LUCAN-R®

Fluconazole USP

PRESENTATION

Lucan-R® 50 mg capsules are maroon colour cap and buff colour body marked RENATA on both cap and body contaning 50mg fluconazole USP.
Lucan-R® 150 mg capsules are Amethyst color cap with imprinted Renata logo and body inmprinted RENATA .
Lucan-R® 200 mg capsules are Green colour cap circular print RENATA and light green body with circular print Lucan-R 200mg.
Lucan-R® Suspension: Dry powder in glass bottle for reconstitution into 35 ml of suspension. After reconstitution, each 5ml contains Fluconazole USP 50mg.

USES:

Fluconazole a member of the triazole class of antifungal agents, is a potent and selective inhibitor of fungal enzymes necessary for the synthesis of ergosterol.

Lucan-R® is indicated for:

1. **Vaginal candidiasis (acute or recurrent) Candidal balanitis.** The treatment of partners who present with symptomatic genital candidiasis should be considered.
2. **Mucosal candidiasis.** These include oropharyngeal, oesophegeal, noninvasive bronchopulmonary infections, candiduria, mucocutaneous and chronic oral atrophic candidiasis (denture sore mouth). Normal hosts and patients with compromised immune function may be treated.
3. **Tinea pedis, tinea cruris, tinea versicolor and dermal Candidial Infections. Lucan-R®** is also indicated for nail fungal infections.
4. **Systemic candidiasis including candidaemia, disseminated candidiasis** and other forms of invasive candidal infections of the peritoneum, endocardium and pulmonary and urinary tracts. Candidal infections in patients with malignancy, in intensive care units or those receiving cytotoxic or immunosuppressive therapy, may be treated.
5. **Cryptococcosis, including cryptococcal meninigitis and infections** of other sites (e.g. pulmonary cutaneous) normal hots and patients with acquired immune deficiency syndrome (AIDS), organ transplants or other causes of immunosuppression may be treated. Lucan-R can be used as maintainance therapy to prevent relapse of cryptococcal disease in patients with AIDS.
6. For the prevention of fungal infections in immunocompromised patients considered at risk as a consequence of neutropenia following cytotoxic chemotherapy or radiotherapy, including bone marrow transplant patients.

DOSAGE AND ADMINISTRATION:

Lucan-R® is administered orally. The daily dose of fluconazole should be based on the nature and severity of the fungal infection. Most cases of vaginal candiasis respond to single dose therapy. Therapy for those types of infection requiring multipile dose treatment should be continued until clinical parameters or laboratory test indicate that active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection. Patients with AIDS and crytococcal meningits usually require maintainance therapy to prevent relapse.

Adults:

1. Candidal balanitis or vaginitis: 150mg single oral dose

2 . Mucosal Candidiasis:

Oropharyngeal candidiasis: the recommamended dose is 50 mg once daily for 7 to 14 days. Treatment should not normally exceed 14 days except in severily immunocompromised patients.

Atrophic oral candidiasis associated with dentures: the recommended dose is 50 mg once daily for 14 days, administared concurrently with local anti septic measures to the denture.

For other candidal infections of the mucosa, (except genital candidiasis see above), e.g. oesophagitis, non-invasive bronchopulmonary infections, candiduria, mucocutaneous candidiasis etc. the recommended dose is 50 mg daily, given for 14 to 30 days.

In unusually difficult cases of mucosal candidal infections the dose may be increased to 100mg daily.

3. For tinea pedis, corporis, cruris, versicolor and dermal Candidal infections: the recommended dose is 50 mg once daily. Duration of treatment is normally 2 to 4 weeks but tinea pedis may require treatment for up to 6 weeks. Duration of treatment should not exceed 6 weeks.

4. **For candidaemia, disseminated candidaemia and other invasive candidal infections :** the recommended dose is 400 mg on the first day followed by 200 mg-400 mg once daily. Depending on the clinical response the dose may be increased to 400 mg once daily. Duration of treatment is based upon the clinical response.

5. **For cryptococcal meningitis and cryptococcal infections at other sites:** the recommanded dose is 400 mg on first day follwed by 200 mg once daily. Duration of treatment for cryptoccoal infections will depend on the clinical and mycological response, but is usually at least 6 to 8 weeks for cryptococcal meningitis.

For the prevention of relapse of cryptococcal meningitis in patients with AIDS, after the patient recives a full course of primary therapy, **Lucan-R®** may be administerd indefinitely at a daily dose of 100-200 mg.

6 . **For the prevention of fungal infections in immunocompromised patients considered at a risk as a consequence of neutropenia** following cytotoxic chemotherapy of radiotherapy, the dose should be 50-400 mg daily based on the patients risk for developing fungal infection. For patients at high risk of systemic infections. e.g patients who are anticipated to have profound or prolonged neutropenia such as during bone marrow transplantation, the recommended dose is 400 mg daily. Start dosage several days before anticipated onset of neutropenia and continue for seven days after the neutrophil count rises above 100 cells per mm.

Children over four weeks of age:

Mucosal candidiasis: The recommended does of fluconazole is 3 mg/kg daily. A loading does of 6mg/kg may be used on the first day to achieve steady state leaves more repidly.

Systemic candidiasis and cryptococcal infection: The recommended dosage of fluconazole is 6-12 mg/kg daily, depending on the severity of the disease.

For the prevention of fungal infections in immunocompromised patients considered at risk as a consequence of neutropenia following cytotoxic chemotherapy or rediotherapy, the dose should be 3-12 mg/kg daily depending on the extent and duration of the induced neutropenia.

Children below four weeks of age: Neonates excrete fluconazole showly. In the first two weeks of life the same mg/kg dosing as in older children should be used but administered every 72 hours. During weeks 2-4 of line the same does should be given 48 hours.

For children with impaired renal function the daily dose should be reduced in accordance with the guidelines give for adults, dependent on the degree of renal impairment.

To facilitate accurate measurement of dose less then 10mg, fluconazole should only be administered to children In hospital using the 50 mg/5 ml suspension orally or the Intravenous Infusion, depending on the clinical condition of the child. A suitable measuring device should be used for administration of the suspension. Once reconstituted, the suspension should not be further diluted.

In serious life threatening infections 12 mg/kg daily has been given to children aged 5-13 years (Maximum 400 mg daily)

Age	Average Weight	dose/Day
1 year	9 kg	½ measuring spoonful
1-2 years	12 kg	1 measuring spoonful
2-3 years	14 kg	1 ½measuring spoonful
3-4 years	16 kg	2 measuring spoonful
4-6 years	20 kg	2 ½ measuring spoonful

Other uses:

i. Fungal urinary tract infections
ii. Disseminated candidiasis
iii. Prophylaxis for fungal infection in neutropenic cancer patients.
iv. Acute treatment of other systemic fungal infections such as coccidioidomycosis and histoplasmosis.

Use in the elderly: The normal dose should be used if there is no evidence of renal impairment. In patients with renal impairment (creatinine clearance less than 40 ml/min.) the dosage intervales or orally dosage should be adjusted as described below.

Use in renal impairment : Fluconazole is excreted predominantly in the urine as unchanged drug. No adjustments in single dose therapy are required. In multiple dose therapy of patients with renal impairment, normal dose should be given on days 1 and 2 of treatment and thereafter the dosage intervals or daily dosage should be modified in accordance with creatinine clearance as follows.

Creatinine clearance ml/min	Dosage interval/daily dose
> 40	24 hours (normal dosage regimen)
21-40	48 hours or half normal daily dose
10-20	72 hours or one-third normal daily dose
Patients receiving regular haemodialysis	One dose after every dialysis session

CONTRA -INDICATION, WARNINGS. ETC

Contra-Indications: Fluconazole should not be used in patients with known hypersensitivity to fluconazole or to related azole compounds.

Use in pregnancy: adverse fetal effects have been seen in animals only at dose levels associated with maternal toxicity. These levels are many times in excess of those recommended for therapeutic use. There has been little use during human pregnancy. Accordingly **fluconazole** should not be used in pregnancy or in women of child bearing potential unless adequate contraception is employed.

Warnings: in some patients, particularly those with serious underlying diseases such as AIDS and cancer, abnormalities of hepatic, renal, haematological and other biochemical function tests have been observed during treatment with fluconazole, but the clinical significance and relationship to treatment is uncertain.

Very rarely. patients who died with severe underlying disease and who had received multiple dose **fluconazole**, had post-mortem findings which included hapatic necrosis. These patients were receiving multiple concomitant medications, some known to be potentially hepatotoxic, and/or had underlying diseases, which could have caused the hepatic necrosis. Consequently, because a causal relationship with fluconazole cannot be excluded, the risk-benefit ratio of continued fluconazole treatment should be assessed in those patients in whom a significant rise of liver enzymes occurs.

Patients have rarely developed exfoliative cutaneous reactions, such pa Stevens Johnson Syndrome and toxic epidermal necrolysis, during treatment with fluconazole. AIDS patients are more prone to the development of severe cutaneous reactions to many drugs.

If a rash develops in a patients treated for a superfaclal fungal infection which is considered attributable to fluconazole further therapy with this agent should be discontinued. In patients with invasive/ systemic fungal infections who develop rashes, they should be monitored closely and fluconazole should be discontinued if bolbous lesions or erythema multiform develop.

Use during lactation: Fluconazole is found in human breast milk at concentrations similar to plasma. hence its use in nursing mothers is not recommended.

Driving/Use of machinery: Experience with fluconazole indicates that therapy a unlikely to impair a patient's ability to drive or use machinery.

DRUG INTERACTION:

In an interaction study, fluconazole increased the prothombin time after warfarin administration in healthy males. Though the magnitude of change was small (12%) careful monitoring of prothombin time in patients receiving coumarin type anticoagulants is recommended.

Fluconazole has been shown to prolong the serum half-life of concomitantly administered oral sulphonyl ureas (chlorpropamide, gilbenclamide, glipizide and tolbutamide) in healthy volunteers. Fluconazole and oral sulphonylureas may be co-administered to diabetic patients, but the possibility of a hypoglycemic episode should be borne in mind.

In a kinetic interaction study, co-administration of multiple-dose hydrochlorothiazide to healthy volunteers receiving fluconazole increased plasma concentrations of fluconazole by 40%. An effect of this magnitude should not necessitate a change in the fluconazole dose regimen in subjects recieving concomitant diureties, although the prescribers should bear it in mind.

Concomitant administration of fluconazole and phenytoin may increase the level of phenytoin to a clinically significant degree. Administration of fluconazole and rifampicin has resulted in a 25% decrease in the AUC and 20% shorter half-life of fluconazole. Patients recieving concomitant rifampicin, an increase in the fluconazole dose should be considered.

Two kinetic studies with combined oral contraceptive have been performed using muitiple dose of fluconazole. There were no relevant effects on either hormone level in the 50 mg fluconazole study, while at 200 mg daily the AUCs of ethinyl estradiol and levonorgestrel were increased 40% and 4% respectively. Thus multipule dose use of fluconazole at these dose is unlikely to have an effect on the efficacy of the combined oral contraceptives.

Lucan-R 50 mg daily does not affect endogenous steroid levels in females. 200-400 mg daily has no clinically singnificant effect on endogenous steroid levels or on ACTH stimulated response in healthy male volunteers.

A kinetic study in renal transplant patients found fluconazole 200 mg daily to slowly increase cyclosporin concentrations. However, in another multiple dose study with 100 mg daily, fluconazole did not affect cyclosporin levels in patients with bone marrow transplants. Cyclosporin plasma concentration monitoring in patients receiving fluconazole is recommended.

Interaction studies have shown that when oral fluconazole is co-administered with food. cemetidine, antacids or following total body irradiation for bone marrow transplantation, no clinically significant impairment of fluconazole absorption occurs.

In placebo-controlled interaction study, the administration of fluconazole 200mg for 14 days resulted in an 18% decrease, in the mean plasma clearance of theophyline, Patients who are receiving dose of theophyline or who are otherwise at increased risk for theophyline toxicity should be observed for sign of toxicity while receiving fluconazole, and the therapy modified appropriately if sign of toxicity while receiving fluconazole, and the therapy modified appropriately if sign of toxicity develop.

Physicians should be aware that drug-drug interaction studies with other medications have not been conducted, but that such interactions may occur.

SIDE-EFFECTS:

Fluconazole is generally well tolerated. The commonest side-effects associated Fluconazole are symptoms associated with the gastrointestinal tract; these include nausea, abdominal discomfort, diarrhoea and flatulence. Other adverse events such as rash are rarely encountered (Incidence less than 1%). In rare cases, as with other azoles, anaphylaxis has been reported.

See "warnings" for information on hepatic necrosis and cutaneous reaction in AIDS patients.

OVERDOSAGE:

In the event of overdosage, supportive measures and symptomatic treatment with gastric lavage if necessary may be adequate.

As fluconazole is excreted largely in the urine, forced volume diuresis would probably increase the elimination rate. A three hour session of haemodialysis decreases plasma levels by approximately 50%

PHARMACEUTICAL PRECAUTIONS:

Store in a cool and dry place. Away from light and children.

SUPPLY:

Lucan-R® 50 mg Capsule : Each Box contains 5X8's Capsules in blister pack.
Lucan-R® 150 mg Capsule Each Box contains 2x6's Capsules in blister pack.
Lucan-R® 200 mg Capsule Each Box contains 2x6's Capsules in blister pack.
Lucan-R® Suspension: Each Box contains dry powder for reconstitute 35 ml suspension In glass bottle

® Trade Mark

Manufactured by:
RENATA LIMITED
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