Ciprodar®

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Ciprofloxacin

DESCRIPTION:
Ciprodar® (ciprofloxacin hydrochloride monohydrate) is a synthetic broad spectrum antibacterial agent, belonging to the fluoroquinolones class intended for oral administration.

PHARMACOLOGY:
Ciprofloxacin interferes intracellularly by inhibiting the DNA gyrase enzyme which is needed for the synthesis of bacterial DNA.
Ciprofloxacin is rapidly and well-absorbed from the gastrointestinal tract, after oral administration. Maximum serum concentrations are attained within 1 to 2 hours. Mean plasma concentrations obtained 12 hours after dosing with 250, 500 mg are 0.1, 0.2 mcg/ml respectively. The serum elimination half-life in subjects with normal renal function is approximately 4 hours. In patients with reduced renal function, the half-life of ciprofloxacin is slightly prolonged, and dosage adjustment may be required.
About 40-50% of the orally administered dose is excreted unchanged in the urine. Fecal excretion over 5 days has accounted for 20 to 35%.
Food may delay absorption.

INDICATIONS:
Adults:
For the treatment of uncomplicated and complicated infections caused by organisms susceptible to ciprofloxacin:
- Respiratory tract infections. Many of the organisms known as "problem germs" (e.g. Klebsiella, Enterobacter, Proteus, Pseudomonas, Legionella, Staphylococcus, Escherichia coli) react very sensitively to ciprofloxacin. Most cases of pneumonia which do not require hospital treatment are caused by Streptococcocus pneumoniae. In such cases ciprofloxacin is not the drug of first choice.
- Otitis media and sinusitis, particularly when they are caused by problem germs such as Pseudomonas or Staphylococcus. A different antibiotic should be used for acute tonsillitis.
- Infections of the eyes.
- Infections of the kidneys and/or efferent urinary tract.
- Infections of the reproductive organs, including inflammation of the ovaries and fallopian tubes (adnexitis), gonorrhoea and infections of the prostate gland (prostatitis).
  Ciprofloxacin is not effective against Treponema pallidum (the causative organism in syphilis).
- Infections of the abdominal cavity, e.g. the gastrointestinal tract, the biliary tract and peritoneum.
- Skin and soft tissues infections.
- Bones and joints infections.
- Blood poisoning (sepsis).
- Infections or the risk of infection (prophylaxis) in patients with a compromised immune system, e.g. who are being treated with immunosuppressants or whose blood contains a reduced number of certain white blood cells (neutropenia).
- Targeted elimination of gut bacteria (selective gut decontamination) during therapy with immunosuppressants.

For children and adolescents aged between 5 and 17:
- For acute infection episodes of cystic fibrosis caused by P. aeruginosa, provided that oral therapy seems sufficient or more effective parenteral treatment options do not appear practicable. Ciprofloxacin is not recommended for other indications.

CONTRAINDICATIONS:
Ciprodar® is contraindicated in:
- Patients who are hypersensitive to ciprofloxacin or other drugs from the same substance group (quinolone type, gyrase inhibitors).
- Pregnant and breast-feeding women.
- Patients under 18 years of age and growing children or adolescents.

SIDE EFFECTS:
- Effects on the gastrointestinal tract: loss of appetite, nausea, vomiting, abdominal pain, flatulence, digestive problems, diarrhoea.
  If severe and persistent diarrhoea develops during or after therapy, a doctor should be consulted as this may be a sign of a serious, possibly life–threatening intestinal disease (pseudomembranous colitis) which requires immediate treatment. In such cases **Ciprodar®** should be discontinued and suitable therapy should be initiated by the doctor.
- Effects on the central nervous system: dizziness, headaches, fatigue, agitation, trembling ; in very rare cases: insomnia, impaired sensation in the arms and legs, perspiration, unsteady gait, seizures, increased intracranial pressure, anxiety, nightmares, distress, depression, hallucinations; in isolated cases: psychotic reactions. In some cases these reactions have occurred after first use. In such cases **Ciprodar®** must be discontinued immediately and the attending physician must be informed.
- Effects on the sense organs: in very rare cases: impaired sense of taste and smell, including a potential loss of the sense of smell which is usually reversible after discontinuation of therapy; visual disturbances, tinnitus, transient loss of hearing, particularly with high tones.
- Hypersensitivity reactions: in some cases the following reactions have occurred after first use of the product. If this happens, **Ciprodar®** must be discontinued immediately, and the attending physician must be informed. Skin reactions such as rashes, pruritus, drug fever.
  In very rare cases:
  - spots of bleeding in the skin, blisters containing blood and small nodules with encrustations indicative of vascular involvement, erythema nodosum, disc-shaped reddening of the skin including severe forms of this condition (Stevens-Johnson syndrome), blister-like detachment of the top layers of the skin and oral and nasal mucous membranes (Lyell's syndrome).
  - kidney and liver damage (interstitial nephritis, hepatitis, liver cell necrosis ranging up to life-threatening liver failure).
  Reactions similar to those associated with serum sickness (with, for example, fever, swelling of the lymph nodes, reddening of the skin, urticaria, oedema); severe immediate allergic reactions involving oedema of the face, blood vessels and larynx and difficulty in breathing ranging up to life-threatening shock (anaphylactic/anaphylactoid reactions), in some cases after first use of the product. If this happens, use of **Ciprodar®** must be discontinued immediately and medical treatment (e.g. shock therapy) must be given.
- Effects on the cardiovascular system: palpitations; in very rare cases: swelling of the legs (peripheral oedema). Hot flushes, migraine, unconsciousness.
- Effects on the locomotor system: pain and swelling in the joints; in very rare cases: muscle pain, tenosynovitis.
  In isolated cases: treatment with fluoroquinolone drugs has been associated with inflammation of the tendons and torn tendons. Events of this type have been observed predominantly in elderly patients who had previously been treated with corticosteroid drugs. If inflammation of a tendon is suspected, treatment with **Ciprodar®** must be discontinued immediately, physical strain must be avoided and appropriate therapy may have to be given. In isolated cases, the symptoms of myasthenia gravis may worsen.
- Effects on blood and its components: changes in the blood count, e.g. an increase in a certain type of white blood cell (eosinophilia), a reduction in white (leucocytopenia, granulocytopenia) or red blood corpuscles (anaemia) or platelets (thrombocytopenia); in very rare cases: proliferation of white blood cells (leucocytosis) or platelets (thrombocytosis), increased degradation of red blood corpuscles (haemolytic anaemia), a reduction in all blood cells (pancytopenia), a severe decrease in a certain type of white blood cell with the possible symptoms of shivering, fever, blisters in the oral and throat mucosa (agranulocytosis), altered blood coagulation factors (prothrombin time).
- Effects on laboratory and urine parameters: liver function may be affected temporarily, especially in patients with existing liver damage; this may result in an increase in liver enzymes and even jaundice; raised levels of urea, creatinine and bilirubin in the blood; in isolated cases: raised levels of blood glucose and blood or crystals in the urine.
- Other effects: In very rare cases: general debility, temporary impairment of kidney function ranging up to transient kidney failure, sensitivity to light with reddening of the skin. Patients undergoing treatment with **Ciprodar®** should therefore not be exposed unnecessarily to sunlight and should avoid exposure to UV light. Treatment must be discontinued if light-sensitivity is observed.
  Long-term or repeated use of **Ciprodar®** can reduce the susceptibility of disease-causing organisms to ciprofloxacin; this means that the patient may become infected again by the same organism or yeast-like organisms before the initial infection has been eradicated.

WARNINGS AND PRECAUTIONS:
- In patients who suffer from seizures (epilepsy) or any other form of damage to the central nervous system, **Ciprodar®** should only be used after careful consideration of the possible risks and expected benefits. Patients in this category are at risk of side effects in the central nervous system.
- In common with other gyrase inhibitors, ciprofloxacin is known to cause damage to the weight-bearing joints of juvenile animals. Evaluation of the safety data of patients aged less than 18 who were mainly suffering from cystic fibrosis did not reveal evidence of joint/cartilage damage. Current findings support the use of ciprofloxacin for treatment of acute infection episodes of cystic fibrosis caused by P. aeruginosa in children and adolescents aged between 5 and 17; at present, only inadequate experience is available in regard to its use in children and adolescents with other infections and children aged less than 5. Ciprofloxacin should therefore not be used for other infections and not for children aged less than 5 in general.
- Even when used correctly, this medicine may impair reaction speed so much that the patient's ability to drive, operate machinery or work without a secure foothold may be reduced, or the patient may not be capable of doing these things at all. This applies particularly at the start of treatment, when the dosage is increased, when the patient is switched from one medicine to another and when this medicine is taken in conjunction with alcohol.
- Pregnancy and lactation: ciprofloxacin must not be used at any stage during pregnancy because no experience has been gained with its use in pregnant women and it is not known whether it is safe to use in this category of patients. Animal experiments have not produced any evidence for malformation of the foetus, but it is not entirely improbable that damage to cartilage may be caused in organisms which have not reached maturity.
  It is also recommended on principle that ciprofloxacin should not be used while breast-feeding.

DRUG INTERACTIONS:
- Products containing iron/antacids and products with a high buffering capacity which contain magnesium, aluminum or calcium.
  Simultaneous use of ciprofloxacin and any of the above-mentioned products reduces the absorption of ciprofloxacin; the same applies, for example to sucralfate, drugs containing the antiviral agent didanosine, oral nutrient solutions and large quantities of dairy products. For this reason, **Ciprodar®** should be taken either 1-2 hours before or at least 4 hours after these products. This restriction does not apply to medications of the H_2-receptor blocker type taken to reduce excess stomach acid (antacids).
- Xanthines: taking ciprofloxacin and theophlline at the same time can lead to an unwanted increase in the concentration of theophlline in the blood and, accordingly, to side effects caused by theophylline which, in isolated cases, may be life-threatening or fatal. If it is imperative to use both medicines at the same time, the theophylline concentration in the blood should be monitored and the dosage should be reduced as required. There have been reports of raised concentrations of the xanthine derivatives caffeine and pentoxifylline in the blood when these substances are administered at the same time as ciprofloxacin.
- Non-steroidal anti-inflammatory drugs: animal experiments have shown that using a combination of very high doses of quinolones (gyrase inhibitors) and non-steroidal anti-inflammatory agents can trigger seizures. This does not apply to medicines containing acetylsalicylic acid.
- Cyclosporine: temporary impairment of kidney function associated with an increase in the concentration of creatinine in the blood has been observed in isolated cases when ciprofloxacin is taken at the same time as cyclosporine. For this reason, the creatinine concentration in the blood of patients in this category should be monitored closely (twice a week).
- Warfarin: the simultaneous use of ciprofloxacin and warfarin may increase the action of warfarin.
- Glibenclamide: in isolated cases the simultaneous use of ciprofloxacin and glibenclamide may increase the action of glibenclamide to such an extent that hypoglycaemia may occur.
- Probenecid: probenecid affects the excretion of ciprofloxacin in the urine (renal secretion). The simultaneous use of ciprofloxacin and probenecid increases the concentration of ciprofloxacin in the blood (serum).
- Metoclopramide: metoclopramide accelerates the absorption of ciprofloxacin into the blood and causes the maximum concentration in the blood (plasma) to be reached more rapidly than usual. No effect on the bioavailability of ciprofloxacin in the human body has been observed.
- Mexiletine: simultaneous use of these two medicines may lead to a raised concentration of mexiletine in the body.
- Phenytoin: elevated or lowered concentrations of phenytoin in the blood have been reported following the simultaneous use of these two medicines.
- Diazepam: there have been reports that simultaneous use of these two medicines delays the decomposition of diazepam in the body. Accordingly, careful monitoring of diazepam treatment is recommended.

DOSAGE AND ADMINISTRATION:
- Swallow the film-coated tablets whole with liquid. You can take them at mealtimes or at other times. Taking them on an empty stomach speeds up absorption of the active ingredient into the body.
- If you have not taken enough **Ciprodar®** or have forgotten to take it, do not take **Ciprodar®** the next time. Simply take the next prescribed dose at the correct time.
- If you want to interrupt treatment with **Ciprodar®** or stop it early, for example because you are feeling better or because you are experiencing side effects, talk to your doctor. First, the bacteria which caused your infection will be able to start reproducing again and your condition may worsen considerably.

Adults:
Unless otherwise prescribed, the following doses are recommended:

Indications	Single/daily doses for adults
	Quantity of active ingredient (mg ciprofloxacin)
Respiratory tract infections* (e.g. bronchitis) - depending on severity and causative agent	2 x 250 - 500
Urinary tract infections - acute uncomplicated - cystitis in women of childbearing age (premenopausal) - complicated	 2 x 125 or 1 x up to 500 Single dose of 250 2 x 250 - 500
Gonorrhoea, acute, uncomplicated	Single dose of 250
Gastrointestinal infections	1 x up to 500
Other infections* (cf. indications)	2 x 500

*In particularly severe, life-threatening infections, especially those involving Pseudomonas, Staphylococcus or Streptococcus, e.g. pneumonia caused by Streptococcus, recurrent infection episodes in patients with cystic fibrosis, bone and joint infections, blood poisoning (sepsis) and infections of the abdominal cavity, therapy may be given with 2 x 750 mg ciprofloxacin.
In Chlamydial infections of the urinary tract and reproductive organs, the daily dose may be increased to 2 x 750 mg ciprofloxacin if necessary.

Elderly patients:
Elderly patients should receive as low a dose as is compatible with the severity of the infection and their kidney function (creatinine clearance).

Children and adolescents (5 to 17):
The recommended oral dose for acute infection episodes caused by P. aeruginosa in mucoviscidosis patients is 2 x daily 15 (-20) mg/ kg (maximum 1,500 mg/day).

Impaired renal and hepatic function:
Adults:
1. The following doses are recommended for moderate to severe impairment of renal function:
   - For patients with a creatinine clearance between 31 ml/min and 60 ml/min (serum creatinine between 1.4 mg/100 ml and 1.9 mg/100ml), the maximum dose for oral administration is 1,000 mg ciprofloxacin per day.
   - For patients with a creatinine clearance ≤ 30 ml/min (serum creatinine ≥ 2 mg/100 ml), the maximum dose for oral administration is 500 mg ciprofloxacin per day.
2. Patients with impaired renal function who are undergoing haemodialysis should receive the same dose after each dialysis session as patients with moderate to severe impaired renal function (see point 1).
3. In patients with impaired renal function who use continuous ambulatory peritoneal dialysis (CAPD), 500 mg ciprofloxacin must be given 4 x daily at 6-hour intervals to treat peritonitis.
4. It is not necessary to adjust the dosage for patients with impaired hepatic function.
5. In patients with impaired renal and hepatic function, the dosage should be adjusted as for impaired renal function; the concentration of ciprofloxacin in the blood may have to be monitored.

Children and adolescents:
No information is available on the influence of impaired renal and hepatic function on the dosage for children and adolescents.

Average duration of therapy:
Adults:
- 1 day for acute uncomplicated gonorrnoea and cystitis.
- Up to 7 days for infections of the kidneys, urinary tract and abdominal cavity.
- In patients with a compromised immune system, therapy should be continued for as long as the total white blood cell count is depressed.
- A maximum of 2 months for inflammations of the bone marrow (osteomyelitis).
- 7–14 days for all other infections.

Therapy should always be continued systematically for at least 3 days after the fever has subsided and the clinical signs have disappeared.
In streptococcal infections therapy should be continued for at least 10 days because of the risk of late complications.
Chlamydial infections should also be treated for at least 10 days.
Children and adolescents:
For acute infection episodes of cystic fibrosis caused by P. aeruginosa in children and adolescents aged between 5 and 17, the duration of treatment is 10–14 days.

OVERDOSAGE:
A few cases of transient (reversible) kidney damage have been reported following extremely large overdoses. In such cases, therefore, kidney function should be checked by a doctor. Administration of products containing magnesium or calcium neutralizes stomach acid and thus reduces the absorption of ciprofloxacin into the bloodstream.

PRESENTATIONS:
Ciprodar® 250 Film Coated Tablets: Packs of 10 and 500 tablets. Each tablet contains 250 mg Ciprofloxacin (as ciprofloxacin hydrochloride monohydrate).
Ciprodar® 500 Film Coated Tablets: Packs of 8, 10 and 500 tablets. Each tablet contains 500 mg Ciprofloxacin (as ciprofloxacin hydrochloride monohydrate).

STORAGE CONDITIONS:
Protect from light. Store in a dry place 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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