading dose and undetectable levels with single dose application. Comparing the concentrations with the minimum inhibitory concentrations (MIC) of yeasts determined by the National Committee for Clinical Laboratory Standards showed that concentrations achieved with single dose applications were higher than MICs of *Candida albicans* and *Candida parapsilosis* and concentrations achieved after loading dose applications were higher than MICs of *C. parapsilosis, C. albicans* and *Candida tropicalis*. Topical fluconazole 0.2% penetrates into the aqueous humor in concentrations that satisfy MICs of most of the Candida strains.

5.3 Preclinical Safety Data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the human exposure indicating little relevance to clinical use.

Carcinogenesis: Fluconazole showed no evidence of carcinogenic potential in mice and rats treated orally for 24 months at doses of 2.5, 5, or 10 mg/kg/day (approximately 2-7 times the recommended human dose). Male rats treated with 5 and 10 mg/kg/day had an increased incidence of hepatocellular adenomas.

Mutagenesis: Fluconazole, with or without metabolic activation, was negative in tests for mutagenicity in 4 strains of *Salmonella typhimurium*, and in the mouse lymphoma L5178Y system. Cytogenetic studies *in vivo* (murine bone marrow cells, following oral administration of fluconazole) and *in vitro* (human lymphocytes exposed to fluconazole at 1000 μg/ml) showed no evidence of chromosomal mutations.

Reproductive Toxicity: Fluconazole did not affect the fertility of male or female rats treated orally with daily doses of 5, 10, or 20 mg/kg or with parenteral doses of 5, 25, or 75 mg/kg.

There were no foetal effects at 5 or 10 mg/kg; increases in foetal anatomical variants (supernumerary ribs, renal pelvis dilation) and delays in ossification were observed at 25 and 50 mg/kg and higher doses. At doses ranging from 80 mg/kg to 320 mg/kg embryolethality in rats was increased and foetal abnormalities included wavy ribs, cleft palate, and abnormal cranio-facial ossification. The onset of parturition was slightly delayed at 20 mg/kg orally and dystocia and prolongation of parturition were observed in a few dams at 20 mg/kg and 40 mg/kg intravenously. The disturbances in parturition were reflected by a slight increase in the number of still-born pups and decrease of neonatal survival at these dose levels. These effects on parturition are consistent with the species specific oestrogen-lowering property produced by high doses of fluconazole. Such a hormone change has not been observed in women treated with fluconazole.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Disodium hydrogen Phosphate Dodecahydrate (Sodium Phosphate), Sodium Dihydrogen phosphate dehydrate (Sodium Acid Phosphate), Disodium Edetate, Sodium Chloride, Benzalkonium Chloride, Water for Injection.

6.2 Incompatibilities

Not available.

6.3 Shelf-life

24 months

6.4 Special Precautions for Storage

Store at a temperature not exceeding 25^0C. Protect from light.

6.5 Nature and Contents of Container

5ml solution filled in 5ml labelled LDPE vial with spike HIPS cap packed in a carton.

6.6 Special Precautions for Disposal and Other Handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Registered Office:

Name: FDC Limited

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8. MARKETING AUTHORISATION NUMBER(S)

Certificate No; 07091/08056/REN/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Feb 4, 2022

10. DATE OF REVISION OF THE TEXT

August 2023.