Tiniflox®

swipha

Tinidazole + Ofloxacin 600/200 mg Tablets

Composition

Each film coated tablet contains:
Tinidazole ph. Eur……600mg
Ofloxacin Ph. Eur.....…200mg

Description
White oblong tablet with 600 + 200 Swipha above and break score line below

Clinical Pharmacology

Mechanism of action

Ofloxacin:
Ofloxacin inhibits bacterial DNA replication by inhibiting bacterial topoisomerases, particularly DNA gyrase and topoisomerase IV. It is active after oral administration. Therapeutic doses of Ofloxacin are devoid of pharmacological effects on the voluntary or autonomic nervous system.
The main mechanism of bacterial resistance to Ofloxacin involves one or more mutations in the target enzymes, which generally confer resistance to other active substances in the class. Efflux pump and impermeability mechanisms of resistance have also been described and may confer variable resistance to active substances in other classes.

Tinidazole:
Tinidazole is active against both protozoa and obligate anaerobic bacteria. The activity against protozoa involves Trichomonas vaginalis, Entamoeba histolytica and Giardia lamblia. The mode of action of Tinidazole against anaerobic bacteria and protozoa involves penetration of the drug into the cell of the micro-organism and subsequent damage of DNA strands or inhibition of their synthesis.
Tinidazole is active against Helicobacter pylori, Gardnerella vaginalis and most anaerobic bacteria including Bacteroides fragilis, Bacteroides melaninogenicus, Bacteroides spp., Clostridium spp., Eubacterium spp., Fusobacterium spp., Peptococcus spp., Peptostreptococcus spp. and Veillonella spp. Helicobacter pylori (H.pylori) is associated with acid peptic disease including duodenal ulcer and gastric ulcer in which about 95% and 80% of patients respectively are infected with this agent. Clinical evidence has shown that the combination of Tinidazole with omeprazole and clarithromycin eradicates 91-96% of H.pylori isolates.

Pharmacokinetics
Absorption:
The administration of oral doses to fasting volunteers was followed by a rapid and almost complete absorption of Ofloxacin. The peak plasma concentration after a single oral dose of 200mg averaged 2.6 micrograms/ml and was reached within one hour. The plasma elimination half-life was 5.7 to 7.0 hours and was not dose related.
Tinidazole is rapidly and completely absorbed following oral administration. In studies with healthy volunteers receiving 2g Tinidazole orally, peak serum levels of 40-51 micrograms/ml were achieved within two hours and decreased to between 11-19 micrograms/ml at 24 hours. Plasma levels decline slowly and Tinidazole can be detected in plasma at concentrations of up to 1 microgram/ml at 72 hours after oral administration.

Distribution:
The apparent distribution volume of Ofloxacin was 120 litres. The plasma concentration did not materially rise with repeat doses (accumulation factor for twice daily dosage: 1.5).
Tinidazole is widely distributed in all body tissues and also crosses the blood brain barrier, obtaining clinically effective concentrations in all tissues. The apparent volume of distribution is about 50 litres. About 12% of plasma Tinidazole is bound to plasma protein.

Biotransformation:
The biotransformation of Ofloxacin was below 5%. The two main metabolites found in the urine were N- desmethyl-ofloxacin and Ofloxacin-N-oxide.
Tinidazole is significantly metabolized in humans prior to excretion. Tinidazole is partly metabolized by oxidation, hydroxylation, and conjugation.

Elimination:
Excretion of Ofloxacin is primarily renal. Between 80 and 90% of the dose were recovered from the urine as unchanged substance.
Tinidazole is excreted by the liver and kidneys. Studies in healthy patients have shown that over 5 days, 60- 65% of an administered dose is excreted by the kidneys with 20-25% of the administered dose excreted as unchanged Tinidazole. Up to 5% of the administered dose is excreted in the faeces.

Indications:
Tiniflox® tablets are indicated for the treatment of a wide variety of infections caused by susceptible Gram-positive and Gram-negative organisms along with anaerobes and protozoa.
Such as: Cystitis Pyelonephritis, Urethritis, Amebiasis, Trichomoniasis, Bacterial Vaginosi, Skin & tissue infections

Dosage and Administration
1 tablet to be taken twice daily or as prescribed by a physician.

Interactions

Antacids, Sucralfate, Metal Cations, Multivitamins:
Quinolones form chelates with alkaline earth and transition metal cations. Administration of quinolones with antacids containing calcium, magnesium, or aluminum, with sucralfate, with divalent or trivalent cations such as iron, or with multivitamins containing zinc, may substantially interfere with the absorption of quinolones resulting in systemic levels considerably lower than desired. These agents should not be taken within the two-hour period before or within the two-hour period after Ofloxacin administration.

Alcohols, Disulfiram
Alcoholic beverages and preparations containing ethanol or propylene glycol should be avoided during Tinidazole therapy and for 3 days afterward because abdominal cramps, nausea, vomiting, headaches, and flushing may occur. Psychotic reactions have been reported in alcoholic patients using metronidazole and disulfiram concurrently. Though no similar reactions have been reported with Tinidazole, Tinidazole should not be given to patients who have taken disulfiram within the last two weeks.

Contraindication

Ofloxacin
The use of Ofloxacin is contraindicated as follows:
- Hypersensitivity to the active substance, to any other fluoroquinolone antibacterials, or to any of the excipients
- In patients with a history of epilepsy or an existing central nervous system disorder with a lowered seizure threshold.
- In patients with a history of tendon disorders related to fluoroquinolone administration
- In children or growing adolescents, and in pregnant or breastfeeding women, since animal experiments do not entirely exclude the risk of damage to the growth-plate cartilage in the growing organism cannot be entirely excluded
- In patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity, because they may be prone to haemolytic reactions when treated with quinolone antibacterial agents

Tinidazole
Hypersensitivity to the active substance or to any of the excipients as with other drugs of similar structure. Tinidazole is contraindicated in patients having, or with a history of blood dyscrasia, although no persistent haematological abnormalities have been noted in clinical or animal studies.
Tinidazole should be avoided in patients with organic neurological disorders.
Tinidazole, other 5-nitroimidazole derivatives or any of the components of this product should not be administered to patients with known hypersensitivity to the drug.
Use of Tinidazole is contraindicated during the first trimester of pregnancy and nursing mothers.

Warnings & Precautions

Ofloxacin:
Ofloxacin tablets are not the drug of first choice in pneumonia caused by Streptococcus pneumoniae or Chlamydia pneumoniae.

Methicillin-resistant S. aureus:
Are very likely to possess co-resistance to fluoroquinolones, including Ofloxacin. Therefore Ofloxacin is not recommended for the treatment of known or suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to Ofloxacin (and commonly recommended antibacterial agents for the treatment of MRSA-infections are considered inappropriate).

Resistance to fluoroquinolones of E. coli:
The most common pathogen involved in urinary tract infections varies across regions. Prescribers are advised to take into account the local prevalence of resistance in E. coli to fluoroquinolones.
Cases of severe bullous skin reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with Ofloxacin. Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Tendonitis:
Tendonitis, rarely observed with quinolones, may occasionally lead to rupture involving Achilles tendon in particular. Tendinitis and tendon rupture, sometimes bilateral, may occur within 48 hours of starting treatment with Ofloxacin and have been reported up to several months after discontinuation of Ofloxacin. The risk of tendinitis and tendon rupture is increased in patients aged over 60 years and in patients using corticosteroids. The daily dose should be adjusted in elderly patients based on creatinine clearance. Close monitoring of these patients is therefore necessary if they are prescribed Ofloxacin. All patients should consult their physician if they experience symptoms of tendinitis. If tendinitis is suspected, treatment with Ofloxacin must be halted immediately, and appropriate treatment (e.g. immobilization) must be initiated for the affected tendon.

Hypersensitivity:
Hypersensitivity and allergic reactions have been reported for fluoroquinolones after first administration. Anaphylactic and anaphylactoid reactions can progress to life-threatening shock, even after the first administration. In these cases Ofloxacin should be discontinued and suitable treatment (e.g. treatment for shock) should be initiated.

Diseases caused by Clostridium difficile:
Diarrhoea, especially if severe, persistent and/or bloody, occurring during or after treatment with Ofloxacin (including several weeks after treatment), may indicate a condition caused by Clostridium difficile, the most severe form of which is pseudo-membranous colitis (CDAD). CDAD may range in severity from mild to life threatening, the most severe form of which is pseudo membranous colitis. It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with Ofloxacin. If pseudo-membranous colitis is suspected, treatment should be discontinued immediately. Appropriate specific antibiotic therapy must be started without delay (e.g. oral vancomycin, oral teicoplanin or metronidazole). Medicinal products that inhibit peristalsis are contraindicated in such cases.

Patients predisposed to seizures:
Quinolones may lower the seizure threshold and may trigger seizures. Ofloxacin is contraindicated in patients with history epilepsy or with a known predisposition to seizures.Patients with a known predisposition to seizures may include those with pre-existing central nervous system lesions, concomitant treatment with fenbufen and similar non-steroidal anti-inflammatory drugs (NSAIDs), or with drugs which lower the cerebral seizure threshold, such as theophylline.
In case of convulsive seizures, treatment with Ofloxacin should be discontinued.

Patients with impaired renal function:
Since Ofloxacin is eliminated primarily via the kidneys, the dose should be adjusted in patients with impaired renal function.

Patients with history of psychotic disorder:
Psychotic reactions have been reported in patients receiving fluoroquinolones including Ofloxacin. In some cases these have progressed to suicidal thoughts or self-endangering behavior including suicide attempt, sometimes after a single dose of Ofloxacin. In the event that a

patient develops these reactions, Ofloxacin should be discontinued and appropriate measures instituted.Ofloxacin should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric diseases.

Patients with impaired liver function:
Ofloxacin should be used with caution in patients with impaired liver function, as liver damage may occur.
Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with fluoroquinolones. Patients should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, pruritus or tender abdomen.

Patients treated with vitamin K antagonists:
Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with fluoroquinolones, including Ofloxacin, in combination with a vitamin K antagonist (e.g. warfarin), coagulation tests should be monitored when these drugs are given concomitantly.

Myasthenia gravis:
Fluoroquinolones, including Ofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Post marketing serious adverse reactions, including deaths and the requirement for respiratory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Ofloxacin is not recommended in patients with a known history of myasthenia gravis.

Super infection:
As with other antibiotics, the use of Ofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms, resistant strains of some organisms or Candida. Repeated evaluation of the patient's condition is essential and periodic in-vitro susceptibility tests may be useful. If secondary infection occurs during therapy, appropriate measures should be taken.

Prevention of photosensitization:
Photosensitization has been reported with Ofloxacin. It is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), during treatment and for 48 hours following treatment discontinuation in order to prevent photosensitization.

QT interval Prolongation
Very rare cases of QT interval prolongation have been reported in patients taking fluoroquinolones.

Therefore, caution should be taken when using fluoroquinolones, including Ofloxacin, in patients with known risk factors for prolongation of the QT interval such as elderly patients and women may be more sensitive to QTc-prolonging medications. Uncorrected electrolyte imbalance (e.g. hypokalemia, hypomagnesemia) causes congenital long QT syndrome. Concomitant use of drugs that are known to prolong the QT interval (e.g. Class IA and III anti- arrhythmic, tricyclic antidepressants, macrolides, antipsychotics)

Cardiac Disease (e.g. heart failure, myocardial infarction, bradycardia)

Dysglycaemia:
As with all quinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g., glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In these diabetic patients, careful monitoring of blood glucose is recommended.

Peripheral neuropathy:
Sensory or sensorimotor peripheral neuropathy has been reported in patients receiving fluoroquinolones, including Ofloxacin, which can be rapid in its onset. Ofloxacin should be discontinued if the patient experiences symptoms of neuropathy. This would minimise the possible risk of developing an irreversible condition.

Patients with glucose-6-phosphate-dehydrogenase deficiency:
Patients with latent or diagnosed glucose-6-phosphate-dehydrogenase deficiency may be predisposed to haemolytic reactions if they are treated with quinolones. Therefore if Ofloxacin has to be used in these patients, potential occurrence of haemolysis should be monitored.

Interference with laboratory tests:
In patients treated with Ofloxacin, determination of opiates or porphyrin levels in urine may give false- positive results. It may be necessary to confirm positive opiate or porphyrin screens by more specific methods.
Vision disorders:
If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

Tinidazole:
As with related compounds, alcoholic beverages should be avoided during Tinidazole therapy because of the possibility of a disulfiram-like reaction (flushing, abdominal cramps, vomiting, and tachycardia). Alcohol should be avoided until 72 hours after discontinuing Tinidazole.
Drugs of similar chemical structure have also produced various neurological disturbances such as dizziness, vertigo, incoordination and ataxia. If during therapy with Tinidazole abnormal neurological signs develop, therapy should be discontinued.
Carcinogenicity has been seen in mice and rats treated chronically with metronidazole, another nitroimidazole agent. Although carcinogenicity data is not available for Tinidazole, the two drugs are structurally related and therefore there is a potential for similar biological effects. Mutagenicity results with tinidazole were mixed (positive and negative).The use of Tinidazole for longer treatment than usually required should be carefully considered.

Pregnancy and Lactation
Pregnancy:
This medicine is not recommended for use by pregnant women, unless absolutely necessary. Kindly consult your physician for all risks and benefits.

Lactation:
Ofloxacin is excreted into human breast milk in small amounts. Because of the potential for arthropathy and other serious toxicity in the nursing infant, breast-feeding should be discontinued during treatment with Ofloxacin.
Tinidazole is excreted in breast milk. Tinidazole may continue to appear in breast milk for more than 72 hours after administration. Women should not nurse until at least 3 days after having discontinued taking Tinidazole.

Adverse Reaction:
Reactions may include nausea, headache, insomnia, external genital pruritus in women, dizziness, vaginitis, diarrhea, vomiting, constipations, central nervous system, and hypersensitivity reaction.

Symptoms of overdosage and Antidotes:

Ofloxacin:

Symptoms
The most important signs to be expected following acute overdose are CNS symptoms such as confusion, dizziness, impairment of consciousness. Convulsive seizures increases in QT interval as well as gastrointestinal reactions such as nausea and mucosal erosions.
Other CNS effects such as confusional state, convulsion, hallucination, and tremor have been observed in post marketing experience.

Management
In the case of overdose steps to remove any unabsorbed Ofloxacin e.g. gastric lavage, administration of adsorbants and sodium sulphate, if possible during the first 30 minutes, are recommended; antacids are recommended for protection of the gastric mucosa.
In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. A fraction of Ofloxacin may be removed from the body with haemodialysis. Peritoneal dialysis and CAPD are not effective in removing Ofloxacin from the body. No specific antidote exists.

Tinidazole:
There is no specific antidote for the treatment of overdosage with tinidazole; therefore, treatment should be symptomatic and supportive. Gastric lavage may be helpful. Hemodialysis can be considered because approximately 43% of the amount present in the body is eliminated during a 6-hour hemodialysis session.

THIS PRODUCT CONTAINS A FLUOROQUINOLONE (OFLOXACIN) WHICH HAS POTENTIAL TO CAUSE PERMANENT PERIPHERAL NEUROPATHY

Storage Condition:
Protect from light
store below 30°C

Presentation
Packs of 1 x 10 and 2 x 10 tablets

NAFDAC REG NO.: A4-4153

Medicine: Keep out of reach of children

swipha

Manufactured by:
swiss pharma nigeria Ltd.,
5, Dopemu Road, Agege, Lagos.

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