For the use only of a Dermatologist or a Hospital or a Laboratory

SERIVA
(SERTACONAZOLE NITRATE LOTION, 2% w/v)

COMPOSITION:
Sertaconazole Nitrate BP ..... 2.0% w/v
Propylene Glycol IP Base .....q.s.

CLINICAL PHARMACOLOGY:
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. 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.

Pharmacokinetics: 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% lotion. 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% lotion. In a multiple dose pharmacokinetic study that included 5 male patients with interdigital tinea pedis (range of diseased area, 42-140 cm2; mean, 93 cm2), Sertaconazole nitrate lotion, 2%, was topically applied every 12 hours for a total of 13 doses to the diseased skin (0.5 grams sertaconazole nitrate per 100 cm2). 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.

INDICATIONS
Sertaconazole nitrate lotion, 2%, is indicated for the topical treatment of superficial fungal infections of skin including tenia pedis.

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

DIRECTION FOR USE
Sufficient Sertaconazole nitrate lotion, 2%, should be applied to cover both the affected areas and the immediately surrounding healthy skin.

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

WARNINGS
Sertaconazole nitrate lotion, 2%, is not indicated for ophthalmic, oral or intravaginal use.

PRECAUTIONS
General: Sertaconazole nitrate lotion, 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.

Information for Patients: The patient should be instructed to:
FOR TOPICAL USE ONLY, NOT FOR ORAL, OPHTHALMIC OR INTRAVAGINAL USE.

1. Use SERIVA, 2%, as directed by the physician. The hands should be washed after applying the medication to the affected area(s).
1. 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.
4. Notify the physician if there is no improvement after the end of the prescribed treatment period, or sooner, if the condition worsens.
5. Inform the physician if the area of application shows signs of increased irritation, redness, itching, burning, blistering, swelling or oozing.
6. Avoid the use of occlusive dressings unless otherwise directed by the physician.
7. Do not use this medication for any disorder other than that for which it was prescribed.

Drug/Laboratory Test Interactions: Potential interactions between Sertaconazole nitrate Lotion, 2%, and other drugs or laboratory tests have not been systematically evaluated.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY
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).

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 lotion, 2%, in pregnant women. Because animal reproduction studies are not always predictive of human response, Sertaconazole nitrate lotion, 2%, should be used during pregnancy only if clearly needed.

Nursing Mothers: 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 lotion, 2%, have not been established in pediatric patients below the age of 12 years.

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

ADVERSE EVENTS
In clinical trials, cutaneous adverse events occurred in 7 of 297 (2%) patients (2 of them severe) receiving Sertaconazole nitrate lotion, 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 lotion 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 lotion, 2%, the following cutaneous adverse events were reported: contact dermatitis, erythema, pruritus, vesiculation, desquamation, and hyperpigmentation.

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

STORAGE
Store below 25°C. Do not freeze. Keep out of reach of children.

PRESENTATION
SERIVA is available in 10 g tube.

MARKETED BY

TORRENT PHARMACEUTICALS LTD.
Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA

IN/SERIVA LOTION 2%/Mar-2018/01/PI