

SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of medicinal product

Ciprofloxacin & Tinidazole Tablets (TINACIP)

2. Composition:

Each film coated tablet contains:

Ciprofloxacin Hydrochloride BP Eq. To

Ciprofloxacin BP.....500 mg

Tinidazole BP.....600 mg

Excipients Q.S.

Colors: Sunset Yellow & Titanium Dioxide BP

3. Pharmaceutical Form:

Solid Oral- Film coated Tablet

4. Clinical Particulars

4.1 Therapeutic Indications:

Ciprofloxacin and Tinidazole 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.

4.2 Posology and Administration

Posology

Ciprofloxacin and Tinidazole Tablets should be taken 1 hour before or 2 hours after meals with a glass of water. Adults One tablet twice daily for 5-10 days, depending on severity and response. Children Not recommended for children.

Method of administration

Oral use.

4.3 Contraindication

Ciprofloxacin is contraindicated in persons with a history of hypersensitivity to ciprofloxacin, any member of the quinolone class of antibacterial, or any of the product components Concomitant administration with tizanidine is contraindicated In patients with a previous history of hypersensitivity to tinidazole or other nitroimidazole derivatives. Reported reactions have ranged in severity from urticaria to Stevens-Johnson syndrome during first trimester of pregnancy In nursing mothers: Interruption of breastfeeding is recommended during tinidazole therapy and for 3 days following the last dose.

4.4 Special Warning & precautions for use

Disabling and Potentially Irreversible Serious Adverse Reactions, Including Tendinitis and Tendon Rupture, Peripheral Neuropathy, and CNS Effects

Fluoroquinolones, including ciprofloxacin, have been associated with disabling and potentially irreversible serious adverse reactions from different body systems that can occur together. Commonly seen adverse reactions include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and CNS effects (hallucinations, anxiety, depression, insomnia, severe headaches, and confusion). These reactions can occur within hours to weeks after starting ciprofloxacin. Patients of any age or without pre-existing risk factors have experienced these adverse reactions.

Discontinue ciprofloxacin immediately at the first signs or symptoms of any serious adverse reaction. In addition, avoid the use of fluoroquinolones, including ciprofloxacin, in patients who have experienced any of these serious adverse reactions associated with fluoroquinolones.

Tendinitis and Tendon Rupture

Fluoroquinolones, including ciprofloxacin, have been associated with an increased risk of tendinitis and tendon rupture in all ages. This adverse reaction most frequently involves the Achilles tendon, and has also been reported with the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendons. Tendinitis or tendon rupture can occur, within hours or days of starting ciprofloxacin, or as long as several months after completion of fluoroquinolone therapy. Tendinitis and tendon rupture can occur bilaterally.

The risk of developing fluoroquinolone-associated tendinitis and tendon rupture is increased in patients over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Other factors that may independently increase the risk of tendon rupture include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis. Tendinitis and tendon rupture have also occurred in patients taking fluoroquinolones who do not have the above risk factors. Discontinue ciprofloxacin immediately if the patient experiences pain, swelling, inflammation or rupture of a tendon. Avoid fluoroquinolones, including ciprofloxacin, in patients who have a history of tendon disorders or have experienced tendinitis or tendon rupture.

Peripheral Neuropathy

Fluoroquinolones, including ciprofloxacin, have been associated with an increased risk of peripheral neuropathy. Cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons, resulting in paraesthesia, hypoesthesia, dysaesthesia and weakness, have been reported in patients receiving fluoroquinolones, including ciprofloxacin. Symptoms may occur soon after initiation of ciprofloxacin and may be irreversible in some patients.

Discontinue ciprofloxacin immediately if the patient experiences symptoms of peripheral neuropathy including pain, burning, tingling, numbness, and/or weakness, or other alterations in sensations including light touch, pain, temperature, position sense and vibratory sensation, and/or motor strength in order to minimise the development of an irreversible condition. Avoid fluoroquinolones,

including ciprofloxacin, in patients who have previously experienced peripheral neuropathy.

CNS Effects:

Fluoroquinolones, including ciprofloxacin, have been associated with an increased risk of CNS effects, including convulsions, increased intracranial pressure (including pseudotumour cerebri), and toxic psychosis. Ciprofloxacin may also cause CNS events, including nervousness, agitation, insomnia, anxiety, nightmares, paranoia, dizziness, confusion, tremors, hallucinations, depression, and psychotic reactions progressing to suicidal ideations/thoughts and self-injurious behaviour such as attempted or completed suicide. These reactions may occur following the first dose. Advise patients receiving ciprofloxacin to inform their healthcare provider immediately if these reactions occur, discontinue the drug, and institute appropriate care. Ciprofloxacin, like other fluoroquinolones, is known to trigger seizures or lower the seizure threshold. As with all fluoroquinolones, use ciprofloxacin with caution in epileptic patients and patients with known or suspected CNS disorders that may predispose to seizures or lower the seizure threshold (e.g. severe cerebral arteriosclerosis, previous history of convulsion, reduced cerebral blood flow, altered brain structure, or stroke), or in the presence of other risk factors that may predispose to seizures or lower the seizure threshold (e.g. certain drug therapy, renal dysfunction). Use ciprofloxacin when the benefits of treatment exceed the risks, since these patients are endangered because of possible undesirable CNS side effects. Cases of status epilepticus have been reported. If seizures occur, discontinue ciprofloxacin.

Exacerbation of Myasthenia Gravis

Fluoroquinolones, including ciprofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Postmarketing serious adverse reactions, including deaths and requirement for ventilatory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Avoid ciprofloxacin in patients with known history of myasthenia gravis.

Tinidazole Neurological Adverse Reactions

Convulsive seizures and peripheral neuropathy, the latter characterised mainly by numbness or paraesthesia of an extremity, have been reported in patients treated with tinidazole. The appearance of abnormal neurologic signs demands the prompt discontinuation of tinidazole therapy.

Vaginal Candidiasis

The use of tinidazole may result in Candida vaginitis. In a clinical study of 235 women who received tinidazole for bacterial vaginosis, a vaginal fungal infection developed in 11 (4.7%) of all study subjects.

Blood Dyscrasia

Tinidazole should be used with caution in patients with evidence of or a history of blood dyscrasia.

4.5 Interaction with other medicinal products and other forms of interaction

Contraindication of concomitant use

Ciprofloxacin is an inhibitor of human CYP450 1A2 (CYP1A2)-mediated metabolism. Co-administration of ciprofloxacin with other drugs primarily metabolised by CYP1A2 results in increased plasma concentrations of these drugs and could lead to clinically significant adverse events of the co-administered drug.

Tinidazole

Although not specifically identified in studies with tinidazole, the following drug interactions were reported for metronidazole, a chemically-related nitroimidazole. Therefore, these drug interactions may occur with tinidazole.

4.6 Fertility, Pregnancy and lactation

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Ciprofloxacin should not be used during pregnancy unless the potential benefit justifies the potential risk to both foetus and mother. An expert review of published data on experiences with ciprofloxacin use during pregnancy by TERIS (the Teratogen Information System) concluded that therapeutic doses during pregnancy are unlikely to pose a substantial teratogenic risk (quantity and quality of data = fair), but the data are insufficient to state that there is no risk.

Lactating Women Ciprofloxacin

Ciprofloxacin is excreted in human milk. The amount of ciprofloxacin absorbed by the nursing infant is unknown. Because of the potential risk of serious adverse reactions (including articular damage) in infants nursing from mothers taking ciprofloxacin, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Tinidazole

Tinidazole is excreted in breast milk. Tinidazole may continue to appear in breast milk for more than 72 hours after administration. Interruption of breastfeeding is recommended during tinidazole therapy and for 3 days following the last dose.

4.7 Effects on ability to drive and use machines

Due to its neurological effects, ciprofloxacin may affect reaction time. Thus, the ability to drive or to operate machinery may be impaired.

Drugs of similar chemical structure, including tinidazole, have been associated with various neurological disturbances such as dizziness, vertigo, ataxia, peripheral neuropathy (paraesthesia, sensory disturbances, hypoesthesia) and rarely convulsions. If any abnormal neurological signs develop during tinidazole therapy, the drug should be discontinued.

4.8 Undesirable effects

- Disabling and Potentially Irreversible Serious Adverse Reactions
- Tendinitis and Tendon Rupture
- Peripheral Neuropathy
- CNS Effects
- Exacerbation of Myasthenia Gravis
- Other Serious, and Sometimes Fatal, Adverse Reactions
- Hypersensitivity Reactions
- Hepatotoxicity
- Serious Adverse Reactions with Concomitant Theophylline
- Clostridium difficile-associated Diarrhoea
- Prolongation of the QT Interval
- Musculoskeletal Disorders in Paediatric Patients and Arthropathic Effects in Animals
- Photosensitivity/Phototoxicity
- Development of Drug-resistant Bacteria

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS)

<https://pv.pharmacyboardkenya.org>

4.9 Overdose

Ciprofloxacin:

In the event of acute overdosage, reversible renal toxicity has been reported in some cases. Empty the stomach by inducing vomiting or by gastric lavage. Observe the patient carefully and give supportive treatment, including monitoring of renal function, urinary pH and acidify, if required, to prevent crystalluria and administration of magnesium, aluminium- or calcium-containing antacids, which can reduce the absorption of ciprofloxacin. Adequate hydration must be maintained. Only a small amount of ciprofloxacin (less than 10%) is removed from the body after haemodialysis or peritoneal dialysis.

Tinidazole

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Ciprofloxacin

Pharmacotherapeutic group: Fluoroquinolones, **ATC code:** J01 MA02

The bactericidal action of ciprofloxacin results from inhibition of the enzymes, topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair and recombination. The mechanism of action of fluoroquinolones, including ciprofloxacin, is different from that of penicillins, cephalosporins, aminoglycosides, macrolides and tetracyclines; therefore, microorganisms resistant to these classes of drugs may be susceptible to ciprofloxacin. There is no known cross-resistance between ciprofloxacin and other classes of antimicrobials. In vitro resistance to ciprofloxacin develops slowly by multiple-step mutations.

Tinidazole

Pharmacotherapeutic group: Anti-infective for systemic use; **ATC code:** J 01 XD02

Tinidazole is an antiprotozoal, antibacterial agent. The nitro-group of tinidazole is reduced by cell extracts of *Trichomonas*. The free nitro-radical generated as a result of this reduction may be responsible for the antiprotozoal activity. Chemically reduced tinidazole was shown to release nitrites and cause damage to purified bacterial DNA in vitro. Additionally, the drug caused DNA base changes in bacterial cells and DNA strand breakage in mammalian cells. The mechanism by which tinidazole exhibits activity against *Giardia* and *Entamoeba* species is not known. Culture and sensitivity testing of bacteria are not routinely performed to establish the diagnosis of bacterial vaginosis; standard methodology for the susceptibility testing of potential bacterial pathogens, i.e. *Gardnerella vaginalis*, *Mobiluncus* spp. or *Mycoplasma hominis*, has not been defined. The following in vitro data are available, but their clinical significance is unknown. Tinidazole is active in vitro against most strains of the following organisms that have been reported to be associated with bacterial vaginosis: Tinidazole does not appear to have activity against most strains of vaginal lactobacilli.

5.2 Pharmacokinetic properties

Ciprofloxacin

Absorption

Ciprofloxacin given as an oral tablet is rapidly and well absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability is approximately 70%, with no substantial loss by first-pass metabolism.

Distribution

The binding of ciprofloxacin to serum proteins is 20-40%, which is not likely to be high enough to cause significant protein-binding interactions with other drugs. After oral administration, ciprofloxacin is widely distributed throughout the body. Tissue concentrations often exceed serum concentrations in both men and women, particularly in genital tissue, including the prostate. Ciprofloxacin is present in active form in the saliva, nasal and bronchial secretions, mucosa of the sinuses, sputum, skin blister fluid, peritoneal fluid, bile, and prostatic secretions. Ciprofloxacin has also been detected in the lungs, skin, fat, muscle, cartilage and bone. The drug diffuses into the cerebrospinal fluid (CSF); however, CSF concentrations are generally less than 10% of peak serum concentrations. Low levels of the drug have been detected in the aqueous and vitreous humours of the eye.

Metabolism

Four metabolites have been identified in human urine, which together account for approximately 15% of an oral dose. The metabolites have antimicrobial activity, but are less active than unchanged ciprofloxacin. Ciprofloxacin is an inhibitor of human cytochrome (CY) P450 1A2 (CYP1A2)-mediated metabolism. Co-administration of ciprofloxacin with other drugs primarily metabolised by CYP1A2 results in increased plasma concentrations of these drugs and could lead to clinically significant adverse events of the co-administered drug.

Excretion

The serum elimination half-life in subjects with normal renal function is approximately 4 hours. Approximately 40-50% of an orally administered dose is excreted in the urine as unchanged drug. After a 250 mg oral dose, urine concentrations of ciprofloxacin usually exceed 200 µg/mL during the first 2 hours, and are approximately 30 µg/mL at 8-12 hours after dosing. The urinary excretion of ciprofloxacin is virtually complete within 24 hours after dosing. The renal clearance of ciprofloxacin, which is approximately 300 ml/minute, exceeds the normal glomerular filtration rate of 120 ml/minute. Thus, active tubular secretion would seem to play a significant role in its elimination. Co-administration of probenecid with ciprofloxacin results in about a 50% reduction in the ciprofloxacin renal clearance and a 50% increase in its concentration in the systemic circulation. Although bile concentrations of ciprofloxacin are several-fold higher than serum concentrations after oral dosing, only a small amount of the dose administered is recovered from the bile as unchanged drug. An additional 1-2% of the dose is recovered from the bile in the form of metabolites. Approximately 20-35% of an oral dose is recovered from the faeces within 5 days after dosing. This may arise from either biliary clearance or transintestinal elimination.

Tinidazole**Absorption**

After oral administration, tinidazole is rapidly and completely absorbed. A bioavailability study of tinidazole tablets was conducted in adult healthy volunteers. All subjects received a single oral dose of 2 g (four 500 mg tablets) of tinidazole following an overnight fast. Oral administration of four 500 mg tablets of tinidazole

under fasted conditions produced a mean peak plasma concentration (C_{max}) of 47.7 (±7.5) µg/ml with a mean time to peak concentration (T_{max}) of 1.6 (±0.7) hours, and a mean area under the plasma concentration time curve (AUC, 0-infinity) of 901.6 (±126.5) µg.hr/mL at 72 hours. The elimination half-life (T_{1/2}) was 13.2 (±1.4) hours. Mean plasma levels decreased to 14.3 µg/mL at 24 hours, 3.8 µg/mL at 48 hours and 0.8 µg/mL at 72 hours following administration. Steady-state conditions are reached in 2½ - 3 days of multi-day dosing.

Administration of tinidazole tablets with food resulted in a delay in T_{max} of approximately 2 hours and a decline in C_{max} of approximately 10%, compared with fasted conditions. However, administration of tinidazole with food did not affect AUC or T_{1/2} in this study. In healthy volunteers, administration of crushed tinidazole tablets in artificial cherry syrup after an overnight fast had no effect on any pharmacokinetic parameter as compared with tablets swallowed whole under fasted conditions.

Distribution

Tinidazole is distributed into virtually all tissues and body fluids and also crosses the bloodbrain barrier. The apparent volume of distribution is about 50 litres. Plasma protein binding of tinidazole is 12%. Tinidazole crosses the placental barrier and is secreted in breast milk.

Metabolism

Tinidazole is significantly metabolised in humans prior to excretion. Tinidazole is partly metabolised by oxidation, hydroxylation and conjugation. Tinidazole is the major drug-related constituent in plasma after human treatment, along with a small amount of the 2hydroxymethyl metabolite. Tinidazole is biotransformed mainly by CYP3A4. In an in vitro metabolic drug interaction study, tinidazole concentrations of up to 75 µg/mL did not inhibit the enzyme activities of CYP1A2, CYP2B6, CYP2C9, CYP2D6, CYP2E1 and CYP3A4. The potential of tinidazole to induce the metabolism of other drugs has not been evaluated.

Elimination

The plasma half-life of tinidazole is approximately 12-14 hours. Tinidazole is excreted by the liver and the kidneys. Tinidazole is excreted in the urine mainly as unchanged drug (approximately 20- 25% of the administered dose). Approximately 12% of the drug is excreted in the faeces.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics

6. Pharmaceutical Particulars:

6.1 List of Excipients:

Starch

Purified Water
Magnesium Stearate
Colloidal silicon dioxide
Cross carmellose Sodium
Sunset Yellow

6.2 Incompatibilities: None

6.3 Shelf Life: 36 months.

6.4 Special precautions for storage

Store in a cool and dry place below 30 °C, protect from light

6.5 Nature and contents of the container

10 x1X 10 tablets Alu. PVC Blister.

7. Marketing Authorization Holder And Manufacturing Site Addresses

Marketing Authorization Holder:

Simba Pharmaceuticals Limited, Tulsi Business Park, Chady Road, Off Airport Road, Syokimau, Mavoko, Machakos County P.O. Box 1541-00606 Nairobi, Kenya.

8. MARKETING AUTHORIZATION NUMBER

Simba Pharmaceuticals Limited, Tulsi Business Park, Chady Road, Off Airport Road, Syokimau, Mavoko, Machakos County P.O. Box 1541-00606 Nairobi, Kenya.

9. MANUFACTURER

Aksharam Pharma Pvt. Ltd Plot No,1&2, Akshar Ind,Estate, Rajkot Highway Road, Opp. Tri-Mandir,.Kherali, Dist. Surendranagar(363020), Gujarat, India

10. DATE OF REVISION OF THE TEXT

17/6/2026