VAMIADAR CAPSULE (Furazolidone 100mg BP)

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

VAMIADAR CAPSULE
Furazolidone

2. Qualitative and quantitative composition

Each capsule Contains:

Furazolidone BP	100 mg

3. Pharmaceutical form

Capsule
A light green and gray capsules with granular powder inside having “VAMIADAR” on the Gelatin shell

4. Clinical particulars

4.1 Therapeutic indications

Vamiadar is indicated in the treatment of amoebiasis, balantidiasis, giardiasis, trichomoniasis, Bacterial vaginosis, cholera, dysentery protozoales, bacterial or mixed origin of bacillary dysentery

4.2 Posology and method of administration

For oral administration:.

As directed by a the Physician

4.3 Contraindications

Blood dyscrasias, Hypersensitivity, Neurological Disease, Convulsions, porphyria, and Pregnancy. Not to be used in children below 1 year of age.

4.4 Special warnings and precautions for use

Regular clinical and laboratory monitoring (especially leucocyte count) are advised if administration of Vamiadar for more than 10 days is considered to be necessary and patients should be monitored for adverse reactions such as peripheral or central neuropathy (such as paraesthesia, ataxia, dizziness, convulsive seizures).

There is the possibility that after *Trichomonas vaginalis* has been eliminated a gonococcal infection might persist.

In patients undergoing haemodialysis, metronidazole and metabolites are efficiently removed during an eight-hour period of dialysis. Metronidazole should therefore, be re-administered immediately after haemodialysis.

No routine adjustment in the dosage of Vamiadar need be made in patients with renal failure undergoing intermittent peritoneal dialysis (IPD) or continuous ambulatory peritoneal dialysis (CAPD).

Significant cumulation may occur in patients with hepatic encephalopathy and the resulting high plasma concentrations of metronidazole may contribute to the symptoms of encephalopathy.

Vamiadar should be administered with caution to patients with hepatic encephalopathy. The daily dosage may be reduced to one third and may be administered once daily.

Due to inadequate evidence on the mutagenicity risk in humans (see section 5.3), the use of Vamiadar for longer treatment than usually required should be carefully considered.

Use with caution in pregnancy and with alcohol consumption.

Avoid tyramine and other high pressor amine containing foods and beverages, OTC appetite suppressants, cough and cold medications, and other medications unless prescribed by physician; also avoiding these products for at least 2 weeks after discontinuing furazolidone; asking health care professional to provide list of products that may or may not cause serious problems with Furazolidone.

4.5 Interaction with other medicinal products and other forms of interaction

Psychotic reactions have been reported in patients who were using metronidazole and disulfiram concurrently.

Some potentiation of anticoagulant therapy has been reported when metronidazole has been used with the warfarin type oral anti-coagulants. Dosage of the anticoagulant may require reducing. Prothrombin time should be monitored. No interactions have been reported of the heparin type.

Lithium retention accompanied by evidence of possible renal damage has been reported in patients treated simultaneously with lithium and metronidazole. Lithium treatment should be tapered or withdrawn before administering metronidazole.

Plasma concentration of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

Patients receiving phenobarbital metabolise metronidazole at a much greater rate than normally, reducing the half-life to approximately three hours.

Aspartate amino transferase assays may give spuriously low values in patients taking metronidazole, depending on the method used.

Clinicians who contemplate continuous therapy for the relief of chronic conditions, for periods no longer than those recommended, are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Patients receiving ciclosporin or tacrolimus with metronidazole are at risk of elevated ciclosporin / tacrolimus serum levels. Serum ciclosporin / tacrolimus and serum creatinine should be closely monitored when coadministration is necessary.

4.6 Pregnancy and lactation

There is inadequate evidence of the safety of metronidazole in pregnancy. Vamiadar should not therefore be given during pregnancy or during lactation unless the physician considers it essential, in these circumstances short, high dosage regimes are not recommended.

A significant amount of metronidazole is found in breast milk and breast feeding should be avoided after a large dose. This could give a bitter taste to the milk.

Pregnancy:

Furazolidone Studies in humans have not been done. However, teratogenic effects on the human fetus or newborn infants have not been reported. Studies in animals have not shown that furazolidone, given in doses far exceeding recommended human doses for long periods of time, causes adverse effects on the fetus.

It is not known whether furazolidone is distributed into breast milk. However, breast-feeding is not recommended in nursing infants up to 1 month of age because of the possibility of hemolytic anemia due to glutathione instability in the early neonatal period.

4.7 Effects on ability to drive and use machines

Patients should be warned about the potential for drowsiness, dizziness, confusion, hallucinations, convulsions or transient visual disorders, and advised not to drive or operate machinery if these symptoms occur.

4.8 Undesirable effects

The frequency of adverse events listed below is defined using the following convention:

very common (≥ 1/10); common (≥
1/100 to < 1/10); uncommon (≥
1/1,000 to < 1/100); rare (≥
1/10,000 to < 1/1,000);
very rare (< 1/10,000), not known (cannot be estimated from the available data).

Frequency, type and severity of adverse reactions in children are the same as in adults.

Serious adverse reactions occur very rarely with standard recommended regimens. However, clinicians who contemplate continuous therapy for the relief of chronic conditions, for periods longer than those recommended are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Blood and lymphatic system disorders:

Very rare: agranulocytosis, neutropenia, thrombocytopenia and pancytopenia, often reversible on drug withdrawal, although fatalities have occurred.

Not known: A moderate leucopenia has been reported in some patients but the white cell count has always returned to normal before or after treatment has been completed.

Immune system disorders:

Rare: Anaphylaxis

Not known: urticaria, angioedema and fever

Metabolism and nutrition disorders:

Not known: anorexia

Psychiatric disorders:

Very rare: psychotic disorders, including confusion and hallucinations

Not known: depressed mood

Nervous system disorders:

Very rare:

• Encephalopathy (eg. confusion, fever, headache, hallucinations, paralysis, light sensitivity, disturbances in sight and movement, stiff neck) and subacute cerebellar syndrome (eg. ataxia, dysathria, gait impairment, nystagmus and tremor) have been reported very rarely which may resolve on discontinuation of the drug.

• Drowsiness, dizziness, convulsions, headache, ataxia, inco-ordination of movement

Not known:

• During intensive and/or prolonged metronidazole therapy a few instances of peripheral neuropathy or transient epileptiform seizures have been reported. In most cases neuropathy disappeared after treatment was stopped or when dosage was reduced.

• Aseptic meningitis has been reported

Eye disorders:

Very rare: transient visual disorders such as diplopia and myopia have been reported

Not known: Optic neuropathy/neuritis has been reported

Gastrointestinal disorders:

Not known: Unpleasant taste in the mouth, oral mucositis, furred tongue, nausea, vomiting, gastro-intestinal disturbances such as epigastric pain and diarrhoea.

Hepatobiliary disorders:

Very rare:

• Abnormal liver function tests, increase in liver enzymes (AST, ALT, alkaline phosphatase), cholestatic or mixed hepatitis, and hepatocellular liver injury, jaundice and pancreatitis, reversible on drug withdrawal have been reported.

• Cases of liver failure requiring liver transplant have been reported in patients treated with metronidazole in combination with other antibiotic drugs.

Skin and subcutaneous tissue disorders:

Very rare: skin rashes, pustular eruptions, pruritus, flushing

Not known: Erythema multiforme may occur, which may be reversed on drug withdrawal. Stevens-Johnson syndrome or toxic epidermal necrolysis.

Musculoskeletal, connective tissue and bone disorders:

Very rare: myalgia, arthralgia

Renal and urinary disorders:

Very rare: darkening of the urine (due to metronidazole metabolite)

FUMET contains glycerol, which can cause headache, gastro-intestinal disturbance and diarrhoea.

The para hydroxyl benzoates used in Vamiadar may cause immediate or delayed hypersensitivity reactions.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

Uneventful recovery has followed attempts at suicide with quantities of between 6 and 12g. There is no specific treatment for gross overdose of Metronidazole, however, early gastric lavage and symptomatic support is advised.

There is no specific antidote for Furazolidone overdosage. In cases of suspected massive overdose, symptomatic and supportive treatment should be instituted.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

ANTIINFECTIVES AND ANTISEPTICS; **FURAZOLIDONE**

ATC code:

FURAZOLIDONE: G01AX06

A nitrofuran derivative with antiprotozoal and antibacterial activity. Furazolidone has a broad antibacterial spectrum covering the majority of gastrointestinal tract pathogens

including E. coli, staphylococci, Salmonella, Shigella, Proteus, Aerobacter aerogenes, Vibrio cholerae and Giardia lamblia. Its bactericidal activity is based upon its interference with DNA replication and protein production; this antimicrobial action minimizes the development of resistant organisms.

Furazolidone and its related free radical products are believed to bind DNA and induce cross-links. Bacterial DNA is particularly susceptible to this drug leading to high levels of mutations (transitions and transversions) in the bacterial chromosome.

5.2 Pharmacokinetic properties

Furazolidone:

Furazolidone is well absorbed following oral administration. Furazolidone is rapidly and extensively metabolized; the primary metabolic pathway identified begins with nitro-reduction to the aminofuran derivative.

Two major metabolites are produced: 3-amino-2-oxazolidone (AOZ) or beta-hydroxyethylhydrazine (HEH). AOZ is responsible for monoamine oxidase inhibition. Detoxification and elimination of the drug is done primarily by conjugation with glutathione.

Half Life

Furazolidone Half Life is 10 minutes.

Elimination

More than 65% of an oral dose was recovered in the urine of humans and animals. Also found in feces

Radio labeled drug studies indicate that Furazolidone is well absorbed following oral administration. Limited pharmacokinetic information is available in humans; however, recent data have reported that variable plasma concentrations were measured in subjects given therapeutic doses. One study of 8 meningitis patients showed that cerebral spinal fluid (CSF) concentrations reached levels comparable to serum concentrations. Also, significant concentrations have been measured in the bile of rats.

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5.3 Preclinical safety data

Several studies in rodents, given chronic, high-dose Furazolidone orally, have shown that this medication is tumorigenic. Furazolidone has been shown to cause mammary neoplasia in two strains of rats. In addition, Furazolidone has been shown to cause pulmonary tumors in mice.

6. Pharmaceutical particulars

6.1 List of excipients

Maize Starch,
Gelatine,
Lactose,
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at a temperature not exceeding 30^0 C.
Protect from light.

6.5 Nature and contents of container

ALU-PVC Blister pack of 1 X 10 Capsules in a printed monocarton

6.6 Special precautions for disposal and other handling

Keep out of the reach of children..

7. Marketing authorization holder

TUYIL PHARMACEUTICAL INDUSTRY LIMITED
22 New Yidi Road, Ilorin, Kwara State