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

SERIVA

1. Generic Name

Sertaconazole Nitrate Cream I.P. 2% w/w

2. Qualitative and quantitative composition

Sertaconazole Nitrate I.P. .....… 2.0 % w/w
Cream base ……..... q.s.
Preservative : Benzyl Alcohol I.P. ..…1.0 % w/w

The excipients used are Stearyl Alcohol, Cetyl Alcohol, Myristyl Alcohol, Speziol C14, Glyceryl Monostearate, Sorbitan Monostearate, Polysorbate 60, Octyl Dodecanol, Light Liquid Paraffin, Benzyl Alcohol.

3. Dosage form and strength

Dosage form: Cream

Strength: 2% w/w

4. Clinical particulars

4.1 Therapeutic indication

Sertaconazole nitrate cream, 2%, is indicated for the topical treatment of superficial mycosis like dermatophytosis

4.2 Posology and method of administration

In the treatment of superficial fungal infections of skin Sertaconazole nitrate cream, 2%, should be applied twice daily for 2 weeks.
In the treatment of interdigital tenia pedis, Sertaconazole nitrate cream, 2%, should be applied twice daily for 4 weeks.

DIRECTION FOR USE:
Sufficient Sertaconazole nitrate cream, 2%, should be applied to cover both the affected areas and the immediately surrounding healthy skin. (for topical use only, not for oral, ophthalmic or intravaginal use.)

4.3 Contraindications

Sertaconazole nitrate cream, 2%, is contraindicated in patients who have a known or suspected sensitivity to sertaconazole nitrate or any of its components or to other imidazoles.

4.4 Special warnings and precautions for use

Warnings
Sertaconazole nitrate cream, 2%, is not indicated for ophthalmic, oral or intravaginal use.

Precautions
Sertaconazole nitrate cream, 2%, is for use on the skin only. If irritation or sensitivity develops with the use of SERIVA, 2%, treatment should be discontinued and appropriate therapy instituted. Physicians should exercise caution when prescribing SERIVA, 2%, to patients known to be sensitive to imidazole antifungals, since cross-reactivity may occur.

4.5 Drugs interactions

Potential interactions between Sertaconazole nitrate Cream, 2%, and other drugs or laboratory tests have not been systematically evaluated.

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

Pregnancy: Teratogenic Effects
Pregnancy Category C
Oral reproduction studies in rats and rabbits did not produce any evidence of maternal toxicity, embryotoxicity or teratogenicity of sertaconazole nitrate at an oral dose of 160 mg/kg/day (40 times (rats) and 80 times (rabbits) the maximum recommended human dose on a body surface area comparison). In an oral peripostnatal study in rats, a reduction in live birth indices and an increase in the number of still-born pups was seen at 80 and 160 mg/kg/day. There are no adequate and well-controlled studies that have been conducted on topically applied Sertaconazole nitrate cream, 2%, in pregnant women. Because animal reproduction studies are not always predictive of human response, Sertaconazole nitrate cream, 2%, should be used during pregnancy only if clearly needed.

Breastfeeding
It is not known if sertaconazole is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when prescribing to a nursing women.

Pediatric Use
The efficacy and safety of Sertaconazole nitrate cream, 2%, have not been established in pediatric patients below the age of 12 years.

Geriatric Use
Clinical studies of Sertaconazole nitrate cream, 2%, did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive or use machines have been performed.
Sertaconazole has no known side effects that are likely to affect the ability to drive and use or operate machines.

4.8 Undesirable effects

In clinical trials, cutaneous adverse events occurred in 7 of 297 (2%) patients (2 of them severe) receiving Sertaconazole nitrate cream, 2% and in 7 of 291 (2%) patients (2 of them severe) receiving vehicle. These reported cutaneous adverse events included contact dermatitis, dry

skin, burning skin, application site reaction and skin tenderness. In a dermal sensitization study, 8 of 202 evaluable patients tested with sertaconazole nitrate cream 2%, and 4 of 202 evaluable patients tested with vehicle, exhibited a slight erythematous reaction in the challenge phase. There was no evidence of cumulative irritation or contact sensitization in a repeated insult patch test involving 202 healthy volunteers. In post-marketing surveillance for sertaconazole nitrate cream, 2%, the following cutaneous adverse events were reported: contact dermatitis, erythema, pruritus, vesiculation, desquamation, and hyperpigmentation.

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

4.9 Overdose

Overdosage with Sertaconazole nitrate cream, 2%, has not been reported to date. Sertaconazole nitrate cream, 2%, is intended for topical dermatologic use only. It is not for oral, ophthalmic, or intravaginal use.

5. Pharmacological properties

5.1 Mechanism of Action

The mechanism of antifungal action of sertaconazole nitrate is similar to that of other imidazoles, in that it inhibits fungal biosynthesis of ergosterol, resulting in disorganization of the fungal plasma membrane and altered permeability.

5.2 Pharmacodynamic properties

The antifungal action of sertaconazole nitrate is similar to that of other imidazoles, in that it inhibits fungal biosynthesis of ergosterol, resulting in disorganization of the fungal plasma membrane and altered permeability. Like other imidazoles, sertaconazole has demonstrated a broad spectrum of antifungal activity both in vitro and in experimental in vivo models, which includes dermatophytes (eg, Epidermophyton, Microsporum, Trichophyton), opportunistic filamentous fungi (eg, Aspergillus, Alternaria, Scopulariopsis, Fusarium), and pathogenic yeasts such as Malassezia furfur, Candida albicans, Candida tropicalis, Torulopsis, and Trichosporon. Activity has also been observed against Trichomonas and some gram-positive organisms (staphylococci, streptococci). One preclinical investigation has suggested the greater activity of sertaconazole compared to miconazole (equivalent doses) against dermatophytes and candida. In vitro testing of antifungal agents showed that sertaconazole (MIC 1.36 mg/L) was more active against Candida yeast isolates than bifonazole (MIC 7.2 mg/L) and terbinafine (MIC 13.77 mg/L). Other experimental data suggest the drug may also be more active than other imidazoles.

5.3 Pharmacokinetic properties

Sertaconazole achieves high epidermal concentrations following cutaneous application. Cutaneous absorption was 64% of the dose at 12 hours and 72% at 24 hours following topical application of a 2% cream. Systemic absorption is minimal to undetectable. The drug was

undetectable in serum or urine samples from healthy subjects for up to 24 hours with 16 g of sertaconazole 2% cream. In a multiple dose pharmacokinetic study that included 5 male patients with interdigital tinea pedis (range of diseased area, 42-140 cm^2; mean, 93 cm^2), Sertaconazole nitrate cream, 2%, was topically applied every 12 hours for a total of 13 doses to the diseased skin (0.5 grams sertaconazole nitrate per 100 cm^2). Sertaconazole concentrations in plasma measured by serial blood sampling for 72 hours after the thirteenth dose were below the limit of quantitation (2.5 ng/mL) of the analytical method used.

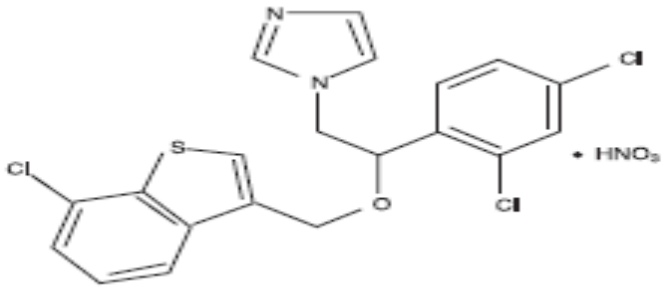
6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Long-term studies to evaluate the carcinogenic potential of sertaconazole nitrate have not been conducted. No clastogenic potential was observed in a mouse micronucleus test. Sertaconazole nitrate was considered negative for sister chromatid exchange (SCE) in the in vivo mouse bone marrow SCE assay. There was no evidence that sertaconazole nitrate induced unscheduled DNA synthesis in rat primary hepatocyte cultures. Sertaconazole nitrate exhibited no toxicity or adverse effects on reproductive performance or fertility of male or female rats given up to 60 mg/kg/day orally by gastric intubation (16 times the maximum recommended human dose based on a body surface area comparison).

7. Description

Sertaconazole Nitrate Cream 2%, contains the imidazole antifungal, sertaconazole nitrate. Sertaconazole nitrate contains one asymmetric carbon atom and exists as a racemic mixture of equal amounts of R and S enantiomers. Sertaconazole nitrate is designated chemically as (±)-1-[2,4-dichloro-ß-[(7-chlorobenzo[b]thien-3-yl)methoxy]phenethyl] imidazole nitrate. It has a molecular weight of 500.8. The molecular formula is $C_{20}H_{15}Cl_3N_2OS \cdot HNO_3$, and the structural formula is:



Sertaconazole nitrate is a white or almost white powder. It is practically insoluble in water, soluble in methanol, sparingly soluble in alcohol and in methylene chloride.

Sertaconazole Nitrate Cream is a white semisolid cream. The excipients used are Stearyl Alcohol, Cetyl Alcohol, Myristyl Alcohol, Speziol C14, Glyceryl Monostearate, Sorbitan Monostearate, Polysorbate 60, Octyl Dodecanol, Light Liquid Paraffin, Benzyl Alcohol.

8. Pharmaceutical particulars

8.1 Incompatibilities

None stated

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

SERIVA is available in 10 g & 30g tube.

8.4 Storage and handing instructions

Store below 25^{o} C. Do not freeze.

Keep out of reach of children.

Replace the cap tightly after use.

9. Patient counselling information

SERIVA

Sertaconazole Nitrate Cream I.P. 2% w/w

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

• Keep this leaflet. You may need to read it again.

• Dosage will be as directed by the Physician

• Keep all medicines out of reach of children

• Direction for use: Sufficient Sertaconazole nitrate cream, 2%, should be applied to cover both the affected areas and the immediately surrounding healthy skin.

• 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 SERIVA is and what it is used for

SERIVA CREAM 2%, contains the imidazole antifungal, sertaconazole nitrate.

SERIVA CREAM, 2%, is indicated for the topical treatment of superficial mycosis like dermatophytosis.

9.2 What you need to know before you apply SERIVA

Do not apply SERIVA

- If you are allergic to sertaconazole nitrate or any of its components or to other imidazoles.

Warnings and precautions

- SERIVA cream, 2%, is for use on the skin only and not indicated for ophthalmic, oral or intravaginal use. If irritation or sensitivity develops with the use of SERIVA cream, treatment should be discontinued and appropriate therapy instituted.

Pediatric Use

- The efficacy and safety of SERIVA cream, 2%, have not been established in pediatric patients below the age of 12 years.

Other medicines and SERIVA

- Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

Pregnancy and breast-feeding

- If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before applying this medicine.
- You should not stop your treatment without discussing this with your doctor.

Driving and using machines

- Sertaconazole has no known side effects that are likely to affect the ability to drive and use or operate machines.

9.3 How to apply SERIVA

1. Use SERIVA, 2%, as directed by the physician. The hands should be washed after applying the medication to the affected area(s).

Avoid contact with the eyes, nose, mouth and other mucous membranes. SERIVA, 2%,is for external use only.

2. Dry the affected area(s) thoroughly before application, if you wish to use SERIVA, 2%, after bathing.

3. Use the medication for the full treatment time recommended by the physician, even though symptoms may have improved.

Notify the physician if there is no improvement after the end of the prescribed treatment period, or sooner, if the condition worsens.

4. Inform the physician if the area of application shows signs of increased irritation, redness, itching, burning, blistering, swelling or oozing.

5. Avoid the use of occlusive dressings unless otherwise directed by the physician.

6. Do not use this medication for any disorder other than that for which it was prescribed.

If you stop applying SERIVA

Should your doctor decide to stop your SERIVA CREAM treatment, he/she will instruct you about the gradual withdrawal of SERIVA CREAM.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

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

Tell your doctor immediately or contact the casualty department at your nearest hospital, if you get any of the following serious side effects:

- Area of application shows signs of increased irritation, redness, itching, burning, blistering, swelling or oozing.
- contact dermatitis, erythema, pruritus, vesiculation, desquamation, and hyperpigmentation

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. 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: http://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 SERIVA

Store below 25ºC. Do not freeze.
Keep out of reach of children.

9.6 Contents of the pack and other information

What SERIVA contains
• The active substance is Sertaconazole Nitrate I.P. 2.0 % w/w
• The excipients used are Stearyl Alcohol, Cetyl Alcohol, Myristyl Alcohol, Speziol C14, Glyceryl Monostearate, Sorbitan Monostearate, Polysorbate 60, Octyl Dodecanol, Light Liquid Paraffin, Benzyl Alcohol.

10. Details of manufacturer

Manufactured in India by:
Glenmark Pharmaceuticals Ltd.
Glenmark House, HDO-Corp Bldg, Wing-A, B.D.Sawant Marg,
Chakala, Andheri (East) – Mumbai – 400099.
At: Village – Saini Majra, Ropar Road, Nalagarh, Dist. Solan (H.P.) – 174101.

11. Details of permission or licence number with date

Mfg Lic No. L/06/369/MNB issued on 14.02.2017.

12. Date of revision

DEC 20

MARKETED BY
torrent PHARMA

TORRENT PHARMACEUTICALS LTD.
IN/ SERIVA CREAM 2% w/w/Dec 20/02/PI