KINODROX®

Prulifloxacin film-coated tablets

DESCRIPTION

Kinodrox® (Prulifloxacin) is an antibacterial agent of the fluoroquinolone group.
Kinodrox® is available for oral administration in yellow oblong-shaped, scored film-coated tablets, containing 600 mg of prulifloxacin.
Inactive ingredients include: Lactose monohydrate; Microcrystalline cellulose; Croscarmellose sodium; Povidone; Anhydrous colloidal silica and Magnesium stearate.
The film coating consists of: Hypromellose; Propylene glycol; Titanium dioxide (E171); Talc and Ferric oxide (E172).

CLINICAL PHARMACOLOGY

Mechanism o Action:
Prulifloxacin is a prodrug. Following oral administration, prulifloxacin is absorbed in the gastrointestinal tract and rapidly converted by esterases to the active metabolite, ulifloxacin. Ulifloxacin is a broad-spectrum oral fluoroquinolone that prevents bacterial DNA replication and transcription through the inhibition of the bacterial DNA gyrase.

Antibacterial Spectrum:
The *in vitro* antimicrobial activity studies were performed using ulifloxacin. Prulifloxacin showed potent and broad-spectrum antibacterial activity against Gram-negative and Gram-positive bacteria.
Gram-negative bacteria including community and nosocomial isolates of: *Escherichia coli; Klebsiella spp.; Proteus spp.; Providencia spp.; Moraxella catarrhalis; Morganella spp.; Haemophilus spp. and Pseudomonas aeruginosa.*
Gram-positive organisms including: *Methicillin- or Oxacillin-susceptible Staphylococcus aureus ; Enterococcus spp. and Streptococcus pneumoniae.*

Pharmacokinetics:
After administration of a single oral dose of prulifloxacin 600 mg in young healthy volunteers, the peak plasma concentration (C_{max}) of ulifloxacin (1.6 µg/mL) was achieved in a median time to C_{max} (T_{max}) of 1 hour. The area under the plasma concentration / time curve from zero to infinity (AUC_{∞}) was 7.3 µg.h/mL, and AUC_{∞} values showed linearity over a dose range of 300-600 mg. Ulifloxacin is ≈ 45% bound to serum proteins *in vivo*. It is extensively distributed throughout tissues with an apparent volume of distribution of 1231 L after a single dose of prulifloxacin 600 mg and shows good penetration into many body tissues.
The elimination half-life ($t_{1/2}$) of ulifloxacin after single-dose prulifloxacin 300-600 mg ranged from 10.6 to 12.1 hours.
After absorption from the gastrointestinal tract, prulifloxacin undergoes extensive first-pass metabolism (hydrolysis by esterases, mainly paraoxonase to form ulifloxacin). Unchanged ulifloxacin is predominantly eliminated by renal excretion.

INDICATIONS AND USAGE

Kinodrox® is indicated for the treatment of infections caused by susceptible germs, in the following conditions:
- Acute uncomplicated lower urinary tract infections (cystitis)
- Complicated lower urinary tract infections
- Acute exacerbation of chronic bronchitis
- Acute bacterial rhinosinusitis
- Traveler's diarrhea

DOSAGE AND ADMINISTRATION

For adult patients, the indicated dosage is as follows:
- Patients with acute uncomplicated lower urinary tract infections (cystitis): a single 600 mg tablet
- Patients with complicated lower urinary tract infections: one 600 mg tablet once a day for a maximum treatment period of 10 days
- Patients with acute exacerbation of chronic bronchitis: one 600 mg tablet once a day for a maximum treatment period of 10 days
- Patients with acute bacterial rhinosinusitis: one 600 mg tablet once a day for a treatment period of 10 days
- Patients with traveler's diarrhea: a 600 mg tablet once a day for 3 days.

Treatment duration in complicated lower urinary tract infections and acute exacerbation of chronic bronchitis depends on the severity of the disease and on the patient's clinical outcome and must be continued for at least 48–72 hours after remission/recovery of the symptoms.
Kinodrox® tablets should be swallowed whole with water, taking food intake into consideration (see drug interactions).
ince there are no specific studies, it is impossible to determine the dosage in patients with renal impairment (patients with creatinine clearance < 60 ml/min) and in patients with hepatic impairment. Therefore, in these patients, the dosage should be adjusted.

CONTRAINDICATIONS

The use of Kinodrox® is contraindicated in the following conditions:
- Hypersensitivity to prulifloxacin, to other quinolone antibacterial agents or to any of the excipients
- Pre-pubertal children or adolescents below the age of 18 years with incomplete skeletal development
- Patients with anamnesis of tendon diseases related to the administration of quinolones
- Patients with celiac disease
- Pregnancy and lactation

WARNINGS AND PRECAUTIONS

CNS disorders: Convulsions have been reported in patients receiving quinolones. Prulifloxacin must be used with caution in patients with CN disorders that may predispose to convulsions or lower the seizure threshold.

Cardiovascular disorders: Preclinical studies have not shown prulifloxacin effect on the QTc interval. However, this possibility cannot be excluded, as this effect has been observed with medications of the same therapeutic group. Therefore, in patients with hypokalemia and hypocalcemia or in patients who suffer from rhythm disorders, the use of quinolones should be carefully evaluated, with monitoring of the QTc interval where appropriate.

Tendinopathy and tendon rupture: After the administration of other drugs of the same therapeutic group, tendinitis may rarely occur.
Most frequently affected is the Achilles tendon, which may rupture. The risk of tendinitis and tendon rupture is increased in elderly patients and patients under corticosteroid treatment. Patients should be advised to discontinue the treatment in case of signs of tendon inflammation, myalgia, pain or articular inflammation and to rest the concerned limb until the diagnosis of tendinitis has been excluded.

Pseudo-membranous colitis: Treatment with antimicrobial agents, including quinolones, may cause the development of pseudo-membranous colitis. Therefore, this possibility should be considered in case of diarrhea following the administration of antibiotics.

De iciency in G6PD: When treated with antimicrobial agents of the quinolone group, patients with latent or known deficiencies in glucose-6-phosphate dehydrogenase activity are predisposed to hemolytic reactions and for this reason prulifloxacin should be administered with caution.

Rhabdomyolysis: As reported for other quinolones, rhabdomyolysis characterized by myalgia, asthenia, increased CPK and myoglobin plasma values and rapid deterioration of renal function may rarely occur. In these cases, the patient should be carefully monitored and appropriate measures must be taken, including the possibility of treatment discontinuation.

Crystalluria: The use of quinolones is occasionally correlated to the appearance of crystalluria; patients under treatment with medicinal products belonging to this therapeutic group should maintain an adequate water balance to avoid excessive urine concentration.

Hepatic Impairment: The tolerability and efficacy of prulifloxacin in patients with hepatic function impairment have not been assessed.

Phototoxicity: As with other quinolones, exposure to the sun or ultraviolet rays may cause phototoxicity reactions in patients treated with prulifloxacin. Excessive exposure to the sun or ultraviolet rays should be avoided during treatment with prulifloxacin; in case of phototoxicity reactions, treatment should be discontinued.

Pregnancy and lactation: No clinical data are available concerning the use of prulifloxacin during confirmed pregnancy. Animal studies did not indicate teratogenic effects. Other reproductive toxicity effects were only observed in cases of maternal toxicity. Nevertheless, in rats, prulifloxacin has been observed to cross the placental barrier and pass in large quantities into breast milk. As with other quinolones, prulifloxacin has been shown to cause arthropathies in young animals and therefore its use is contraindicated during pregnancy and nursing.

Ability to drive and use machines: Quinolones can cause dizziness and lightheadedness and therefore patients should be aware of how they react to the treatment before driving or using machines or beginning activities that require attention and coordination.

Galactose intolerance: The medicinal product contains lactose; therefore patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not use the medicinal product.

DRUG INTERACTIONS

Cimetidine, antacids containing Al and Mg or preparations containing iron and calcium: The co-administration of prulifloxacin with these products reduces the absorption of prulifloxacin; therefore prulifloxacin should be administered 2 hours before or at least 4 hours after administration of these compounds.

Food/Milk: Concomitant ingestion of prulifloxacin and milk causes a decrease in the area under the concentration/time curve (AUC) and reduces the urinary elimination of prulifloxacin, while the ingestion of food delays and reduces peak levels.

Probenecid: The urinary excretion of prulifloxacin decreases when it is administered together with probenecid.

Fenbu en: The concomitant administration of fenbufen with certain quinolones can cause increased risk of convulsions; the administration of prulifloxacin and fenbufen should therefore be carefully evaluated.

Hypoglycemic agents: Quinolones may cause hypoglycemia in diabetic patients under treatment with hypoglycemic agents.

Theophylline: Concomitant administration of prulifloxacin and theophylline may cause a slightly decreased theophylline clearance that should have no clinical significance. However, as for other quinolones, theophylline plasma levels should be monitored in patients with metabolic disorders or presenting risk factors.

War arin: Quinolones may enhance the effects of oral anticoagulants such as warfarin and its derivatives; when these medicinal products are administered together with prulifloxacin, the close monitoring of the prothrombin test or the conduct of appropriate coagulation tests are recommended.

Nicardipine: Preclinical data have shown that nicardipine may potentiate the phototoxicity of prulifloxacin.

ADVERSE REACTIONS

The undesirable effects stated below were reported during the clinical trials carried out on prulifloxacin. Most of the adverse events were of mild or moderate intensity.
Rate values used are as follows: very common (≥ 10%), common (from 1% to 10%), uncommon (from 0.1% to 1%), rare (from 0.01% to 0.1%) and very rare (< 0.01%, including isolated reports).

General disorders and administration site condition:
Rare: fever.
Nervous system disorders:
Uncommon: headache, dizziness
Rare: altered taste
Psychiatric disorders:
Rare: sleep disorders, drowsiness, lightheadedness
Ear and labyrinth disorders:
Rare: hearing impairment
Ocular disorders:
Rare: ocular hyperemia
Gastrointestinal disorders:
Common (only for prolonged treatment): epigastralgia, nausea
Uncommon: diarrhea, epigastralgia, nausea, gastritis and vomiting
Rare: abdominal pain, gastrointestinal disorders, angular stomatitis, dyspepsia, flatulence, indigestion, oral cavity discomfort, oral moniliasis, glossitis, gastric dilation.
The rate of epigastralgia and nausea may increase during prolonged treatment.
Musculoskeletal and connective tissue disorders:
Rare: muscular spasms, rhabdomyolysis
Skin and subcutaneous tissue disorders:
Uncommon: pruritus, skin rash
Rare: facial eczema, phototoxicity and urticaria
Vascular disorders:
Rare: hot flush
Laboratory analysis:
Rare: increase in gamma GTs levels, increase in bilirubin levels
Metabolic and nutritional disorders:
Uncommon: anorexia
The following adverse reactions have been reported very rarely (<0.01%):
Anaphylactic/anaphylactoid reaction, tevens–Johnson syndrome, hypoglycemia, hypoesthesia, drug-induced dermatitis.
Treatment with prulifloxacin may be associated with asymptomatic crystalluria with no change in creatinine levels, with alterations in hepatic function parameters and with eosinophilia. In the observed cases, these alterations were asymptomatic and transient.
During treatment with prulifloxacin, the development of adverse reactions and altered laboratory parameters not mentioned above, but reported with other quinolones, cannot be excluded.

OVERDOSE

There is no information regarding overdose in humans. Prulifloxacin has been tested in healthy volunteers at a dose of up to 1200 mg/ day for 12 days with a good tolerability.
In the event of acute overdosage, the stomach should be emptied by inducing vomiting or by gastric lavage; the patient should be carefully observed and given supportive treatment.

STORAGE CONDITIONS

tore in a dry place below 30°C, protected from light. Do not refrigerate.

PRESENTATION

Kinodrox® is available in blister packs of 5 tablets.

This is a medicament

-A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
-Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
-The doctor and the pharmacist are experts in medicine, its benefits and risks.
-Do not by yourself interrupt the period of treatment prescribed.
-Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children.

Do not use after expiry date.

Manufactured in Zouk Mosbeh, Lebanon, by
ALGORITHM S.A.L.
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