CIANKIT

Azithromycin, Fluconazole & Secnidazole Tablets Combi-kit

COMPOSITION:

Each combi-kit contains:

(A) One Azithromycin Tablet USP

Each film coated tablet contains:

Azithromycin Dihydrate USP	
Eq to Azithromycin (Anhydrous)	1000 mg
Excipients	q.s

Colour: Titanium Dioxide BP

(B) One Fluconazole Tablet USP

Each uncoated tablet contains:

Fluconazole USP	150 mg
Excipients	q.s.

(C) Two Secnidazole Tablets

Each film coated tablet contains:

Secnidazole	1000 mg
Excipients	q.s.

Colour: Titanium Dioxide BP & Sunset Yellow

PHARMACODYNAMICS:

A. Azithromycin Tablets USP:

Pharmacotherapeutic group: antibacterials for systemic use; macrolides; azithromycin, ATC code: J01FA10

Mode of action:

Azithromycin is an azalide, a sub-class of the macrolides antibiotics. By binding to the 50S-ribosomal sub-unit, azithromycin avoids the translocation of peptide chains from one side of the ribosome to the other. As a consequence of this, RNA-dependent protein synthesis in sensitive organisms is prevented.

PK/PD relationship

For azithromycin the AUC/MIC is the major PK/PD parameter correlating best with the efficacy of azithromycin.

Mechanism of resistance:

Resistance to azithromycin may be inherent or acquired. There are three main mechanisms of resistance in bacteria: target site alteration, alteration in antibiotic transport and modification of the antibiotic.

Complete cross resistance exists among Streptococcus pneumoniae, betahaemolytic streptococcus of group A, Enterococcus faecalis and Staphylococcus aureus, including methicillin resistant S. aureus (MRSA) to erythromycin, azithromycin, other macrolides and lincosamides.

B. Fluconazole Tablets USP:

Pharmacotherapeutic group: Antimycotics for systemic use – triazole derivatives

ATC classification: J02A C01

Mode of action

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.

Fluconazole is highly specific for fungal cytochrome P-450 dependent enzymes. Fluconazole 50mg daily given for up to 28 days has been shown not to affect testosterone plasma concentrations in males or steroid concentrations in females of child-bearing age. Fluconazole 200-400mg daily has no clinically significant effect on endogenous steroid levels or on ACTH stimulated response in healthy male volunteers.

C. Secnidazole Tablets:

Secnidazole is the first nitroimidazole to offer a 3-day antiprotozoal activity from one single dose. With its prolonged half life, Secnidazole offers an effective treatment and thus ensures improved patient compliance because of the short duration of treatment with excellent therapeutic efficacy.

Secnidazole exhibits activity against anaerobic protozoa Entamoeba histolytica, Giardia lamblia and Trichomonas vaginalis.

PHARMACOKINETICS:

A. Azithromycin Tablets USP:

Absorption

After oral administration the bioavailability of azithromycin is approximately 37%. Peak plasma levels are reached after 2-3 hours (Cmax after a single dose of 500 mg orally was approximately 0.4 mg/l).

Distribution

Kinetic studies have shown markedly higher azithromycin levels in tissue than in plasma (up to 50 times the maximum observed concentration in plasma) indicating that the active substance is heavily tissue bound (steady state distribution volume of approximately 31 l/kg). In serum the protein binding of azithromycin is variable and depending on the serum concentration varies from 50% in 0.05 mg/l to 12% in 0.5 mg/l.

Excretion

Plasma terminal elimination half-life closely reflects the tissue depletion half-life of 2 to 4 days. Biliary excretion of azithromycin, predominantly in unchanged form, is a major route of elimination. The identified metabolites (formed by N- and O- demethylising, by hydroxylising of the desosamine and aglycone rings, and by the splitting of the cladinose conjugate) are microbiologically inactive.

After a 5 day treatment slightly higher (29%) AUC values were seen in the elderly volunteers (>65 years of age) compared to the younger volunteers (< 45 years of age). However these differences are not regarded as clinically relevant; therefore a dose adjustment is not recommended.

B. Fluconazole Tablets USP:

Absorption

After oral administration fluconazole is well absorbed, and plasma levels (and systemic bioavailability) are over 90% of the levels achieved after intravenous administration. Oral absorption is not affected by concomitant food intake. Peak plasma concentrations in the fasting state occur between 0.5 and 1.5 hours post dose with a plasma elimination half-life of approximately 30 hours. Plasma concentrations are proportional to dose. Ninety percent steady state levels are reached by day 4-5 with multiple once daily dosing. Administration of a loading dose (on day 1) of twice the usual daily dose enables plasma levels to approximate to 90% steady state level by day 2.

Distribution

The apparent volume of distribution approximates to total body water. Plasma protein binding is low (11-12%).

Fluconazole achieves good penetration in all body fluids studied. The levels of fluconazole in saliva and sputum are similar to plasma levels. In patients with fungal meningitis fluconazole levels in the CSF are approximately 80% of the corresponding plasma levels.

Elimination

The major route of excretion is renal with approximately 80% of the administered dose appearing in the urine as unchanged product. Fluconazole clearance is proportional to creatinine clearance. There is no evidence of circulating metabolites.

The long plasma elimination half-life provides the basis for single dose therapy for vaginal candidiasis, once daily and once weekly dosing for other indications.

Interaction studies with antipyrine indicate that fluconazole does not affect its metabolism.

C. Secnidazole Tablets:

Secnidazole is rapidly absorbed following oral administration. The maximum serum level is obtained after 3 hours following oral administration of 2 gm secnidazole. The plasma elimination half life is about 20 hours. The majority of Secnidazole is eliminated via urine (50% of the ingested dose is excreted within 120 hours).

The pharmacokinetic profile of secnidazole gives it the longest half-life of all the second generation nitroimidazoles, ensuring 72-hour therapeutic blood levels from a 2 gm single dose.

INDICATION:

CIANKIT is indicated for treatment of mixed vaginal infections or as empirical cure of suspected mixed vaginal infections such as vulvovaginitis, bacterial vaginosis and trichomoniasis; it is also indicated in syndromic management of pelvic inflammatory disease.

DOSAGE AND ADMINISTRATION:

Adults: 1 CIANKIT as single oral dose, or as prescribed. Both the partners should preferably be treated simultaneously.

CONTRA-INDICATIONS:

CIANKIT is contraindicated in patients with known hypersensitivity to this product or any of its ingredients, or to nitroimidazoles or macrolides. Co-administration of terfenadine and cisapride with fluconazole (in CIANKIT) is contraindicated.

CIANKIT is not advocated during pregnancy, lactation and in children.

SPECIAL WARNING AND PRECAUTION FOR USE:

Warnings:

Those who develop rashes due to fluconazole (in CIANKIT) must be monitored closely. Fluconazole (in CIANKIT) needs to be advocated with due precaution along with oral hypoglycemics, coumarins, phenytoin, cyclosporine, rifampicin, theophylline, astemizole, rifabutin, tacrolimus and short-acting benzodiazepines.

As azithromycin interacts with aluminium and magnesium-containing antacids, digoxin, ergot derivatives, triazolam and drugs metabolized by cytochrome P450 such as carbamazepine, cyclosporine, phenytoin, CIANKIT must be coadministered with care.

Secnidazole also has potential to interact with coumarins and hence CIANKIT must be coadministered with care along with such anticoagulants.

Alcohol beverages must be avoided whilst taking CIANKIT, and for three days thereafter since simultaneous intake of nitroimidazoles like secnidazole could result in abdominal cramps, flushing, nausea, vomiting, headaches and even psychotic reactions.

Precautions:

CIANKIT is to be advocated with due precaution in hepatic and renal disease, and potentially proarrhythmic conditions in view potential of fluconazole and azithromycin to induce liver and kidney dysfunction, and cardiac conduction abnormalities.

CIANKIT should be advocated with care in diarrhea since azithromycin usage could be associated with pseudomembranous colitis.

INTERACTION WITH OTHER MEDICINE AND CONCOMITANT USE:

Fluconazole (in CIANKIT) can interact with oral hypoglycemics, coumarins, phenytoin, cyclosporine, rifampicin, theophylline, astemizole, rifabutin, tacrolimus, terfenadine, cisapride and short-acting benzodiazepines.

Azithromycin (in CIANKIT) absorption can be reduced by antacids having magnesium or aluminium. Elevation of serum levels of digoxin, ergot derivatives, Triazolam and drugs metabolized by liver cytochrome P450 can occur with azithromycin (in CIANKIT).

Secnidazole (in CIANKIT) can potentiate the action of anticoagulants.

PREGNANCY AND LACTATION:

CIANKIT is not advocated during pregnancy and lactation.

EFFECT ON ABILITY TO DRIVE AND USE MACHINES:

When driving vehicles or operating machines it should be taken into account that occasionally dizziness or seizures may occur.

UNDESIRABLE EFFECT:

Single dose of 150 mg fluconazole (in CIANKIT) can cause mild to moderate headache, nausea, abdominal pain, diarrhea, dyspepsia, dizziness and taste perversion. Other rare side effects due to fluconazole (in CIANKIT) include vomiting, seizures, cardiac conduction abnormalities, skin lesions, hematopoietic disturbances, electrolyte and lipid changes.

Azithromycin (in CIANKIT) can cause gastrointestinal side effects such as nausea, vomiting, diarrhea and abdominal pain. Other adverse reactions due to azithromycin (in CIANKIT) include fatigue, asthenia, paresthesia, malaise, hypersensitivity and skin eruptions. Cholestatic jaundice, palpitations, chest pain and arrhythmias, genitourinary affections such as monilia, vaginitis, nephritis and acute renal failure, nervous system manifestations like dizziness, headache, vertigo, somnolence, hyperactivity, nervousness, agitation, syncope, aggressive reaction and anxiety, as well as hearing disturbances and taste perversion can occur with azithromycin (in CIANKIT). Azithromycin (in CIANKIT), like other antimicrobials, can cause pseudomembranous colitis.

Secnidazole (in CIANKIT) can cause mild side effects of gastrointestinal disturbances, and dizziness.

Rarely, angioedema and anaphylactic reactions can occur with CIANKIT ingredients.

OVERDOSE:

A. Azithromycin Tablets USP:

The undesirable effects at doses in excess of those recommended were similar to those after normal doses. The typical symptoms of an overdose with macrolide antibiotics include reversible loss of hearing, severe nausea, vomiting and diarrhoea. In cases of overdose, administration of medicinal charcoal and general symptomatic treatment as well as measures to support vital functions are indicated where necessary.

B. Fluconazole Tablets USP:

There have been reports of overdosage with fluconazole and hallucination and paranoid behaviour have been concomitantly reported

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

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

C. Secnidazole Tablets:

At therapeutic doses the secnidazole is well tolerated, however, if an overdose should keep watch on the patient, and presenting nausea, vomiting (or other toxicity data), it is taken to hospital and general measures of support.

In case of accidental or intentional massive dose try to remove the drug by vomiting or gastric lavage.

SHELF LIFE:

3 years

PACKAGING:

One Azithromycin Tablet USP, one Fluconazole Tablet USP & two Secnidazole Tablets are packed in a Alu-PVC blister and such 1 blister is packed in a carton along with insert.

STORAGE CONDITION:

Store in a dry place, below 30°C. Keep out of reach of children.

Marketed by :
MEDICARE LESOTHO PTY LTD.
MAIN STREET, HLOTSE.LERIBE LESOTHO
PHONE NUMBER: 00266 22400407/731.

Manufactured by :

CIAN HEALTHCARE LTD.
(An ISO 9001 : 2015 & WHO GMP Certified Co.)
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