Matador®

دار الدواء
Dar Al Dawa

Levofloxacin Hemihydrate

DESCRIPTION:
Matador® contains levofloxacin, a synthetic antibacterial fluoroquinolone.

PHARMACOLOGY:
As a fluoroquinolone antibacterial agent, levofloxacin inhibits bacterial DNA synthesis by acting on the DNA gyrase complex and topoisomerase IV. Levofloxacin is highly bactericidal *in vitro*. Its spectrum covers many Gram-positive and Gram-negative bacteria such as staphylococci, streptococci including pneumcocci, enterobacteriaceae, *Haemophilus influenzae*, non-fermentative Gram-negative bacteria and atypical microorganisms. There is generally no-cross resistance between levofloxacin and other classes of antibacterial agents. Nosocomial infections due to *Pseudomonas aeruginosa* may require combination therapy.
Following oral administration, levofloxacin is rapidly absorbed. The absolute bioavailability is approximately 100%. Food has little effect on the absorption of levofloxacin. Approximately 30-40% of levofloxacin are bound to serum protein. Steady state is achieved within 3 days. Penetration into bone tissue, blister fluid and lung tissue is good, but is poor into cerebro-spinal fluid. Levofloxacin is metabolised to a very small extent, the two metabolites account for <5% of the dose excreted in urine. Levofloxacin is eliminated relatively slowly from the plasma ($t_{1/2}$: 6-8 h). Excretion is primarily by the renal route (>85% of the administrated dose). With decreasing renal function, renal elimination and clearance are decreased and elimination half-lives increased (for a creatinine clearance comprised between 20-40 ml/min, $t_{1/2}$ is 27 hours).

INDICATIONS:
Matador® is indicated for the treatment of the following infections due to levofloxacin-susceptible microorganisms:
- Acute sinusitis.
- Acute exacerbation of chronic bronchitis.
- Community-acquired pneumonia.
- Complicated urinary tract infections including pyelonephritis.
- Skin and soft tissue infections.
- Prostatitis.

CONTRAINDICATIONS:
Matador® is contraindicated:
- In patients hypersensitive to levofloxacin, other quinolones or to any of its excipients.
- In patients with epilepsy.
- In patients with history of tendon disorders related to fluoroquinolone administration.
- In children or adolescents.
- During pregnancy and in breast-feeding women.

SIDE EFFECTS:
Please tell your physician or pharmacist, if you experience any adverse effect with the use of this product.
Frequencies of undesirable effects: common (>1/100 and <1/10), uncommon (>1/1000 and <1/100), rare (>1/10 000 and <1/1 000), very rare (<1/10 000), including isolated reported.
The following undesirable effects may occur with the use of **Matador®**:
- Gastrointestinal system: Common: Nausea, diarrhea; Uncommon: Anorexia, vomiting, dyspepsia, abdominal pain; Rare: bloody diarrhea which in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis; Very rare: Hypoglycemia particularly in diabetic patients.
- Skin and allergic reactions: Uncommon: Rash, pruritus; Rare: Urticaria, bronchospasm/dyspnea; Very rare: Quincke's oedema (swelling of the face, tongue, throat or larynx), hypotension, anaphylactic/oid shock, photosensitization; Isolated cases of severe bullous eruptions such as Steven's Johnson syndrome (skin and mucous membrane bullous reactions), toxic epidermal necrolysis (Lyells' syndrome, i.e., bullous reactions) and erythema exudativum multiforme (red inflammatory rash with formation of blisters). Muco-cutaneous and anaphylactic/anaphylactoid reactions may sometimes occur even after the first dose.
- Nervous system: Uncommon: Headache, dizziness/vertigo, drowsiness and insomnia; Rare: Depression, anxiety, psychotic reactions (with e.g. hallucinations), paresthesia, tremor, agitation, confusion, convulsion; Very rare: Hypoesthesia, visual and auditory disturbances, test and smell disorders.
- Cardiovascular system: Rare: Tachycardia, hypotension; Very rare: Shock anaphylactic/anaphylactoid; Isolated cases: QT-interval prolongation (see section Overdose).
- Muscle and skeleton: Rare: Arthralgia, myalgia, tendon disorders including tendinitis (inflammation of tendons, e.g. Achilles tendon); Very rare: Tendon rupture, muscular weakness which may be of special importance in patients with myasthenia gravis; Isolated cases of rhabdomyolysis.
- Liver and kidney: Common: Increase in liver enzymes (transaminases ALT and AST); Uncommon: Increase in bilirubin and serum creatinine; Very rare: hepatitis and acute kidney failure.
- Blood: Uncommon: Eosinophilia and leukopenia; Rare: Neutropenia and thrombocytopenia; Very rare: Agranulocytosis; Isolated cases of hemolytic anemia and pancytopenia.
- Others: Uncommon: Asthenia, fungal overgrowth and proliferation of other resistant microorganisms; Very rare: Allergic pneumonitis, fever. Other possible undesirable effects related to the class of fluoroquinolones: Very rare: Extrapyramidal symptoms and other disorders of muscular coordination, hypersensitivity vasculitis and attacks of porphyria in patients with porphyria.

WARNINGS AND PRECAUTIONS:
- In patients predisposed to seizures, for example in case of simultaneous medications (see interactions), and as with other quinolones, levofloxacin should be used with extreme caution.
- Diarrhea, particularly if severe, persistent and/or bloody, during or after treatment with levofloxacin, may be symptomatic of pseudo-membranous colitis due to *Clostridium difficile*. If pseudo-membranous colitis is suspected levofloxacin must be stopped immediately.
- Tendinitis, rarely observed with quinolones, may occasionally lead to rupture involving Achilles tendon in particular. This undesirable effect may occur within 48 hours of starting of treatment and may be bilateral. Elderly patients are more prone to tendinitis. The risk of tendon rupture may be increased by coadministration of corticosteroids. If tendinitis is suspected, treatment with levofloxacin must be stopped IMMEDIATELY and the affected tendons must be put at rest.
- In patients with renal impairment, since levofloxacin is excreted mainly by the kidneys, the dose of levofloxacin should be adjusted.
- Although photosensitization is very rare with levofloxacin, it is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays.
- As with other antibiotics, the use of levofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during treatment, appropriate measures should be taken.
- Patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity may be prone to hemolytic reactions when treated with quinolone antibacterial agents. This has to be taken into consideration when using levofloxacin.

Driving:
Levofloxacin may cause undesirable affects such as dizziness, vertigo, drowsiness and visual disturbances, which may constitute a risk in situations such as driving a car or operating machinery.

DRUG INTERACTIONS:
In order to avoid possible interactions with other medicines, inform your physician or pharmacist about any other current treatment.
- There is no clinically relevant interaction with food. It is recommended that preparations containing divalent or trivalent cations such as iron salts or magnesium- or aluminium-containing antacids should not be taken 2 hours before or after levofloxacin administration, because of a possible reduction in absorption. The bioavailability of levofloxacin is significantly reduced when administered together with sucralfate, so it is recommended to administer sucralfate 2 hours after the levofloxacin administration.
- No pharmacokinetic interactions of levofloxacin were found with theophylline in a clinical study. However, a pronounced lowering of the cerebral seizure threshold may occur when quinolones are given concurrently with theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs or other agents, which lower the seizure threshold.
- Caution should be exercised when levofloxacin is co-administered with drugs that affect the tubular renal secretion such as probenecid and cimetidine, especially in renally impaired patients.
- Increased coagulation tests (PT/INR) and/or bleeding, which may be severe, have been reported in patients treated with levofloxacin in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests, therefore, should be monitored in patients treated with vitamin K antagonists.

DOSAGE AND ADMINISTRATION:
Strictly follow the recommended dosage unless directed otherwise by the physician.
Dosage and duration of treatment in adults with normal renal function (creatinine clearance >50 ml/min):
- Acute sinusitis: 500 mg once daily for 10 to 14 days.
- Acute exacerbation of chronic bronchitis: 250 to 500 mg once daily for 7 to 10 days.
- Community-acquired pneumonia: 500 mg once or twice daily for 7 to 14 days.
- Complicated urinary tract infections including pyelonephritis: 250 mg once daily for 7 to 10 days.
- Skin and soft tissue infections: 250 mg once daily or 500 mg once or twice daily for 7 to 14 days.
- Prostatitis: 500 mg once daily for 28 days.

Dosage in adult patients with impaired renal function (creatinine clearance≤50 ml/ min):
According to the severity of the infection, three treatment regimens are recommended depending on the creatinine clearance:

Creatinine clearance	Dosage regimen		
50-20 ml/min	First dose: 250 mg then 125 mg/24 h	First dose: 500 mg then 250 mg/24 h	First dose: 500 mg then 250 mg/12 h
19-10 ml/min	First dose: 250 mg then 125 mg/48 h	First dose: 500 mg then 125 mg/24 h	First dose: 500 mg then 125 mg/12 h
<10 ml/min (including hemodialysis and CAPD*)	First dose: 250 mg then 125 mg/48 h	First dose: 500 mg then 125 mg/24 h	First dose: 500 mg then 125 mg/24 h

*No additional doses are required after hemodialysis or Continuous Ambulatory peritoneal dialysis (CAPD).

Special populations:
No dosage adjustment is required in patients with impaired liver function.
No dosage adjustment is necessary in elderly patients. However, special attention to renal function should be paid in elderly patients, and the dosage should be adapted accordingly.
Method of administration:
Matador® tablets should be swallowed without crushing and with sufficient amount of liquid. They may be divided at score line to adapt the dosage. The tablets may be taken during meals or between meals.

OVERDOSAGE:
In case of overdose, contact immediately your physician.
According to toxicity studies in animals, the most important signs to be expected following acute overdose of levofloxacin are central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, gastro-intestinal reactions such as nausea and mucosal erosions.
In clinical pharmacology studies performed with a supra-therapeutic dose increase in QT interval has been seen.
In the event of overdose the patient should be carefully observed (including ECG monitoring) and symptomatic treatment should be implemented. In case of acute oral overdose, gastric lavage should also be considered and antacids may be used for protection of gastric mucosa. Haemodialysis, including peritoneal dialysis and CAPD, are not effective in removing levofloxacin from the body. No specific antidote exists.

PRESENTATIONS:
Matador® 250 Film Coated Tablets: Packs of 7 tablets. Each tablet contains 250 mg Levofloxacin (as levofloxacin hemihydrate).
Matador® 500 Film Coated Tablets: Packs of 7 tablets. Each tablet contains 500 mg Levofloxacin (as levofloxacin hemihydrate).

STORAGE CONDITIONS:
Store below 30°C.

This is a medicament.
- *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 you the medicament.*
- *The doctor and the pharmacist are experts in medicine, its benefits and its 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

Manufactured by Dar Al Dawa, Na'ur - Jordan

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02/08