| Leaflet | | | |
|---|---|---|---|
| Item Code: | PKG1049 | Pharmacode No.: | NA |
| Brand Name: | Fluconazole 200 mg Strides | Cartonator Machine: | NA |
| Generic Name: | Fluconazole 200 mg Capsules | Unfolded Size: | 460 x 140 mm (Width x Height) |
| Country Name: | South Africa | Number of Folds: | Vertical - 2 Zig-zag folds + 2 Folds<br>Horizontal - 1 Fold |
| Customer Name: | Trinity Pharma | | |
| Paper/GSM: | 60 GSM Maplitho Paper | Folded Size: | 38.33 x 70 mm (Approx.) (Width x Height) |
| Grain Direction: | NA | Previous Item Code: | NA |
| | | Reason for revision: | New Development |
| Colour/Pantone: | Black | | |

Signs for approval

| Packaging Development | | Production | Quality Control (QC) | Quality Assurance (QA) | | Head Quality | Customer Approval |
|---|---|---|---|---|---|---|---|
| | | | | | | | |

Claudia Law - Approved - 17.07.2023

Anisa Suliman - Approved - 17.07.2023

**PACKAGE INSERT**

**SCHEDULING STATUS:**

S4

**PROPRIETARY NAME (AND DOSAGE FORM):**
**FLUCONAZOLE 50 STRIDES** (Capsule)
**FLUCONAZOLE 200 STRIDES** (Capsule)

**COMPOSITION:**
The chemical name of FLUCONAZOLE STRIDES (fluconazole), a bis-triazole, is 2-(2,4-difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)-2-propanol. Fluconazole has a molecular weight of 306.3. It is a white to off-white crystalline powder which is sparingly soluble in water and saline.

**FLUCONAZOLE 50 STRIDES:** Each capsule contains 50 mg fluconazole.
**FLUCONAZOLE 200 STRIDES:** Each capsule contains 200 mg fluconazole.

**PHARMACOLOGICAL CLASSIFICATION:**
A. 20.2.2 Antimicrobial (chemotherapeutic) agents. Fungicides.

**PHARMACOLOGICAL ACTION:**
Fluconazole is a triazole antifungal agent. Fluconazole exerts its antifungal effect by inhibition of sterol 14-alpha-demethylase impairing the biosynthesis of ergosterol, the principal sterol in the fungal cell membrane. This damages the cell membrane, producing alterations in membrane function and permeability.

**Pharmacokinetics:**
Fluconazole is well absorbed after oral administration. Oral bioavailability is more than 90 %. Oral bioavailability is not altered by foods or gastric acidity. The time to peak plasma concentrations is 1 to 2 hours. Protein binding is low (12 %). The elimination half-life in adults is approximately 30 hours and is increased in patients with impaired renal function. Fluconazole is primarily excreted by the kidneys. Approximately 80 % of the dose is excreted unchanged in the urine. Fluconazole clearance is proportional to creatinine clearance. However, accumulation is significant over 15 days and concentrations may rise 2 to 3 fold. A small amount of fluconazole undergoes hepatic metabolism. Fluconazole is cleared from the body faster in children than in adults. The half-life in children is 23 hours. During the first 2 weeks of life the half-life is approximately 74 hours on day one and 47 hours on day 13.

**INDICATIONS:**
Anti-infective therapy should be adjusted once the results of the cultures and other laboratory studies become available.
FLUCONAZOLE STRIDES is indicated for the treatment of the following conditions in adults:
- Cryptococcal meningitis in mentally alert patients without localising neurological signs and as a follow-up therapy after amphotericin B therapy.
- Maintenance therapy to prevent relapse of cryptococcal disease in patients with acquired immunodeficiency syndrome (AIDS).
- Oropharyngeal and oesophageal candidiasis.
- Systemic candidiasis.
- Prophylaxis of fungal infections in patients receiving cytotoxic chemotherapy and/or radiation therapy.
- Vaginal candidiasis - Acute or recurrent infections and as prophylaxis to reduce the incidence of recurrent infections.
- Candidial balanitis.
- Dermatomycosis, including tinea corporis, tinea cruris, tinea pedis, tinea unguium (onychomycosis) and dermal *candida* infections.

FLUCONAZOLE STRIDES is indicated for the treatment of the following conditions in children:
- Cryptococcal meningitis in mentally alert patients without localising neurological signs and as a follow-up therapy after amphotericin B therapy.
- Maintenance therapy to prevent relapse of cryptococcal disease in patients with acquired immunodeficiency syndrome (AIDS).
- Oropharyngeal and oesophageal candidiasis.
- Systemic candidiasis.
- Prophylaxis of candidiasis in patients receiving cytotoxic chemotherapy and/or radiation therapy.

**CONTRAINDICATIONS:**
- Hypersensitivity to FLUCONAZOLE STRIDES, other azole antifungal agents or to any of the excipients.
- Co-administration of terfenadine in patients receiving multiple doses of FLUCONAZOLE STRIDES in doses of 400 mg per day or greater (see **INTERACTIONS**).
- Co-administration of cisapride (see **INTERACTIONS**).
- Pregnancy and lactation (see **PREGNANCY AND LACTATION**).
- Therapy with multiple doses of FLUCONAZOLE STRIDES is contra-indicated in patients with renal impairment.
- Concurrent use with astemizole should be avoided.

**WARNINGS:**
FLUCONAZOLE STRIDES has been associated with cases of serious hepatotoxicity, including fatalities related to dose and duration of use, primarily in patients with serious underlying medical conditions. This hepatotoxicity may be reversible when therapy is discontinued. Any patients who develop abnormal liver function tests, while taking FLUCONAZOLE STRIDES, should be carefully monitored for the development of more serious hepatic injury. Should signs and symptoms consistent with liver disease develop, that may be attributable to FLUCONAZOLE STRIDES**,** FLUCONAZOLE STRIDES should be discontinued.
Less frequently, patients have developed rashes, urticaria, pruritus, dry skin, abnormal odour, angioedema and exfoliative cutaneous reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis, during treatment with FLUCONAZOLE STRIDES. Patients with AIDS are more prone to the development of severe cutaneous reactions to numerous medicines. Should patients with systemic/invasive fungal infections develop rashes, they should be monitored closely, and if bullous lesions or erythema multiforme develop, FLUCONAZOLE STRIDES must be discontinued.

**INTERACTIONS:**
FLUCONAZOLE STRIDES may interfere with the metabolism of some medicines if given concomitantly, mainly through inhibition of the cytochrome P450 isoenzymes CYP3A4 and CYP2C9. Co-administration of FLUCONAZOLE STRIDES and medicines metabolised by cytochrome P450 can result in increased serum concentrations of the medicines metabolised by the same enzyme system.
FLUCONAZOLE STRIDES increases plasma concentrations of the following medicines when given concomitantly:
- Warfarin – Anticoagulant effects are increased, resulting in an increase in prothrombin time/INR ratio. Monitoring of the prothrombin time is required and adjustment of the warfarin dose may be necessary.
- Sulfonylurea hypoglycaemics - The plasma concentration of these agents may be increased and hypoglycaemia can result. Blood glucose concentrations should be monitored and the dose of the sulfonylurea may need to be reduced.
- Phenytoin - Decreased metabolism of phenytoin, resulting in increased plasma concentrations and possible phenytoin toxicity.
- Theophylline - Decreased clearance of theophylline which leads to increased theophylline plasma concentrations and possibly toxicity. Theophylline concentrations should be monitored.
- Zidovudine - Increased plasma concentrations of zidovudine. Patients should be monitored for zidovudine related adverse effects.
- Terfenadine - The concurrent use of terfenadine and doses of 400 mg or more of FLUCONAZOLE STRIDES is contraindicated. If co-administration of terfenadine and FLUCONAZOLE STRIDES at doses less than 400 mg is considered, essential terfenadine concentrations should be closely monitored (see **CONTRAINDICATIONS**). Astemizole has also been reported to interact with FLUCONAZOLE STRIDES and concurrent use should be avoided (see **CONTRAINDICATIONS**).
- Cisapride - The concomitant administration of FLUCONAZOLE STRIDES with cisapride is contra-indicated because of the possible increase in serum cisapride concentrations which can increase the risk of serious and life-threatening cardiac arrhythmias including torsade de pointes (see **CONTRAINDICATIONS**).
- Ciclosporin - Clinically significant rises in ciclosporin serum concentrations of two to threefold has been observed in some patients when given fluconazole. Therefore ciclosporin plasma concentrations should be monitored in all patients receiving FLUCONAZOLE STRIDES.
- Midazolam and triazolam - FLUCONAZOLE STRIDES increases the serum concentrations of midazolam and triazolam and their psychomotor effects. This effect appears to be more pronounced following oral administration of FLUCONAZOLE STRIDES than with fluconazole administered intravenously. If these medicines are to be used concurrently, a reduced dose of the benzodiazepine may be necessary and the patient should be monitored.
- Rifabutin - Increase in serum concentration of rifabutin which carries an increased risk of uveitis. Patients on this combination need to be carefully monitored.
- Tacrolimus - Tacrolimus concentrations are considerably increased by FLUCONAZOLE STRIDES. Patients on this combination need to have serum concentrations of tacrolimus monitored and dose reduction is necessary.

The following medicine increases plasma concentrations of FLUCONAZOLE STRIDES when given concomitantly:
- Hydrochlorothiazide

The following medicine decreases plasma concentrations of FLUCONAZOLE STRIDES when given concomitantly:
- Rifampicin - Increased metabolism of FLUCONAZOLE STRIDES, resulting in lower plasma concentrations of FLUCONAZOLE STRIDES.

**Other information on interactions:**
Co-administration of fluconazole and nevirapine resulted in approximately 100 % increase in nevirapine exposure as compared with historical data where nevirapine was administered alone. Because of the risk of increased exposure to nevirapine, caution should be exercised if nevirapine and FLUCONAZOLE STRIDES are given concomitantly and patients should be monitored closely.

**PREGNANCY AND LACTATION:**
The use of FLUCONAZOLE STRIDES during pregnancy has resulted in congenital malformations and should be avoided (see **CONTRAINDICATIONS**).
FLUCONAZOLE STRIDES should not be given to breastfeeding women (see **CONTRAINDICATIONS**).
FLUCONAZOLE STRIDES is distributed into the breast milk at concentrations similar to those in plasma.

**DOSAGE AND DIRECTIONS FOR USE:**
Cryptococcal meningitis:
*Adults:* Initial dose is 400 mg on the first day; followed by 200 mg to 400 mg daily depending on the clinical response. Duration of therapy is based on clinical and mycological response, but is usually 8 weeks, following amphotericin B therapy, and 10 weeks with FLUCONAZOLE STRIDES monotherapy.
*Children over 4 weeks of age:* 6 mg/kg/day to 12 mg/kg/day depending on the severity of infection.
Maintenance therapy to prevent relapse of cryptococcal meningitis in patients with AIDS:
*Adults:* 100 mg to 200 mg per day
Systemic candidiasis:
*Adults:* Initial dose is 400 mg on the first day; followed by 200 mg daily.
The dose may be increased to 400 mg daily depending on the clinical response.
*Children over 4 weeks of age:* 6 mg/kg/day to 12 mg/kg/day depending on the severity of infection.
Duration of therapy is based on clinical and mycological response.
Oropharyngeal candidiasis:
*Adults:* 50 mg to 100 mg daily for 7 to 14 days. Severely immunocompromised patients may require longer treatment periods.
To prevent relapse in AIDS patients: 150 mg of FLUCONAZOLE STRIDES may be given once a week.
*Children over 4 weeks of age:* Initial dose is 6 mg/kg on the first day; followed by 3 mg/kg once daily. Duration of treatment is at least 2 weeks to decrease the risk of relapse.
Oesophageal candidiasis:
*Adults:* Initial dose is 200 mg on the first day; followed by 100 mg to 200 mg daily. Doses up to 400 mg once a day may be used if there is no clinical response after 14 days on the lower dose. Duration of treatment is at least 3 weeks and for an additional 2 weeks after the symptoms have resolved.
*Children over 4 weeks of age:* Initial dose is 6 mg/kg on the first day; followed by 3 mg/kg once daily. Dose may be increased to 12 mg/kg/day based on the condition of the patient and the response to the medicine. Duration of treatment is for at least 3 weeks and for an additional 2 weeks after the symptoms have resolved.
Prophylaxis of fungal infections in patients who receive cytotoxic chemotherapy and/or radiation therapy:
*Adults:* 50 mg to 400 mg daily depending on the patient's risk for developing fungal infections. Treatment should be started several days before the onset of neutropenia is expected and continued for 7 days after the neutrophil count rises above 1000 cells per $mm^3$.
*Children over 4 weeks of age:* 3 to 12 mg/kg/day depending on the extent and duration of the induced neutropenia.
Vaginal candidiasis:
*Adults:* 150 mg administered as a single dose.
Recurrent vaginal candidiasis:
*Adults:* 150 mg administered as a single dose, once a month. The duration of therapy is individualized, but ranges from 4 to 12 months.
*Candida balanitis:*
*Adults:* 150 mg administered as a single dose.
Dermal infections, including tinea pedis, tinea corporis, tinea cruris, tinea unguium (onychomycosis) and dermal *candida* infections:
*Adults:* 150 mg administered as a single dose once a week.
Duration of treatment is usually 2 to 4 weeks, but tinea pedis may require up to 6 weeks of treatment. For tinea unguium treatment should continue until the infected nail grows out and is replaced with an uninfected nail. Fingernails generally require 3 to 6 months to regrow and toenails 6 to 12 months.

Safety and efficacy of FLUCONAZOLE STRIDES in children has not been established for the following indications:
Recurrent vaginal candidiasis, *candida balanitis*, dermal infections, including tinea pedis, tinea corporis, tinea cruris, tinea unguium (onychomycosis) and dermal *candida* infections.
*Elderly:* See dosage in renal failure.
Normal dosage recommendations are used in the elderly unless the patient has decreased renal function, in which case an adjustment in dosage or dosing interval is required.

**DOSAGE IN RENAL FAILURE:**
FLUCONAZOLE STRIDES should be used with caution in patients with renal function impairment. FLUCONAZOLE STRIDES is excreted through the kidneys. A dosage reduction or increase in dosing interval is recommended:
1. The normal loading dose or the initial dose should be given on the first day of treatment.
2. Subsequent doses should be adjusted according to the creatinine clearance.

If creatinine clearance is > 50 ml/min the normal dose can be given.
If creatinine clearance is < 50ml/min and patient is not receiving dialysis, 50 % of the normal dose can be given.
Patients on regular haemodialysis should receive a standard dose of FLUCONAZOLE STRIDES after each dialysis session.
The patient's creatinine clearance (Ccr) can be estimated by using the following formula:

Ccr male = $\frac{\text{Weight(kg)} \times (140 - \text{age})}{72 \times (\text{plasma creatinine (micromol/litre)}\ 88}$

Ccr female = $\frac{0,85 \times \text{Weight(kg)} \times (140 - \text{age})}{72 \times (\text{plasma creatinine (micromol/litre)}\ 88}$

The pharmacokinetics of FLUCONAZOLE STRIDES have not been studied in children with impaired renal function. Recommendations for dosage reduction in such children should parallel the recommendations for adults.

- The dose of FLUCONAZOLE STRIDES and the duration of treatment should be based on the site of infection and the individual's response to therapy.
- Treatment should be continued until clinical parameters and laboratory tests indicate that active fungal infection has subsided.
- AIDS patients with cryptococcal meningitis or recurrent oropharyngeal candidiasis require maintenance therapy to prevent relapse.
- For infants under 2 weeks of age the above children's doses should be used, but only given once every 72 hours. For those aged between 2 and 4 weeks the dose should be given every 48 hours. The maximum adult daily dose (i.e. 400 mg) should not be exceeded in children.
- Normal dosage recommendations are used in the elderly population unless the patient has decreased renal function. In which case an adjustment in dosage or dosing interval is required.

**SIDE EFFECTS AND SPECIAL PRECAUTIONS:**
Side effects:
Haematological:
- *Less frequent:* Leucopenia, neutropenia, agranulocytosis and thrombocytopenia.

Central nervous system:
- *Frequent:* Headache.
- *Less frequent:* Dizziness, vertigo, seizures, insomnia, nervousness, fatigue, rigors, malaise, hyperkinesia.

Endocrine/Metabolic:
- *Less frequent:* Hypokalaemia, hypercholesterolaemia, hypertriglyceridaemia.

Gastrointestinal:
- *Frequent:* Nausea, vomiting, abdominal pain, diarrhoea, flatulence.
- *Less frequent:* Taste perversion, dyspepsia, thirst.

Kidney/Genitourinary:
- *Less frequent:* Female sexual dysfunction, intermenstrual bleeding, menorrhagia, leukorrhoea, polyuria.

Liver:
- *Frequent:* Hepatotoxicity (including elevated serum concentrations of alkaline phosphatase, bilirubin, ALT and AST).
- *Less frequent:* Hepatic failure, hepatitis, hepatocellular necrosis, jaundice.

Musculoskeletal:
- *Less frequent:* Hypertonia.

Ocular:
- *Less frequent:* Abnormal vision.

Skin:
- *Frequent:* Rash.
- *Less frequent:* Alopecia, urticaria, dry skin, abnormal odour, exfoliative cutaneous reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis.

Other:
- *Less frequent:* Anaphylaxis (including angioedema, facial oedema, pruritus), flushing.

Special precautions:
Liver function should be monitored periodically in all patients receiving continuous treatment with FLUCONAZOLE STRIDES for more than one month or when a patient develops signs or symptoms suggestive of liver dysfunction.
FLUCONAZOLE STRIDES should be discontinued if abnormalities in enzyme values persist, worsen or if they are accompanied by symptoms of hepatotoxicity.

FLUCONAZOLE STRIDES should be used with caution in patients with underlying disease such as AIDS or malignancy. Abnormalities in haematological, hepatic and renal function have been observed.

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:**
(See **SIDE EFFECTS AND SPECIAL PRECAUTIONS**).
Symptoms of overdose: The following have been reported with an overdose of FLUCONAZOLE STRIDES: Irritability, insomnia, depressed mood, numbness of the tongue, bulging fontanel, anorexia, vomiting, abdominal pains/cramps, diarrhoea, fatigue, itching, facial rash, generalised urticaria, skin erythema, arthralgia, renal failure, elevation of alkaline phosphatase and gamma-glutamyl transpeptidases and increase in serum calcium.
Treatment of overdose:
Treatment is symptomatic and supportive. There is no specific antidote.
FLUCONAZOLE STRIDES is largely excreted in the urine. Forced diuresis may increase the elimination rate.
Elimination of FLUCONAZOLE STRIDES can be facilitated by haemodialysis. The concentration of FLUCONAZOLE STRIDES can be decreased by about 50 % by a three hour haemodialysis session.

**IDENTIFICATION:**
**FLUCONAZOLE 50 STRIDES Capsules:**
White powder filled in hard gelatin capsule of size '4' with white opaque body and sky blue opaque cap having 'FCZ 50' in linear printing on it in black colour.
**FLUCONAZOLE 200 STRIDES Capsules:**
White powder filled in hard gelatin capsules of size '0' with White body and dark blue cap.

**PRESENTATION:**
**FLUCONAZOLE 50 STRIDES Capsules:**
Carton containing transparent PVC/PVDC and aluminium foil blister pack of 14 capsules.
**FLUCONAZOLE 200 STRIDES Capsules:**
Carton containing transparent PVC/PVDC and aluminium foil blister pack of 28 or 30 capsules.

**STORAGE INSTRUCTIONS:**
Store at or below 25 °C, in a dry place.
**KEEP OUT OF THE REACH OF CHILDREN.**

**REGISTRATION NUMBERS:**
**FLUCONAZOLE 50 STRIDES:** 38/20.2.2/0101
**FLUCONAZOLE 200 STRIDES:** 38/20.2.2/0103

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:**
STRIDES PHARMA (SA) (Pty) LTD
106 16th Road,
Building 2,
Midrand,
1686,
South Africa.

**DATE OF PUBLICATION OF PACKAGE INSERT:**
August 2004

PKG1049

Front

Qualigens Pharma Pvt. Ltd. PDD-001/T05-00

Survey No. 151/2, Umbre, Khopoli-Pali Road, Taluka Khalapur, Dist. - Raigad-410 203

**VOUBILJET**

**SKEDULERINGSTATUS:**

S4

**EIENDOMSNAAM (EN DOSEERVORM):**
**FLUCONAZOLE 50 STRIDES** (Kapsule)
**FLUCONAZOLE 200 STRIDES** (Kapsule)

**SAMESTELLING:**
Die chemiese naam van FLUCONAZOLE STRIDES (flukonasool), 'n bis-triasool, is 2- (2,4-difluorofeniel) -1,3-bis (1H-1,2,4-triasool-l-yl) -2-propanol. Flukonasool het 'n molekulêre gewig van 306,3. Dit is 'n wit tot naaswit kristallyne poeier wat min oplosbaar is in water en normale soutoplossing.

**FLUCONAZOLE 50 STRIDES:** Elke kapsule bevat 50 mg flukonasool.
**FLUCONAZOLE 200 STRIDES:** Elke kapsule bevat 200 mg flukonasool.

**FARMAKOLOGIESE KLASSIFIKASIE:**
A. 20.2.2 Antimikrobiese (chemoterapeutiese) middels. Fungisiede.

**FARMAKOLOGIESE WERKING:**
Flukonasool is 'n triasool antifungale middel. Flukonasool oefen sy antifungiese effek uit deur inhibisie van sterol 14-alfa-demetielase wat die biosintese van ergosterol, die hoofsterol in die fungusmembraan, ondertruk. Dit beskadig die selmembraan, wat veranderinge in membraanfunksie en deurlaatbaarheid veroorsaak.

**Farmakokinetika:**
Flukonasool word goed geabsorbeer na orale toediening. Orale biobeskikbaarheid is meer as 90 %. Orale biobeskikbaarheid word nie beïnvloed deur voedsel of gastriese suur nie. Die tyd tot die maksimum plasmakonsentrasie is 1 tot 2 uur. Proteïenbinding is laag (12 %). Die eliminasiehalfleeftyd by volwassenes is ongeveer 30 uur en word verhoog by pasiënte met ingekorte renale funksie. Flukonasool word hoofsaaklik uitgeskei deur die niere. Ongeveer 80 % van die dosis word onveranderd in die urine uitgeskei. Flukonasool opruiming is eweredig aan kreatinien opruiming. Akkumulasie is egter beduidend oor 15 dae en konsentrasies kan 2 tot 3 voudig toeneem. 'n Klein hoeveelheid flukonasool ondergaan hepatiese metabolisme. Flukonasool word vinniger by kinders opgeruim as by volwassenes. Die halfleeftyd by kinders is 23 uur. Gedurende die eerste 2 weke van die lewe is die halfleeftyd ongeveer 74 uur op dag een en 47 uur op dag 13.

**INDIKASIES:**
Anti-infektiewe terapie moet aangepas word sodra die resultate van die kulture en ander laboratoriumstudies beskikbaar is.
FLUCONAZOLE STRIDES word aangedui vir die behandeling van die volgende toestande by volwassenes:
- Kriptokokkale meningitis by verstandelik wakker pasiënte sonder lokalisering van neurologiese tekens en as 'n opvolgterapie na amfoterisien B-terapie.
- Instandhoudingsterapie om terugkeer van kriptokokkale siekte te voorkom by pasiënte met verworwe immuniteitsgebreksindroom (VIGS).
- Orofaringeale en esofageale kandidiase.
- Sistemiese kandidiase.
- Profilaktiese van fungusinfeksies by pasiënte wat sitotoksiese chemoterapie en/of bestralingsterapie ontvang.
- Vaginale kandidiase - Akute of herhalende infeksies en as profilaktiese om die voorkoms van herhalende infeksies te verminder.
- Kandidiale balanitis.
- Dermatomikose, insluitende tinea corporis, tinea cruris, tinea pedis, tinea unguium (onigomikose) en dermale *candida* infeksies.

FLUCONAZOLE STRIDES word **aangedui vir die behandeling van die volgende toestande by kinders:**
- Kriptokokkale meningitis by verstandelik wakker pasiënte sonder lokalisering van neurologiese tekens en as 'n opvolgterapie na amfoterisien B-terapie.
- Instandhoudingsterapie om terugkeer van kriptokokkale siekte te voorkom by pasiënte met verworwe immuniteitsgebreksindroom (VIGS).
- Orofaringeale en esofageale kandidiase.
- Sistemiese kandidiase.
- Profilaktiese van fungusinfeksies by pasiënte wat sitotoksiese chemoterapie en/of bestralingsterapie ontvang.

**KONTRAÏNDIKASIES:**
- Hipersensitiwiteit vir FLUCONAZOLE STRIDES, ander asool antifungale middels of enige van die hulpstowwe.
- Gelyktydige toediening van terfenadien by pasiënte wat veelvuldige dosisse FLUCONAZOLE STRIDES ontvang in dosisse van 400 mg per dag of meer (sien **INTERAKSIES**).
- Gelyktydige toediening van sisapried (sien **INTERAKSIES**).
- Swangerskap en laktasie (sien **SWANGERSKAP EN LAKTASIE**).
- Terapie met vatsoutige dosisse FLUCONAZOLE STRIDES is gekontraindikeerd by pasiënte met renale inkorting.
- Gelyktydige gebruik met astemisool moet vermy word.

**WAARSKUWINGS:**
FLUCONAZOLE STRIDES is geassosieer met gevalle van ernstige hepatotoksisiteit, insluitende sterftes wat verband hou met dosis en gebruiksduur, hoofsaaklik by pasiënte met ernstige onderliggende mediese toestande. Hierdie hepatotoksisiteit kan omkeerbaar wees wanneer terapie gestaak word. Enige pasiënte wat abnormale lewerfunksietoetsbe ontwikkel, terwyl FLUCONAZOLE STRIDES gebruik word, moet noukeurig gemonitor word vir die ontwikkeling van meer ernstige lewerskade. Indien tekens en simptome in ooreenstemming met lewersiekte ontwikkel, kan dit aan FLUCONAZOLE STRIDES toegeskryf word. FLUCONAZOLE STRIDES moet gestaak word.
Minder dikwels het pasiënte uitslag, urtikariële, pruritus, droë vel, abnormale reuk, angioedeem en eksfoliatiewe kutane reaksies, soos Stevens-Johnson sindroom en toksiese epidermale nekrolise, tydens behandeling met FLUCONAZOLE STRIDES ontwikkel. Pasiënte met VIGS is meer geneig tot die ontwikkeling van ernstige kutane reaksies op talle medisyne. Indien pasiënte met sistemiese/indringende fungusinfeksies 'n uitslag ontwikkel, moet hulle noukeurig gemonitor word, en indien bulleuse letsels of eriteem multiforme ontwikkel, moet FLUCONAZOLE STRIDES gestaak word.

**INTERAKSIES:**
FLUCONAZOLE STRIDES kan met die metabolisme van sommige medisyne inmeng indien dit gesamentlik toegedien word, hoofsaaklik deur inhibisie van die sitochroom P450 iso-ensiem CYP3A4 en CYP2C9. Gesamentlike toediening van FLUCONAZOLE STRIDES en medisyne wat deur sitochroom P450 gemetaboliseer word, kan lei tot verhoogde serumkonsentrasies van die medisyne wat deur dieselfde ensiemstelsel gemetaboliseer word.
- FLUCONAZOLE STRIDES verhoog plasmakonsentrasies van die volgende medisyne wanneer dit gelyktydig gegee word:
- Warfarien - Antikoagulerende effekte word verhoog, wat lei tot 'n toename in protrombien tyd/IGV-verhouding. Monitering van die protrombientyd is nodig en aanpassing van die warfarien dosis kan nodig wees.
- Sulfonielureum hipoglisemiese middels - Die plasmakonsentrasie van hierdie middels kan verhoog word en hipoglisemie kan voorkom. Bloedglukosekonsentrasies moet gemonitor word en die dosis van die sulfonielureum sal dalk verminder moet word.
- Fenitoïen - Verlaagde metabolisme van fenitoïen, wat lei tot verhoogde plasmakonsentrasies en moontlike fenitoïentoksisiteit.
- Teofilliën - Verlaagde opruiming van teofilliën wat lei tot verhoogde teofilliënplasmakonsentrasies en moontlik toksisiteit. Teofilliënkonsentrasies moet gemonitor word.
- Sidovudien - Verhoogde plasmakonsentrasies van sidovudien. Pasiënte moet gemonitor word vir sidovudien-verwante nadelige effekte.
- Terfenadien - Die gelyktydige gebruik van terfenadien en dosisse van 400 mg of meer van FLUCONAZOLE STRIDES is gekontraindikeerd. Indien gelyktydige toediening van terfenadien en FLUCONAZOLE STRIDES by dosisse van minder as 400 mg oorweeg word, moet noodsaaklike terfenadienkonsentrasies noukeurig gemonitor word (sien **KONTRAÏNDIKASIES**). Daar is ook berig dat daar 'n interaksie is met astemisool en FLUCONAZOLE STRIDES en gelyktydige gebruik moet dus vermy word (sien **KONTRAÏNDIKASIES**).
- Sisapried - Die gelyktydige toediening van FLUCONAZOLE STRIDES met sisapried is gekontraindikeerd weens die moontlike toename in serum-sisaprieddkonsentrasies wat die risiko van ernstige en lewensbedreigende kardiale aritmieë, insluitend torsade de pointes kan verhoog (sien **KONTRAÏNDIKASIES**).
- Siklosporien - Kliniese beduidende stygings in die konsentrasies van siklosporien in die serum van twee tot drievoudig is waargeneem by sommige pasiënte wanneer flukonasool toegedien word. Dus, moet die plasmakonsentrasies van siklosporien gemonitor word by alle pasiënte wat FLUCONAZOLE STRIDES ontvang.
- Midasolam en triasolam - FLUCONAZOLE STRIDES verhoog die serumkonsentrasies van midasolam en triasolam en hul psigomotoriese effekte. Hierdie effek blyk meer uitgesproke te wees na orale toediening van FLUCONAZOLE STRIDES as met intraveneuse toegedien van flukonasool. Indien hierdie medisyne gelyktydig gebruik moet word, kan 'n verminderde dosis bensodiasepien nodig wees en die pasiënt moet gemonitor word.
- Rifabutien - Toename in serumkonsentrasie van rifabutien wat 'n verhoogde risiko van uveïtis inhou. Pasiënte op hierdie kombinasie moet noukeurig gemonitor word.
- Takrolimus - Konsentrasies takrolimus word aansienlik verhoog deur FLUCONAZOLE STRIDES. Pasiënte op hierdie kombinasie moet serumkonsentrasies van takrolimus laat monitor en dosisvermindering is nodig.

Die volgende medisyne verhoog plasmakonsentrasies van FLUCONAZOLE STRIDES wanneer dit gesamentlik gegee word:
- Hidrochloortiasied

Die volgende medisyne verminder plasmakonsentrasies van FLUCONAZOLE STRIDES wanneer dit gelyktydig gegee word:
- Rifampisien - Verhoogde metabolisme van FLUCONAZOLE STRIDES, wat lei tot laer plasmakonsentrasies FLUCONAZOLE STRIDES.

**Ander inligting oor interaksies:**
Gesamentlike toediening van flukonasool en nevirapien het gelei tot ongeveer 'n 100 % toename in die blootstelling aan nevirapien in vergelyking met historiese data waar nevirapien alleen toegedien word. As gevolg van die risiko van verhoogde blootstelling aan nevirapien, moet versigtigheid aan die dag gelê word indien nevirapien en FLUCONAZOLE STRIDES gelyktydig toegedien word en pasiënte moet noukeurig gemonitor word.

**SWANGERSKAP EN LAKTASIE:**
Die gebruik van FLUCONAZOLE STRIDES tydens swangerskap het gelei tot kongenitale misvormings en moet vermy word (sien **KONTRAÏNDIKASIES**).
FLUCONAZOLE STRIDES moet nie aan borsvoedende vroue gegee word nie (sien **KONTRAÏNDIKASIES**).
FLUCONAZOLE STRIDES word in die borsmelk uitgeskei teen konsentrasies soortgelyk aan dié in plasma.

**DOSIS EN GEBRUIKSAANWYSINGS:**
Kriptokokkale meningitis:
*Volwassenes:* Aanvangsdosis is 400 mg op die eerste dag; gevolg deur 200 mg tot 400 mg daagliks, afhangende van die kliniese respons. Duur van terapie is gebaseer op kliniese en mikologiese respons, maar is gewoonlik 8 weke, na amfoterisien B-terapie, en 10 weke met FLUCONAZOLE STRIDES monoterapie.
*Kinders ouer as 4 weke:* 6 mg/kg/dag tot 12 mg/kg/dag afhangende van die ems van infeksie.
Instandhoudingsterapie om terugval van kriptokokkale meningitis by pasiënte met VIGS te voorkom:
*Volwassenes:* 100 mg tot 200 mg per dag
Sistemiese kandidiase:
*Volwassenes:* Aanvangsdosis is 400 mg op die eerste dag; gevolg deur 200 mg daagliks.
Die dosis kan verhoog word tot 400 mg daagliks, afhangende van die kliniese respons.
*Kinders ouer as 4 weke:* 6 mg/kg/dag tot 12 mg/kg/dag afhangende van die ems van infeksie.
Duur van terapie is gebaseer op kliniese en mikologiese respons.
Orofaringeale kandidiase:
*Volwassenes:* 50 mg tot 100 mg daagliks vir 7 tot 14 dae. Pasiënte met ernstige immuunonderdrukking kan langer behandelingsperiodes benodig.
Om terugval by VIGS-pasiënte te voorkom: 150 mg FLUCONAZOLE STRIDES kan een keer per week gegee word.
*Kinders ouer as 4 weke:* Aanvangsdosis is 6 mg/kg op die eerste dag; gevolg deur 3 mg/kg een keer per dag. Duur van behandeling is ten minste 2 weke om die risiko van terugval te verminder.
Esofageale kandidiase:
*Volwassenes:* Aanvangsdosis is 200 mg op die eerste dag; gevolg deur 100 mg tot 200 mg daagliks. Dosisse tot 400 mg een keer per dag mag gebruik word indien daar geen kliniese respons na 14 dae op die laer dosis is nie. Duur van behandeling is ten minste 3 weke en vir 'n bykomende 2 weke nadat die simptome opgeklaar het.
*Kinders ouer as 4 weke:* Aanvangsdosis is 6 mg/kg op die eerste dag; gevolg deur 3 mg/kg een keer per dag. Dosis kan verhoog word tot 12 mg/kg/dag gebaseer op die toestand van die pasiënt en die respons op die medisyne. Duur van behandeling is vir ten minste 3 weke en vir 'n addisionele 2 weke nadat die simptome opgeklaar het.
Profilaktiese van fungusinfeksies by pasiënte wat sitotoksiese chemoterapie en/of bestralingsterapie ontvang:
*Volwassenes:* 50 mg tot 400 mg daagliks afhangende van die pasiënt se risiko om fungusinfeksies te ontwikkel. Behandeling moet 'n paar dae voor die aanvang van neutropenie begin word en moet voortgesit word vir 7 dae nadat die *neutrofieletelling* bo 1 000 selle per mm³ styg.
*Kinders ouer as 4 weke:* 3 tot 12 mg/kg/dag afhangende van die omvang en duur van die geïnduseerde neutropenie.
Vaginale kandidiase:
*Volwassenes:* 150 mg toegedien as 'n enkeldosis.
Herhalende vaginale kandidiase:
*Volwassenes:* 150 mg toegedien as 'n enkele dosis, een keer per maand. Die duur van terapie is geïndividualiseer, maar wissel van 4 tot 12 maande.
*Candida balanitis:*
*Volwassenes:* 150 mg toegedien as 'n enkeldosis.
Dermale infeksies, insluitend tinea pedis, tinea corporis, tinea cruris, tinea unguium (onigomikose) en dermale *candida* infeksies:
*Volwassenes:* 150 mg een keer per week as 'n enkeldosis toegedien.
Duur van behandeling is gewoonlik 2 tot 4 weke, maar tinea pedis kan tot 6 weke se behandeling vereis. Vir tinea unguium moet behandeling voortgaan totdat die besmette nael uitgroei en met 'n onbesmette nael vervang is. Vingernaels benodig gewoonlik 3 tot 6 maande om te hergroei en toonnaels 6 tot 12 maande.

Veiligheid en effektiwiteit van FLUCONAZOLE STRIDES by kinders is nie vasgestel vir die volgende indikasies nie:
Herhalende vaginale kandidiase, *candida balanitis*, dermale infeksies, insluitend tinea pedis, tinea corporis, tinea cruris, tinea unguium (onigomikose) en dermale *candida* infeksies.
*Bejaardes:* Sien dosis in renale versaking.
Normale dosisaanbevelings word by bejaardes gebruik, tensy die pasiënt ingekorte renale funksie het, in welke geval 'n aanpassing in dosis of doseringsinterval nodig is.

**DOSIS IN RENALE VERSAKING:**
FLUCONAZOLE STRIDES moet met omsigtigheid gebruik word by pasiënte met ingekorte renale funksie. FLUCONAZOLE STRIDES word deur die niere uitgeskei. 'n Dosisvermindering of verhoging in doseringsinterval word aanbeveel:

1. Die normale ladingsdosis of die aanvangsdosis moet op die eerste dag van behandeling gegee word.
2. Daaropvolgende dosisse moet aangepas word volgens die kreatinienopruiming.

Indien kreatinienopruiming > 50 ml/min is, kan die normale dosis gegee word.
Indien kreatinienopruiming < 50 ml/min is en pasiënt nie dialise ontvang nie, kan 50 % van die normale dosis gegee word.
Pasiënte op gereelde hemodialise moet 'n standaard dosis FLUCONAZOLE STRIDES na elke dialisesessie ontvang.
Die pasiënt se kreatinienopruiming (Kot) kan geskat word deur die volgende formule te gebruik:

$$\text{Kot manlik} = \frac{\text{Gewig (kg) x (140 – ouderdom)}}{\text{72 x (plasmakreatinien (mikromol/liter) 88}}$$

$$\text{Kot vroulik} = \frac{\text{0,85 x Gewig (kg) x (140– ouderdom)}}{\text{72 x (plasmakreatinien (mikromol/liter) 88}}$$

Die farmakokinetika van FLUCONAZOLE STRIDES is nie by kinders met ingekorte renale funksie bestudeer nie. Aanbevelings vir dosisvermindering by sulke kinders moet ooreenstem met die aanbevelings vir volwassenes.

- Die dosis FLUCONAZOLE STRIDES en die duur van behandeling moet gebaseer word op die plek van infeksie en die individu se respons op terapie.
- Behandeling moet voortgesit word totdat kliniese parameters en laboratoriumtoetse aandui dat aktiewe fungusinfeksie opgeklaar het.
- VIGS-pasiënte met kriptokokkale meningitis of herhalende orofaringeale kandidiase benodig onderhoudsterapie om terugval te voorkom.
- Vir pasgebore babas jonger as 2 weke moet die bogenoemde kinderdosisse gebruik word, maar slegs een keer elke 72 uur gegee word. Vir diegene tussen die ouderdomme van 2 en 4 weke moet die dosis elke 48 uur gegee word. Die maksimum daaglikse dosis vir volwassenes (d.w.s. 400 mg) moet nie by kinders oorskry word nie.
- Normale dosisaanbevelings word in die bejaarde populasie gebruik, tensy die pasiënt verslegte renale funksie het. In welke geval 'n aanpassing in dosis of doseringsinterval nodig is.

**NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:**
Newe-effekte:
Hematologies:
- *Minder gereeld:* Leukopenie, neutropenie, agranulositose en trombositopenie.

Sentrale senuweestelsel:
- *Gereeld:* Hoofpyn.
- *Minder gereeld:* Duiseligheid, vertigo, aanvalle, slapeloosheid, senuweeagtigheid, moegheid, stufheid, malaise, hiperkinese.

Endokrien/Metabolies:
- *Minder gereeld:* Hipokalemie, hipercholesterolemie, hipertrigliseriedemie.

Gastrointestinaal:
- *Gereeld:* Naarheid, braking, abdominale pyn, diarree, winderigheid.
- *Minder gereeld:* Smaakversteuring, dispepsie, dorsheid.

Nier/Genitourinêr:
- *Minder gereeld:* Vroulike seksuele disfunksie, intermenstruele bloeding, menorragie, leukorree, poliurie.

Lewer:
- *Gereeld:* Hepatotoksisiteit (insluitend verhoogde serumkonsentrasies van alkaliese fosfatase, bilirubien, ALT en AST).
- *Minder gereeld:* Hepatiese versaking, hepatitis, hepatoselluläre nekrose, geelsug.

Muskuloskeletstel:
- *Minder gereeld:* Hipertonie.
- *Okuïër:*
- *Minder gereeld:* Abnormale visie.

Vel:
- *Gereeld:* Uitslag.
- *Minder gereeld:* Alopesiate, urtikariële, droë vel, abnormale reuk, afskilferende kutane reaksies soos Stevens-Johnson-sindroom en toksiese epidermale nekrolise.

Ander:
- *Minder gereeld:* Anafilakse (insluitend angioedeem, gesigsedeem, pruritus), blosing.

Spesiale voorsorgmaatreëls:
Lewerfunksie moet periodies gemonitor word by alle pasiënte wat deurlopende behandeling met FLUCONAZOLE STRIDES vir meer as een maand ontvang of wanneer 'n pasiënt tekens of simptome ontwikkel wat dui op lewerdisfunksie.
FLUCONAZOLE STRIDES moet gestaak word indien abnormaliteite in ensiemwaardes voortduur, vereger of indien dit gepaard gaan met simptome van hepatotoksisiteit.

FLUCONAZOLE STRIDES moet met omsigtigheid gebruik word by pasiënte met onderliggende siektes soos VIGS of maligniteit. Abnormaliteite in hematologiese, hepatiese en renale funksie is waargeneem.

**BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:**
(Sien **NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS**).
Simptome van oordosering: Die volgende is aangemeld met 'n oordosering van FLUCONAZOLE STRIDES: Prikkelbaarheid, slapeloosheid, depressiewe gemoed, gevoelloosheid van die tong, buitende fontanel, anoreksie, braking, abdominale pyne/krampe, diarree, moegheid, jeuk, gesigsuistlag, algemene urtikariële, vel eriteem, artralgie, renale versaking, verhoging van alkaliese fosfatase en gamma-glutamiel transpeptidase en toename in serum kalsium.
Behandeling van oordosering:
Behandeling is simptomaties en ondersteunend. Daar is geen spesifieke teenmiddel nie.
FLUCONAZOLE STRIDES word grootliks in die urine uitgeskei. Gedwonge diurese kan die eliminasietempo verhoog.
Uitskeiding van FLUCONAZOLE STRIDES kan deur hemodialise aangehelp word. Die konsentrasie van FLUCONAZOLE STRIDES kan met ongeveer 50 % verminder word deur 'n drie uur hemodialise sessie.

**IDENTIFIKASIE:**
**FLUCONAZOLE 50 STRIDES Kapsules:**
Wit poeier gevul in harde gelatienkapsules van grootte '4' met 'n wit opaak lyf en lugblou opaak doppie met 'FCZ 50' in linêre druk daarop in swart kleur.
**FLUCONAZOLE 200 STRIDES Kapsules:**
Wit poeier gevul in harde gelatienkapsules van grootte '0' met donkerblou doppie en wit lyf.

**AANBEIDING:**
**FLUCONAZOLE 50 STRIDES Kapsules:**
Karton wat deursigtige PVC en aluminiumfoelie stolpverpakking van 14 kapsules bevat.
**FLUCONAZOLE 200 STRIDES Kapsules:**
Karton wat deursigtige PVC/PVDC en aluminiumfoelie stolpverpakkings van 28 of 30 kapsules bevat.

**BERGINGSINSTRUKSIES:**
Bêre teen of benede 25 °C op 'n droë plek.
**HOU BUITE BEREIK VAN KINDERS.**

**REGISTRASIENOMMERS:**
**FLUCONAZOLE 50 STRIDES:** 38/20.2.2/0101
**FLUCONAZOLE 200 STRIDES:** 38/20.2.2/0103

**NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:**
STRIDES PHARMA (SA) (Edms.) BPK
106 16de Weg,
Gebou 2,
Midrand,
1686,
Suid Afrika.

**DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:**
Augustus 2004

PKG1049

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