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

CROUSHO GEL

1. Generic Name

Ketoconazole Gel 2 %

2. Qualitative and quantitative composition

Ketoconazole I.P…….2% w/w

In Gel Base……...q.s

Colour : Carmoisine

The excipients used are Disodium EDTA, Citric Acid Monohydrate, Phenoxyethanol, Euxyl PE 9010, Aristoflex AVC, Neelicol Carmoisine, Polysorbate-20, and Propylene Glycol.

3. Dosage form and strength

Dosage form: Gel

Strength: 2% w/w

4. Clinical particulars

4.1 Therapeutic indication

Treatment of indications involving the yeast Pityrosporum or its Mycelial from M. furfur, such as Pityriasis Capitis (dandruff), Seborrhoeic Dermatitis and Pityriasis Versicolor.

4.2 Posology and method of administration

Apply two fingertip units of Crousho Gel and gently massage it over the scalp or the affected area of the skin. Crousho Gel should be left on the scalp or affected area for at least 1 hour.

Method of administration

Instructions for use for the patient

1) Before applying Crousho Gel, Keep the scalp clean and dry. Take two fingertip units of Crousho Gel.

2) Using your fingertips, gently massage Crousho Gel on the scalp or the affected area of the skin till the Gel disappears and leave it on the scalp for at least 30 minutes.

3) Crousho Gel is specially designed for leave on Follow the procedure alternative days Application and is suitable to be left on scalp till your next wash.

4.3 Contraindications

Known hypersensitivity to Ketoconazole or the excipients of this formulation.

4.4 Special warnings and precautions for use

Use of Crousho Gel should be discontinued if any reaction suggesting sensitivity or irritation occurs.

***General*:** Crousho Gel may be irritating to mucous membranes of the eyes and hence contact with eyes or mouth should be avoided. Do not use the Gel if skin is broken or injured.

Pregnancy: Teratogenic effects: Pregnancy category C.

Ketoconazole should be used during pregnancy only if the potential benefit justifies the risk.

Nursing Mothers: It is not recommended for routine use in lactating mothers and should be used with caution when the benefit far outweighs the risks.

Pediatric use: Safety and efficacy in children has not been established.

4.5 Drugs interactions

Formal drug interaction studies with ketoconazole have not been performed. Coadministration of oral ketoconazole with CYP3A4 metabolized HMG-CoA reductase inhibitors such as simvastatin, lovastatin and atorvastatin, may increase the risk of skeletal muscle toxicity, including rhabdomyolysis. These effects have not been observed with topically administered ketoconazole.

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

Pregnancy

Pregnancy Category C:

There are no adequate and well controlled trials in pregnant women. Crousho Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Reproductive toxicity studies have not been performed with Crousho Gel. Ketoconazole was tested for its effects on offspring in the rat at oral doses of 10, 20, 40, 80, and 160 mg/kg. Ketoconazole was teratogenic (syndactylia and oligodactylia) at 80 mg/kg/day and embryotoxic at 160 mg/kg/day (76 and 152 times the human dose, respectively). However, these effects may be related to maternal toxicity, which was also seen at these dose levels.

Oral doses of 10, 20, 40, 80, and 160 mg/kg were studied in pre- and postnatal development studies in rats. Doses of 40 mg/kg (38 times the human dose) and above were associated with maternal toxicity, an increase in the length of gestation, and an increase in the number of stillborn fetuses. These doses of ketoconazole were also toxic to the offspring, resulting in a decrease in fetal/pup weights and viability.

Lactation

It is not known whether Crousho Gel is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Crousho Gel is administered to a nursing woman.

If used during lactation and Crousho Gel is applied to the chest, care should be taken to avoid accidental ingestion by the infant.

Pediatric Use

Safety and effectiveness in pediatric subjects below the age of 12 have not been established.

Geriatric Use

Of the 933 subjects in the three safety and efficacy trials, 193 (20.7%) were 65 and older, while 61 (6.5%) were 75 and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects but greater sensitivity of some older individuals cannot be ruled out.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Topical treatment with Ketoconazole Gel is generally well tolerated.

As with other topicals, a local burning sensation, itching, irritation and oily/dry hair, may occur, but are rare, during the period of use of Ketoconazole Gel 2%.

In rare instances, mainly in patients with chemically damaged hair or grey hair, a discoloration of the hair has been observed. Increase in normal hair loss may occur in <1% patients.

In all such circumstances discontinuation of treatment with Ketoconazole is strongly recommended. A gentle skin/scalp cleanser along with appropriate treatment measures is recommended.

Reporting of side effects

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

4.9 Overdose

CROUSHO GEL is intended for topical use only.

There has been no experience of overdose with CROUSHO GEL. No incidents of accidental ingestion have been reported. A health care provider or poison control center should be

contacted in the event of accidental ingestion.

5. Pharmacological properties

5.1 Mechanism of Action

Not applicable

5.2 Pharmacodynamic properties

Pharmacodynamic effect not identified.

5.3 Pharmacokinetic properties

In a pharmacokinetic absorption trial, eighteen subjects, both males and females, with severe seborrheic dermatitis (range 1-14% of body surface area) applied CROUSHO GEL once daily for 2 weeks. The median total amount of gel applied was 4.6 g (range 1.65–46.3 g). Daily doses ranged from 0.05 to 3.47 g. Mean (± standard deviation [SD]) peak plasma levels were 1.35 (± 3.18) ng/mL on Day 7 (range from <0.1 ng/mL, to 13.9ng/mL), and 0.80 (± 1.22) ng/mL on Day 14 (range from <0.1 ng/mL to 5.4 ng/mL). Median Tmax was 8 hours on Day 7 and 7 hours on Day 14. Mean (± SD) AUC0-24 values were 20.8 (± 44.7) ngwh/mL and 15.6 (± 26.4) ngwh/mL on Day 7 and 14, respectively.

The plasma levels from an oral dose of 200 mg ketoconazole taken with a meal are approximately 250 times higher than the resulting plasma levels of ketoconazole following topical application of CROUSHO GEL.

6. Nonclinical properties

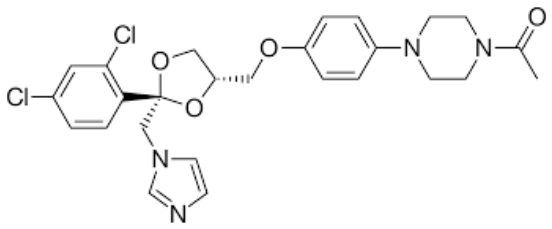
6.1 Animal Toxicology or Pharmacology

Long-term studies to assess the carcinogenic potential of Ketoconazole have not been conducted. A long-term feeding study in Swiss Albino mice and in Wistar rats showed no evidence of oncogenic activity. Ketoconazole gel at a dosage up to 5 mg/kg/dose is not photocarcinogenic when topically applied to hairless mice five days per week for a period of 40 weeks. Ketoconazole produced no evidence of mutagenicity in the dominant lethal mutation test in male and female mice at single oral doses up to 80 mg/kg. When tested in the Ames assay, ketoconazole was found to be non-mutagenic to *Salmonella typhimurium* in the presence and absence of metabolic activation. Ketoconazole, in combination with another drug, gave equivocal results in the mouse micronucleus test. At oral doses of 75 to 80 mg/kg/day (71 to 76 times the human dose) ketoconazole impaired the reproductive performance in female (decreased pregnancy and implantation rates) and male (increased abnormal sperm and decreased sperm motility) rats.

7. Description

<u>Ketoconazole</u>:

Ketoconazole is *cis*-1-acetyl-4-[[(2*RS*,4*RS*)-2-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxyl]phenylpiperazine. The empirical formula is $C_{26}H_{28}Cl_2N_4O_4$, and its molecular weight is 531.4g/mol. The chemical structural formula is:



Crousho Gel:

Ketoconazole Gel is Light pinkish to rose coloured translucent uniform Gel. The excipients used are Disodium EDTA, Citric Acid Monohydrate, Phenoxyethanol, Euxyl PE 9010, Aristoflex AVC, Neelicol Carmoisine, Polysorbate-20, and Propylene Glycol.

8. Pharmaceutical particulars

8.1 Incompatibilities

None known.

8.2 Shelf-life

Do not use later than date of expiry

8.3 Packaging information

CROUSHO GEL is available in pack of 30 gm.

8.4 Storage and handing instructions

Do not store above 30^0C. Store protected from light. Do not freeze.

Keep out of reach of children.

Avoid contact with eyes.

9. Patient Counselling Information

CROUSHO GEL

(Ketoconazole Gel 2 %)

Read all of this leaflet carefully before you start taking this medicine because it contains Important information for you.

· 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 CROUSHO GEL And what they are used for

9.2. What you need to know before you take CROUSHO GEL.

9.3. How to take CROUSHO GEL.

9.4. Possible side effects

9.5. How to store CROUSHO GEL.

9.6. Contents of the pack and other information

9.1 What CROUSHO GEL is and what it is used for

CROUSHO GEL is Contain Ketoconazole Gel 2 %. CROUSHO GEL is used for the treatment of indications involving the yeast Pityrosporum or its Mycelial from M. furfur, such as Pityriasis Capitis (dandruff), Seborrhoeic Dermatitis and Pityriasis Versicolor.

9.2 What you need to know before you take CROUSHO GEL.

Do not take CROUSHO GEL if:

If you are allergic to anything in Ketoconazole

Special warnings and precautions for use

Use of Crousho Gel should be discontinued if any reaction suggesting sensitivity or irritation occurs.

***General*:** Crousho Gel may be irritating to mucous membranes of the eyes and hence contact with eyes or mouth should be avoided. Do not use the Gel if skin is broken or injured.

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Nursing Mothers: It is not recommended for routine use in lactating mothers and should be used with caution when the benefit far outweighs the risks.

Pediatric use: Safety and efficacy in children has not been established.

9.3 How to take Crousho Gel.

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

- Before applying Crousho Gel, Keep the scalp clean and dry. Take two fingertip units of Crousho Gel.
- Using your fingertips, gently massage Crousho Gel on the scalp or the affected area of the skin till the Gel disappears and leave it on the scalp for at least 30 minutes.
- Crousho Gel is specially designed for leave on Follow the procedure alternative days application and is suitable to be left on scalp till your next wash.

9.4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Topical treatment with Ketoconazole Gel is generally well tolerated.

As with other topicals, a local burning sensation, itching, irritation and oily/dry hair, may occur, but are rare, during the period of use of Ketoconazole Gel 2%.

In rare instances, mainly in patients with chemically damaged hair or grey hair, a discoloration of the hair has been observed. Increase in normal hair loss may occur in <1% patients.

In all such circumstances discontinuation of treatment with Ketoconazole is strongly recommended. A gentle skin/scalp cleanser along with appropriate treatment measures is recommended.

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https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting

9.5 How to store Crousho Gel.

Do not store above 30^0C. Store protected from light. Do not freeze.

9.6 Content of the pack and other information

CROUSHO GEL contain active substance Ketoconazole.

The excipients used are Disodium EDTA, Citric Acid Monohydrate, Phenoxyethanol, Euxyl PE 9010, Aristoflex AVC, Neelicol Carmoisine, Polysorbate-20, and Propylene Glycol.

CROUSHO GEL is available in pack of 30 gm.

10. Details of manufacturer

SunBeam Lifesciences Private Limited,

R. S. No. 23/4, Mangalam Road,

Vadmangalam, Villianur Commune,

Puducherry – 605 102, India.

11. Details of permission or licence number with date

Mfg. Licence. No.: 17 13 4264 issued on: 14.09.2022

12. Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/Crousho Gel 30 gm/Jun-23/01/PI