SCHEDULING STATUS:
S4

PROPRIETARY NAME AND DOSAGE FORM:
BIO FLUCONAZOLE IV (Intravenous infusion)

COMPOSITION:
BIO FLUCONAZOLE IV: Each 100 ml solution contains 200 mg fluconazole.
Excipients: Sodium chloride, water for injections.
Sugar free.

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

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties
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.
Pharmacokinetic properties
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:
Once the results of the cultures and other laboratory studies become available, anti-infective therapy should be adjusted. BIO FLUCONAZOLE IV 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).
– Systemic candidiasis.
– Oropharyngeal and oesophageal 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 pedis, tinea corporis, tinea cruris, tinea unguium (onychomycosis) and dermal candida infections.
BIO FLUCONAZOLE IV 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).
– Systemic candidiasis.
– Oropharyngeal and oesophageal candidiasis.
– Prophylaxis of candidiasis in patients receiving cytotoxic chemotherapy and/or radiation therapy.

CONTRAINDICATIONS:
• Hypersensitivity to BIO FLUCONAZOLE IV, other azole antifungal agents or to any of the excipients.
• Co-administration of cisapride (see INTERACTIONS).
• Pregnancy and lactation (see HUMAN REPRODUCTION).
• Multiple dose therapy is contraindicated in patients with renal impairment.
• Concurrent use with astemizole should be avoided.

WARNINGS AND SPECIAL PRECAUTIONS:
BIO FLUCONAZOLE IV 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. Hepatotoxicity may be reversible on discontinuation of therapy. Patients who develop abnormal liver function tests during BIO FLUCONAZOLE IV therapy should be monitored for the development of more serious hepatic injury. BIO FLUCONAZOLE IV should be discontinued if clinical signs or symptoms consistent with the liver disease develop that may be attributable to BIO FLUCONAZOLE IV.
Liver function should be monitored periodically in all patients receiving continuous treatment with
BIO FLUCONAZOLE IV for more than one month or when a patient develops signs or symptoms suggestive of liver dysfunction.
Patients have less frequently developed pruritus, rashes, urticaria, angioedema, dry skin, abnormal odour, exfoliative cutaneous reactions such as Stevens-Johnson Syndrome and toxic epidermal necrolysis during treatment with BIO FLUCONAZOLE IV. AIDS patients are more prone to the development of severe cutaneous reaction to many medicines. If patients with invasive/ systemic fungal infections develop rashes, they should be monitored closely, and BIO FLUCONAZOLE IV discontinued if bullous lesions or erythema multiforme develop.
BIO FLUCONAZOLE IV 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.

INTERACTIONS:
BIO FLUCONAZOLE IV 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 BIO FLUCONAZOLE IV and medicines metabolised by cytochrome P450 can result in increased serum concentrations of the medicines metabolised by the same enzyme system.
BIO FLUCONAZOLE IV 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.
Astemizole has also been reported to interact with BIO FLUCONAZOLE IV and concurrent use should be avoided (see CONTRAINDICATIONS).
Cisapride – The concomitant administration of BIO FLUCONAZOLE IV with cisapride is contraindicated 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 have been observed in some patients when given fluconazole. Therefore, ciclosporin plasma concentrations should be monitored in all patients receiving BIO FLUCONAZOLE IV.
Midazolam and triazolam – BIO FLUCONAZOLE IV increases the serum concentrations of midazolam and triazolam and their psychomotor effects. This effect appears to be more pronounced following oral administration of BIO FLUCONAZOLE IV 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 BIO FLUCONAZOLE IV. Patients on this combination need to have serum concentrations of tacrolimus monitored and dose reduced if necessary.
The following medicine increases plasma concentrations of BIO FLUCONAZOLE IV when given concomitantly:
Hydrochlorothiazide.
The following medicine decreases plasma concentrations of BIO FLUCONAZOLE IV when given concomitantly:
Rifampicin – Increased metabolism of BIO FLUCONAZOLE IV, resulting in lower plasma concentrations of BIO FLUCONAZOLE IV.
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 BIO FLUCONAZOLE IV are given concomitantly, and patients should be monitored closely.

HUMAN REPRODUCTION:
The use of BIO FLUCONAZOLE IV during pregnancy has resulted in congenital malformations and should be avoided (see CONTRAINDICATIONS).
BIO FLUCONAZOLE IV should not be given to breastfeeding women (see CONTRAINDICATIONS).
BIO FLUCONAZOLE IV 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 mycological response, but is usually 8 weeks, following Amphotericin B therapy and 10 weeks with BIO FLUCONAZOLE IV monotherapy.
Children over 4 weeks of age: 6 mg/kg/day to 12 mg/kg/day depending on the severity of the 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. 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 the 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 BIO FLUCONAZOLE IV 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 in 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 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 individualised 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 BIO FLUCONAZOLE IV 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
BIO FLUCONAZOLE IV should be used with caution in patients with renal function impairment.
BIO FLUCONAZOLE IV is excreted through the kidneys. *A dosage reduction or increase in dosing interval is recommended:*
The normal loading dose or the initial dose should be given on the first day of treatment.
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 < 50 ml/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 BIO FLUCONAZOLE IV after each dialysis session.

The patient's creatinine clearance (C_{cr}) can be estimated by using the following modified formula of Cockroft and Gault (for use in adults):

$$\text{eGFR (ml/min)} = \frac{(140 - \text{age}) \times \text{Wt (kg)}}{S_{cr}\ (\mu\text{mol/L})}$$

eGFR = Estimated Glomerular Filtration Rate
S_{cr} = Serum creatinine
For females multiply the GFR by 0,85.

The pharmacokinetics of BIO FLUCONAZOLE IV has 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 BIO FLUCONAZOLE IV 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.
BIO FLUCONAZOLE IV
BIO FLUCONAZOLE IV is formulated in 0,9 % sodium chloride solution, each 200 mg (100 ml bottle) containing 15 mmol each of sodium and chloride ions.
Because BIO FLUCONAZOLE IV is available as a dilute saline solution, consideration should be given to the rate of fluid administration in patients requiring sodium or fluid restriction.
BIO FLUCONAZOLE IV is compatible with the following administration fluids: dextrose 20 %, ringer's solution, normal saline, potassium chloride in dextrose and sodium bicarbonate 4,2 %.
BIO FLUCONAZOLE IV may be infused at a maximum rate of approximately 200 mg/hour through an existing line with one of the above listed fluids. Although no specific incompatibilities have been noted, mixing with any other drug prior to infusion is not recommended.

SIDE EFFECTS:
Immune system disorders
Less frequent: Hypersensitivity (fever and chills; skin rash or itching). Anaphylaxis including angioedema, face oedema, pruritus, flushing.
Blood and the lymphatic system disorders
Less frequent: Agranulocytosis, thrombocytopenia, leucopenia and neutropenia.
Endocrine disorders
Less frequent: Hypercholesterolaemia, hypertriglyceridemia, hypokalaemia.
Skin and subcutaneous tissue disorders
Frequent: Rash.
Less frequent: Exfoliative cutaneous reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis; urticaria, dry skin, abnormal odour and alopecia.
Cardiac disorders
Frequency not known: QT prolongation, torsades de pointes.
Nervous system disorders
Frequent: Headache.
Less frequent: Vertigo, dizziness, seizures, insomnia, nervousness, fatigue, rigors, malaise, hyperkinesia.
Gastrointestinal disorders
Frequent: Abdominal pain, diarrhoea, flatulence, constipation, loss of appetite, nausea, vomiting.
Less frequent: Dyspepsia, taste perversions, thirst.
Renal and urinary disorders
Less frequent: Polyuria, female sexual dysfunction, intermenstrual bleeding, menorrhagia, leucorrhoea.
Hepato-biliary disorders
Frequent: Hepatotoxicity (including elevated serum concentrations of alkaline phosphatase, bilirubin, ALT and AST).
Less frequent: Hepatic failure, hepatitis, hepatocellular necrosis, jaundice.
Eye disorders
Less frequent: Abnormal vision.
Musculoskeletal, connective tissue and bone disorders
Less frequent: Hypertonia.

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

IDENTIFICATION:
BIO FLUCONAZOLE IV: A clear colourless to pale yellow solution.

PRESENTATION:
BIO FLUCONAZOLE IV is packed in a 100 ml transparent white LDPE bottle. Each bottle is wrapped with a transparent clear polypropylene wrapper.

STORAGE CONDITIONS:
BIO FLUCONAZOLE IV: Store at or below 30 °C. Do not freeze. Discard any remaining contents after use.
KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER:
BIO FLUCONAZOLE IV: 42/20.2.2/0683

NAME AND BUSINESS ADDRESS OF HOLDER OF THE REGISTRATION CERTIFICATE:
BIOTECH LABORATORIES (PTY) LTD.
Ground Floor, Block K West, Central Park
400, 16th Road, Halfway House
Midrand
1685

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:
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SKEDULERINGSTATUS:
S4

EIENDOMSNAAM EN DOSEERVORM:
BIO FLUCONAZOLE IV (Intraveneuse infusie)

SAMESTELLING:
BIO FLUCONAZOLE IV: Elke 100 ml oplossing bevat 200 mg flukonasool.
Onaktiewe bestanddele: Natriumchloried, water vir inspuiting.
Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:
A 20.2.2 Swamdoders

FARMAKOLOGIESE WERKING:
Farmakodinamiese eienskappe
Flukonasool is 'n triasoolswamdoder. Flukonasool oefen sy antifungus effek uit deur die sterol 14-alfa-demetielase te inhibeer wat die biosintese van ergosterol, die hoof sterol in die swamselmembraan, benadeel. Dit beskadig die selmembraan wat veranderinge in membraanfunksie en deurlaatbaarheid veroorsaak.
Farmakokinetiese eienskappe
Na orale toediening word flukonasool goed geabsorbeer met 'n sistemiese biobeskikbaarheid van meer as 90 %. Orale biobeskikbaarheid word nie beïnvloed deur voedsel of maagsuur nie. Piek plasmakonsentrasies word binne 1 tot 2 uur bereik. Plasma proteïenbinding is laag (12 %). Die plasma eliminasie halfleeftyd is ongeveer 30 uur en is verhoog in pasiënte met verswakte nierfunksie. Flukonasool word hoofsaaklik deur die niere uitgeskei. Ongeveer 80 % van die dosis word onveranderd in die uriene uitgeskei. Flukonasool uitskeiding is in verhouding tot kreatinieopklaring. Akkumulasie is betekenisvol oor 'n tydperk van 15 dae en die konsentrasies kan 2-3 maal styg. In Klein hoeveelheid flukonasool ondergaan hepatiese metabolisme.
Die uitgeskeiding van flukonasool is vinniger in kinders as in volwassenes, met 'n halfleeftyd van 23 uur. Gedurende die eerste twee weke van die lewe is die halfleeftyd ongeveer 74 uur op dag een en 47 uur op dag 13.
INDIKASIES:
Sodra kultuurkwekings en ander laboratoriumuitslae beskikbaar word, moet infeksiewerende behandeling daarvolgens aangepas word.
BIO FLUCONAZOLE IV word aangedui vir die behandeling van die volgende toestande in volwassenes:
– Kriptokokkale-meningitis in verstandelik wakker pasiënte sonder gelokaliseerde neurologiese tekens en as opvolgterapie na amfoterisien-B behandeling.
– As instandhoudingsterapie om die terugval van kriptokokkale-siekte by pasiënte wat aan VIGS ly, te voorkom.
– Sistemiese kandidiase.
– Orofaringeale en esofageale kandidiase.
– Voorkoming van swaminfeksies by pasiënte wat chemoterapie en/of radioterapie ontvang.
– Vaginale kandidiase – akute of herhalende infeksies of om die insidensie van herhalende infeksies te voorkom.
– Kandidiale balanitis.
– Dermatomikose insluitende tinea pedis, tinea corporis, tinea cruris, tinea unguium (onigomikose) en kandidiale swamvelinfeksies.

BIO FLUCONAZOLE IV word aangedui vir die behandeling van die volgende toestande in kinders:
– Kriptokokkale-meningitis in verstandelik wakker pasiënte sonder gelokaliseerde neurologiese tekens en as opvolgterapie na amfoterisien-B behandeling.
– As instandhoudingsterapie om die terugval van kriptokokkale-siekte by pasiënte wat aan VIGS ly, te voorkom.
– Sistemiese kandidiase.
– Orofaringeale en esofageale kandidiase.
– Voorkoming van swaminfeksies by pasiënte wat chemoterapie en/of radioterapie ontvang.

KONTRA-INDIKASIES:
• Hipersensitiwiteit teenoor flukonasool, ander asoolverbindings of teenoor enige van die onaktiewe bestanddele van BIO FLUCONAZOLE IV.
• Gelyktydige toediening van sisapried (kyk INTERAKSIES).
• Tydens swangerskap en laktasie (kyk MENSLIKE VOORTPLANTING).
• Meervoudige dosis terapie is 'n kontra-indikasie by pasiënte met nierontoereikendheid.
• Gelyktydige gebruik met astemisool moet vermy word.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
Flukonasool is in verband gebring met gevalle van ernstige lewertoksisiteit, insluitende sterftes, hoofsaaklik by pasiënte met ernstige onderliggende mediese toestande. Lewertoksisiteit kan omgekeer word as behandeling gestaak word. Pasiënte wat abnormale lewerfunksietoetse tydens BIO FLUCONAZOLE IV behandeling ontwikkel, moet gemonitor word vir die ontwikkeling van meer ernstige lewerskade. BIO FLUCONAZOLE IV moet gestaak word indien kliniese tekens of simptome van lewersiekte ontwikkel wat toegeskryf kan word aan BIO FLUCONAZOLE IV.
Lewerfunksies moet gereeld gemonitor word by alle pasiënte wat met BIO FLUCONAZOLE IV deurlopend behandel word vir meer as een maand of wanneer 'n pasiënt tekens of simptome ontwikkel wat dui op lewerafwyking.
Pasiënte het minder dikwels pruritis, uitslag, urtikarie, angio-edeem, droë vel, abnormale reuk, afskilferende velreaksies soos Stevens-Johnson-sindroom en toksiese epidermale nekrolise tydens behandeling met BIO FLUCONAZOLE IV ontwikkel. VIGS-pasiënte is meer geneig tot die ontwikkeling van ernstige velreaksies met medisyne. Indien pasiënte met siekte-invalle / sistemiese swaminfeksies uitslag ontwikkel, moet hulle noukeurig gemonitor word, en moet BIO FLUCONAZOLE IV gestaak word indien blaserige letsels of veelvuldige velrooiheid ontwikkel.
BIO FLUCONAZOLE IV moet met omsigtigheid gebruik word by pasiënte met onderliggende siektes soos VIGS of kwaadaardighede. Abnormaliteite in hematologiese, lewer- en nierfunksie is waargeneem.

INTERAKSIES:
BIO FLUCONAZOLE IV kan met die metabolisme van sommige medisyne inmeng na gelyktydige toediening, hoofsaaklik deur inhibisie van die sitochroom P450 iso-ensieme CYP3A4 en CYP2C9. Gelyktydige toediening van BIO FLUCONAZOLE IV en medisyne wat deur sitochroom P450 gemetaboliseer word, kan lei tot verhoogde plasmakonsentrasies van die medisyne wat met dieselfde ensiemstelsel gemetaboliseer word.
BIO FLUCONAZOLE IV verhoog die plasmakonsentrasies van die volgende medisyne wanneer dit gelyktydig gegee word:
Warfarien – antistol effekte word verhoog, wat lei tot 'n toename in protrombientyd / INR-verhouding. Monitering van die protrombientyd is nodig en dosisaanpassing van die warfarien kan nodig wees.
Sulfonielurea hipoglisemiese middels – die plasmakonsentrasie van hierdie medisyne kan verhoog, en kan hipoglisemie tot gevolg hê.
Bloedglukosekonsentrasies moet gemonitor word, en die dosis van die sulfonielureum moet moontlik verminder word.
Fenitoïen – Verminderde metabolisme van fenitoïen, wat lei tot verhoogde plasmakonsentrasies en moontlike fenitoïentoksisiteit.
Teofillien – Verlaagde uitskeiding van teofillien, wat lei tot verhoogde teofillien plasmakonsentrasies en moontlik toksisiteit. Teofillien konsentrasies moet gemonitor word.
Zidovudien – Verhoogde plasmakonsentrasies van zidovudien. Pasiënte moet gemonitor word vir zidovudienverwante nadelige effekte.
Astemisool – Interaksie tussen astemisool en BIO FLUCONAZOLE IV is aangemeld en daarom moet gelyktydige gebruik vermy word (kyk KONTRA-INDIKASIES).
Sisapried – Die gelyktydige toediening van BIO FLUCONAZOLE IV met sisapried word gekontraïndikeer weens die moontlike toename in serum sisapried konsentrasies, wat die risiko van ernstige en lewensbedreigende hartdisritmieë insluitende torsade de pointes kan verhoog (kyk KONTRA-INDIKASIES).
Siklosporien – Twee tot drievoudige styging in die serumkonsentrasies van siklosporien is waargeneem in sommige pasiënte wat flukonasool ontvang en klinies beduidend is. Daarom moet die plasmakonsentrasies van siklosporien gemonitor word by alle pasiënte wat BIO FLUCONAZOLE IV ontvang.
Midasolam en triasolam – BIO FLUCONAZOLE IV verhoog die serumkonsentrasies van midasolam en triasolam en hul psigomotoriese effekte. Hierdie effek blyk meer uitgespreek te wees na orale toediening van BIO FLUCONAZOLE IV as met intraveneuse toediening van flukonasool. As 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, en 'n verhoogde risiko vir uveïtis. Pasiënte wat hierdie kombinasie ontvang moet noukeurig gemonitor word.
Takrolimus – Die konsentrasie van takrolimus word aansienlik deur BIO FLUCONAZOLE IV verhoog. Pasiënte wat hierdie kombinasie ontvang se serumkonsentrasie moet noukeurig gemonitor word en dosis vermindering kan nodig wees.
Die volgende medisyne verhoog die plasmakonsentrasies van BIO FLUCONAZOLE IV wanneer dit gelyktydig toegedien word:
Hidrochloortiasied.
Die volgende medisyne verlaag die plasmakonsentrasies van BIO FLUCONAZOLE IV wanneer dit gelyktydig toegedien word:
Rifampisien – Verhoogde metabolisme van BIO FLUCONAZOLE IV, wat lei tot laer plasmakonsentrasies van BIO FLUCONAZOLE IV.
Ander inligting met betrekking tot interaksies:
Gelyktydige toediening van flukonasool en nevirapien het gelei tot ongeveer 100 % toename in nevirapien blootstelling in vergelyking met historiese data waar nevirapien alleen toegedien is. As gevolg van die risiko van verhoogde blootstelling aan nevirapien, moet nevirapien en BIO FLUCONAZOLE IV met omsigtigheid gelyktydig toegedien word en pasiënte moet noukeurig gemonitor word.

MENSLIKE VOORTPLANTING:
Die gebruik van BIO FLUCONAZOLE IV tydens swangerskap het kongenitale afwykings veroorsaak en moet vermy word (kyk KONTRA-INDIKASIES).
BIO FLUCONAZOLE IV moet nie gegee word vir vroue wat borsvoed nie (kyk KONTRA-INDIKASIES).
BIO FLUCONAZOLE IV word uitgeskei in borsmelk in konsentrasies soortgelyk aan dié in plasma.

DOSIS EN GEBRUIKSAANWYSINGS:
Kriptokokkale meningitis
Volwassenes: Die aanvangsdosis is 400 mg op dag een; gevolg deur 200 mg tot 400 mg daagliks, afhangend van die kliniese respons. Die duur van behandeling hang af van die kliniese reaksie, maar is gewoonlik 8 weke, na afloop van behandeling met Amfoterisien B, of 10 weke met BIO FLUCONAZOLE IV as monoterapie.
Kinders ouer as 4 weke: 6 mg/kg/dag tot 12 mg/kg/dag afhangende van die erns van die infeksie.
Instandhoudingsbehandeling vir die voorkoming van kriptokokkale meningitis by pasiënte met VIGS
Volwassenes: 100 tot 200 mg per dag.
Sistemiese kandidiase
Volwassenes: Aanvangdosis is 400 mg op die eerste dag; gevolg deur 200 mg. Die dosis kan na 400 mg daagliks, verhoog word, afhangende van die kliniese reaksie.
Kinders ouer as 4 weke: 6 mg/kg/dag tot 12 mg/kg/dag afhangende van die erns van die infeksie.
Die behandelingstydperk hang af van die kliniese respons.
Orofaringeale kandidiase
Volwassenes: 50 tot 100 mg daagliks vir 7 tot 14 dae. Pasiënte wat se immuniteit verswak is mag langer behandelingstydperke benodig.
Om in terugslag te voorkom by pasiënte met VIGS: 150 mg BIO FLUCONAZOLE IV kan een keer per week toegedien word.
Kinders ouer as 4 weke: Aanvangdosis is 6 mg/kg op die eerste dag; gevolg deur 3 mg/kg een keer per dag. Die behandeling moet vir minstens 2 weke gegee word om die risiko van in 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 per dag kan gebruik word indien daar geen kliniese respons is na 14 dae op die laer dosis nie. Duur van behandeling is minstens 3 weke en vir nog 2 weke nadat 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, afhangende van die toestand van die pasiënt en die reaksie op die medisyne. Duur van behandeling is vir ten minste 3 weke en dan vir nog 2 weke nadat die simptome opgeklaar het.
Voorkoming van swaminfeksies by pasiënte wat sitotoksiese chemoterapie en/of bestraling ontvang
Volwassenes: 50 mg tot 400 mg daagliks, afhangende van die pasiënt se risiko om swaminfeksies te ontwikkel. Behandeling moet 'n paar dae voor die verwagte aanvang van neutropenie in aanvang neem en vir 7 dae voortgesit word nadat die neutrofieltelling tot bo 1000 selle per mm^3 gestyg het.
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 enkele dosis.
Herhalende vaginale kandidiase
Volwassenes: 150 mg toegedien as 'n enkele dosis, eenkeer per maand. Die duur van behandeling hang af van persoon tot persoon, maar wissel van 4 tot 12 maande.
Kandida balanitis
Volwassenes: 150 mg toegedien as 'n enkele dosis.
Dermale infeksies insluitend tinea pedis, tinea corporis, tinea cruris, tinea unguium (onigomikose) en dermale kandida infeksies
Volwassenes: 150 mg toegedien as 'n enkele dosis eenkeer per week. Duur van behandeling is gewoonlik 2 tot 4 weke, maar tinea pedis moet behandel word vir 6 weke. Die behandeling vir tinea unguium moet volgehou word totdat die besmette nael uitgegroei het en daar 'n nuwe onbesmette nael gegroei het. Vingernaels neem gewoonlik 3 tot 6 maande om uit te groei en toonnaels 6 tot 12 maande.
Veiligheid en doeltreffendheid van BIO FLUCONAZOLE IV by kinders, is nie vir die volgende indikasies vasgestel nie:
Herhalende vaginale kandidiase, kandida balanitis, dermale infeksies insluitende tinea pedis, tinea corporis, tinea cruris, tinea unguium (onychomycosis) en dermale candida infeksies.
Bejaardes: sien dosering van nierversaking.
Normale dosis vir bejaardes word aanbeveel, tensy die pasiënt se nierfunksie verswak is. In sulke gevalle moet die dosis of dosisinterval aangepas word.
Dosis in nierversaking
BIO FLUCONAZOLE IV moet met omsigtigheid gebruik word by pasiënte met verswakte nierfunksie.
BIO FLUCONAZOLE IV word deur die niere uitgeskei. 'n Vermindering in dosis of toename in dosisinterval word aanbeveel:
Die normale dosislading of aanvangsdosis moet op die eerste dag van behandeling gegee word.
Daaropvolgende dosisse moet volgens die kreatinienopruiming aangepas word.
Die normale dosis kan toegedien word indien die kreatinienopruiming > 50 ml/min is.
Indien die kreatinienopruiming < 50 ml/min is en die pasiënt nie op dialise is nie, kan 50 % van die normale dosis toegedien word.
Pasiënte wat gereelde hemodialise ondergaan moet na elke dialise sessie 'n standaard dosis BIO FLUCONAZOLE IV ontvang.

Die pasiënt se kreatinienopruiming kan bereken word deur die volgende gewysigde formule van Cockroft en Gault (vir gebruik by volwassenes) te gebruik:

$$eGFS\ (ml/min) = \frac{(140 - ouderdom) \times Gewig\ (kg)}{S_{cr}\ (\mu mol/L)}$$

eGFS = Geskatte Glomerulêre Filtrasie Spoed
S_{cr} = Serumkreatinien
Vir vroulike pasiënte vermenigvuldig die GFS met 0,85.

Die farmakokinetika van BIO FLUCONAZOLE IV is nie by kinders met verswakte nierfunksie ondersoek nie. Die daaglikse dosis moet in ooreenstemming met die riglyne vir volwassenes verlaag word, afhangende van die graad van nierontoereikendheid.
Die dosis van BIO FLUCONAZOLE IV en die duur van die behandeling moet bepaal word deur die area van infeksie en die individu se reaksie op die behandeling. Behandeling moet voortgesit word tot kliniese parameters en laboratoriumtoetse aandui dat aktiewe swaminfeksie opgeklaar het.
Pasiënte met VIGS en kriptokokkale meningitis of herhalende orofaringeale kandidiase benodig gewoonlik instandhoudingsterapie om 'n terugslag te voorkom.
Vir babas jonger as 2 weke moet die bogenoemde kinders se dosisse gebruik word, maar moet slegs elke 72 uur toegedien word. Vir babas tussen die ouderdomme van 2 tot 4 weke moet die dosis elke 48 uur gegee word. Die maksimum volwasse daaglikse dosis (400 mg) moet nie by kinders oorskry word nie.
Normale dosisse word vir bejaardes aanbeveel, tensy die pasiënt verswakte nierfunksie het. In hierdie geval is 'n aanpassing in dosis of dosisinterval nodig.
BIO FLUCONAZOLE IV
BIO FLUCONAZOLE IV word geformuleer in 0,9 % natriumchloriedoplossing. Elke 200 mg (100 ml bottel) bevat 15 mmol Na+ en 15 mmol Cl-.
Aangesien BIO FLUCONAZOLE IV as 'n verdunde soutoplossing beskikbaar is, behoort die tempo van toediening by pasiënte wat natrium- of vloeistofbeperking vereis noukeurig oorweeg te word.
BIO FLUCONAZOLE IV is verenigbaar met die volgende toedieningsvloeistowwe: dekstrose 20 %, ringers oplossing, normale soutoplossing, kaliumchloried in dekstrose en natriumbikarbonaat 4,2 %.
BIO FLUCONAZOLE IV kan teen 'n maksimum spoed van ongeveer 200 mg / uur deur 'n bestaande ingieting saam met een van die bogenoemde vloeistowwe toegedien word. Alhoewel geen spesifieke onverenigbaarhede opgemerk is nie, word vermenging met enige ander medisyne voor infusie nie aanbeveel nie.

NEWE-EFFEKTE:
Immuunstelsel versteurings
Minder algemeen: Hipersensitiwiteit (koors en kouekoors, veluitslag of jeuk). Anafilakse insluitende angioedeem, gesigedeem, pruritis, gloede.
Bloed en limfstelsel versteurings
Minder algemeen: Agranulositose, trombositopenie, leukopenie en neutropenie.
Endokrienstelsel versteurings
Minder algemeen: Hipercholesterolemie, hipertrigliseridemie, hipokalemie.
Vel en subkutane weefsel versteurings
Algemeen: Uitslag.
Minder algemeen: Afskilferende velsiektes insluitende Stevens-Johnsonsindroom en toksiese epidermis-nekrolise, urtikarie, droë vel, abnormale reuk en haarverlies.
Kardiale versteurings
Frekwensie onbekend: QTc-interval verlenging, torsades de pointes.
Senuweestelsel versteurings
Algemeen: Hoofpyn.
Minder algemeen: Vertigo, duiseligheid, konvulsies, slaaploosheid, senuweeagtigheid, moegheid, styfheid, ongemak, hiperkinesie.
Gastro-intestinale versteurings
Algemeen: Abdominale pyn, diarree, winderigheid, hardlywigheid, aptytverlies, naarheid, braking.
Minder algemeen: Dispepsie, smaakversteurings, dors.
Nier en urienweg versteurings
Minder algemeen: Poliurie, vroue seksuele disfunksie, bloeding tussen menstruasies, menoragie, leukoree.
Hepato-bilière versteurings
Algemeen: Lewertoksisiteit (insluitende verhoogde serumkonsentrasies van alkaliese fosfatase, bilirubien, ALT en AST).
Minder algemeen: Lewerversaking, hepatitis, hepatosellulêre nekrose, geelsug.
Oog versteurings
Minder algemeen: Abnormale sig.
Spier, bindweefsel- en been versteurings
Minder algemeen: Hipertonie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
(Kyk NEWE-EFFEKTE)
Simptome van oordosering:
Die volgende is aangemeld met oordosering van BIO FLUCONAZOLE IV: slaaploosheid, prikkelbaarheid, braking, diarree, abdominale pyn en of krampe, anoreksie, bultende fontanel, verhoging van alkaliese fosfate en gammaglutamiel transpeptidase, toename in serumkalsium, nierversaking, moegheid; gesigsuitslag, vel-eriteem, verspreide urtikarie, artralgie, jeuk, gevoelloosheid van die tong en terneergedruktheid.
Behandeling:
Behandeling is simptomaties en ondersteunend. Daar is geen spesifieke teenmiddel nie.
BIO FLUCONAZOLE IV word hoofsaaklik in die urien uitgeskei. Gedwonge waterafdrywing sal waarskynlik die uitskeidingstempo verhoog. Eliminasie van BIO FLUCONAZOLE IV kan deur hemodialise bewerkstellig word. Plasmavlakke kan ongeveer 50 % verlaag word deur 'n drie uur hemodialise sessie.

IDENTIFIKASIE:
BIO FLUCONAZOLE IV: Helder kleurlose tot liggeel oplossing.

AANBIEDING:
BIO FLUCONAZOLE IV word verpak in 100 ml deurskynende, wit, plastiek (LDPE) bottels. Elke bottel is toegedraai met 'n helder deurskynende polipropileen omhulsel.

BERGINGSINSTRUKSIES:
BIO FLUCONAZOLE IV: Bewaar teen of benede 30 °C. Moenie vries nie. Gooi enige oorblywende inhoud weg na gebruik.
HOU BUITE BEREIK VAN KINDERS

REGISTRASIENOMMER:
BIO FLUCONAZOLE IV: 42/20.2.2/0683

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