SOUTH AFRICAN PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

ASPEN FLUCONAZOLE 50 mg (capsule)

ASPEN FLUCONAZOLE 100 mg (capsule)

ASPEN FLUCONAZOLE 150 mg (capsule)

ASPEN FLUCONAZOLE 200 mg (capsule)

COMPOSITION

Each ASPEN FLUCONAZOLE 50 mg capsule contains 50 mg of fluconazole.

Each ASPEN FLUCONAZOLE 100 mg capsule contains 100 mg of fluconazole.

Each ASPEN FLUCONAZOLE 150 mg capsule contains 150 mg of fluconazole.

Each ASPEN FLUCONAZOLE 200 mg capsule contains 200 mg of fluconazole.

Excipients:

ASPEN FLUCONAZOLE 50 mg contains colloidal silicon dioxide, FD&C Red 3 (C.I. 45430), gelatin, lactose monohydrate, magnesium stearate, Patent Blue V (C.I. 42051), pregelatinised starch, sodium lauryl sulphate, titanium dioxide (C.I. 77891).

Contains sugar: Lactose monohydrate 57,40 mg

ASPEN FLUCONAZOLE 100 mg and ASPEN FLUCONAZOLE 200 mg contain colloidal silicon dioxide, gelatin, lactose monohydrate, magnesium stearate, Patent Blue V (C.I. 42051), pregelatinised starch, sodium lauryl sulphate, titanium dioxide (C.I. 77891).

Contains sugar:

ASPEN FLUCONAZOLE 100 mg: Lactose monohydrate 114,80 mg

ASPEN FLUCONAZOLE 200 mg: Lactose monohydrate 229,60 mg

ASPEN FLUCONAZOLE 150 mg contains colloidal silicon dioxide, gelatin, lactose monohydrate, magnesium stearate, pregelatinised starch, sodium lauryl sulphate, titanium dioxide (C.I. 77891).

Contains sugar: Lactose monohydrate 172,20 mg

CATEGORY AND CLASS

A 20.2.2 Antimicrobial (chemotherapeutic) agents: Fungicides

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Fluconazole is a triazole antifungal. It inhibits cytochrome P450 in the fungal membrane, which results in impairment of ergosterol synthesis. This results in alterations in membrane function and permeability and eventually death of the fungal cell. In yeast infections particularly Candida Albicans, fluconazole inhibits the transformation of blastospores into invasive mycelial form.

Pharmacokinetic properties

Fluconazole is well absorbed orally. A single administration of fluconazole orally in a fasting state, reaches peak plasma concentrations within 1 to 2 hours. Steady state concentrations are reached within 2 to 10 days depending on the loading dose given to a patient. Only about 11 % to 12 % of fluconazole is protein bound. Fluconazole is widely distributed in the body, including

the eye, peritoneal fluid, saliva, sputum and breast milk. Concentrations in the cerebrospinal fluid (CSF) range from 50 % to 90 % of plasma values. Fluconazole is excreted via the kidneys with an elimination half-life of about 30 hours, which is increased with impaired renal function. Fluconazole is removed by dialysis.

INDICATIONS

ASPEN FLUCONAZOLE 50 mg capsules, ASPEN FLUCONAZOLE 100 mg capsules and ASPEN FLUCONAZOLE 200 mg capsules are indicated for the treatment of:

- Cryptococcal meningitis and maintenance therapy to prevent regression of cryptococcal disease in patients with acquired immune deficiency syndrome (AIDS).
- Systemic and oropharyngeal candidiasis.
- Prevention of fungal infections in patients who are at risk of such infections as a result of cytotoxic chemotherapy and radiotherapy.

ASPEN FLUCONAZOLE 150 mg capsules are indicated for the treatment of:

- Dermatomycosis including tinea pedis, tinea corporis, tinea cruris, onychomycosis and dermal candida infections.
- Vaginal candidiasis and prophylaxis to reduce the incidence of recurrent vaginal candidiasis.

CONTRAINDICATIONS

ASPEN FLUCONAZOLE is contraindicated in:

- Patients with hypersensitivity to fluconazole or to triazole compounds, or to any of the excipients in ASPEN FLUCONAZOLE (see COMPOSITION).
- Concomitant use with astemizole, cisapride and terfenadine due to the risk of cardiac arrhythmias.
- Pregnancy and lactation (see HUMAN REPRODUCTION).

WARNINGS AND SPECIAL PRECAUTIONS

Hepatic function

ASPEN FLUCONAZOLE has been associated with cases of serious hepatic toxicity. Hepatotoxicity may be reversible on discontinuation of ASPEN FLUCONAZOLE therapy. Patients who already show abnormal liver function tests during ASPEN FLUCONAZOLE therapy should be monitored continuously. AIDS patients are prone to the development of severe cutaneous reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis during treatment. These patients should be monitored closely and ASPEN FLUCONAZOLE should be discontinued if bullous lesions or erythema multiforme develop.

In some patients, particularly those with underlying disease such as AIDS and cancer, abnormalities of hepatic, renal and haematological function have been observed during treatment with ASPEN FLUCONAZOLE.

Effects on ability to drive and use machines

Since adverse reactions such as dizziness has been reported in patients receiving ASPEN FLUCONAZOLE, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that ASPEN FLUCONAZOLE does not adversely affect their ability to do so (see SIDE EFFECTS).

Excipients

Lactose warning:

ASPEN FLUCONAZOLE contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take

ASPEN FLUCONAZOLE.

INTERACTIONS

ASPEN FLUCONAZOLE may have interactions with the following medicines:

- Rifampicin causes a decrease in ASPEN FLUCONAZOLE levels in plasma**.**
- Administration of hydrochlorothiazides with ASPEN FLUCONAZOLE has resulted in an increase in plasma ASPEN FLUCONAZOLE levels.
- Concurrent use of ASPEN FLUCONAZOLE with phenytoin, zidovudine, rifabutin, ciclosporin, warfarin and nortriptyline causes an increase in plasma concentration of these medicines**.** Prothrombin time must be carefully monitored in patients receiving warfarin together with ASPEN FLUCONAZOLE**.**
- ASPEN FLUCONAZOLE may decrease the clearance of theophylline, which may result in toxic levels in the body. Therefore theophylline concentrations should be monitored.
- The effectiveness of oral contraceptives may be decreased when taken together with ASPEN FLUCONAZOLE.
- Serious dysrhythmias have occurred in some patients receiving other azole antifungals in combination with terfenadine. Interaction studies have been conducted and no clinically significant drug interaction was present, however when terfenadine and ASPEN FLUCONAZOLE are given in combination, the patient should be carefully monitored.
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HUMAN REPRODUCTION

The safety of ASPEN FLUCONAZOLE in pregnancy and lactation has not been established (see CONTRAINDICATIONS).

DOSAGE AND DIRECTIONS FOR USE

Adults:

- **Vaginal candidiasis** - 150 mg (one capsule) orally as a single dose

- **Candida balanitis** - 150 mg (one capsule) orally as a single dose
- **Tinea pedis, cruris, corporis** - 150 mg (one capsule) orally once weekly for 2 to 4 weeks. Treatment for up to 6 weeks may be necessary for Tinea pedis
- **Tinea unguium or onychomycosis** - 150 mg (one capsule) orally once weekly until regrowth of a normal nail which may take 3 to 6 months for fingernails, and 6 to 12 months for toenails.

For cryptococcal meningitis the dose is 400 mg on the first day followed by 200 mg once daily. The dose may be increased to 400 mg depending on the patient's response. Duration of treatment for cryptococcal meningitis is 6 to 8 weeks.

For systemic candidiasis the dose is 400 mg on the first day followed by 200 mg daily. Duration of treatment is based on the clinical response.

Children:

Safety and efficacy in children has not been established.

Geriatrics:

The dosage is the same as for adults, but the possibility of decreased liver and kidney function should be considered, in which case the dosage must be adjusted.

Dosage in patients with impaired renal function:

ASPEN FLUCONAZOLE is cleared by renal excretion as unchanged medicine. In patients with impaired renal function, an initial loading dose of 50 mg to 400 mg is given. The daily dose thereafter is determined using the creatinine clearance. If the creatinine clearance is more than 50 ml per minute, the standard dose may be given. If the creatinine clearance is 11 ml to 50 ml per minute, then 50 % of the recommended dose is given. Patients receiving regular

haemodialysis should receive the standard dose.

SIDE EFFECTS

Gastrointestinal symptoms include:

- Abdominal pain
- Nausea
- Diarrhoea
- Flatulence
- Loss of appetite
- Vomiting

Skin reactions include:

- Toxic epidermal necrolysis
- Stevens-Johnson syndrome
- Rash

If rash develops which is considered attributable to ASPEN FLUCONAZOLE, further therapy should be avoided.

Other side effects include:

- Headache
- Dizziness
- Seizures
- Alopecia
- Leucopenia
- Thrombocytopenia
- Raised liver enzymes values

- Less frequent reports of anaphylaxis and angioedema

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Symptoms

A case of overdosage with fluconazole, as contained in ASPEN FLUCONAZOLE, has been reported. An HIV infected patient developed hallucinations and exhibited paranoid behaviour after administering 8 200 mg of fluconazole, as contained in ASPEN FLUCONAZOLE. The patient was admitted to hospital and recovered within 48 hours.

Treatment

Symptomatic treatment of an overdose may be adequate. Forced diuresis would increase elimination rate as ASPEN FLUCONAZOLE is excreted in the urine. Treatment would include haemodialysis.

IDENTIFICATION

ASPEN FLUCONAZOLE 50 mg:

A No. 4 capsule with a white opaque body and a dark blue cap containing a white to off-white powder.

ASPEN FLUCONAZOLE 100 mg:

A No. 2 capsule with a white opaque body and light blue cap containing a white to off-white powder.

ASPEN FLUCONAZOLE 150 mg:

A No. 1 capsule with a white opaque body and a white opaque cap containing a white to off-white powder.

ASPEN FLUCONAZOLE 200 mg:

A No. 0 capsule with a white opaque body and a blue cap containing a white to off-white powder.

PRESENTATION

ASPEN FLUCONAZOLE 50 mg:

14 capsules are packed in transparent polyvinyl chloride/polyvinylidene chloride or opaque polyvinyl chloride/ACLAR blister strips sealed with an aluminium foil backing. The blister strips are packed into a pre-printed unit cardboard carton together with a leaflet.

60 capsules are packed in a white cylindrical polypropylene securitainer sealed with a white cylindrical low-density polyethylene tamper evident Snap-On cap together with a white low-density polyethylene filler and a leaflet.

ASPEN FLUCONAZOLE 100 mg:

10 capsules are packed in colourless polyvinyl chloride/polyvinylidene chloride or transparent to opaque colourless polyvinyl chloride/ACLAR blister strips sealed with an aluminium foil backing. The blister strips are packed into a pre-printed unit cardboard carton together with a leaflet.

60 capsules are packed in a white cylindrical polypropylene container sealed with a white cylindrical low-density polyethylene tamper evident Snap-On cap together with a white low-density polyethylene filler and a leaflet.

ASPEN FLUCONAZOLE 150 mg:

1 or 4 capsules are packed in transparent polyvinyl chloride/polyvinylidene chloride or opaque polyvinyl chloride/ACLAR blister strips sealed with an aluminium foil backing. The blister strips

are packed into a pre-printed unit cardboard carton together with a leaflet.

60 capsules are packed in a white cylindrical polypropylene container sealed with a white cylindrical low-density polyethylene tamper evident Snap-On cap together with a white low-density polyethylene filler and a leaflet.

ASPEN FLUCONAZOLE 200 mg:

28 capsules are packed in transparent polyvinyl chloride/polyvinylidene chloride or opaque polyvinyl chloride/ACLAR blister strips sealed using an aluminium foil backing. The blister strips are packed into a pre-printed unit cardboard carton together with a leaflet.

60 capsules are packed in a white cylindrical polypropylene securitainer sealed with a white cylindrical low-density polyethylene tamper evident Snap-On cap together with a white low-density polyethylene filler and a leaflet.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C in a dry place.

Keep in the original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

ASPEN FLUCONAZOLE 50 mg: 37/20.2.2/0369

ASPEN FLUCONAZOLE 100 mg: 37/20.2.2/0370

ASPEN FLUCONAZOLE 150 mg: 37/20.2.2/0371

ASPEN FLUCONAZOLE 200 mg: 37/20.2.2/0372

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

Date of registration: 28 May 2004

Date of the most recently revised professional information as approved by the Authority:

28 May 2004

Botswana:	S2
ASPEN FLUCONAZOLE 50 mg:	BOT0801272
ASPEN FLUCONAZOLE 150 mg:	BOT0801274
ASPEN FLUCONAZOLE 200 mg:	BOT0801273

Namibia:	NS2
ASPEN FLUCONAZOLE 50 mg:	10/20.2.2/0523
ASPEN FLUCONAZOLE 150 mg:	10/20.2.2/0524
ASPEN FLUCONAZOLE 200 mg:	10/20.2.2/0525

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