PACKAGE LEAFLET: INFORMATION FOR THE USER

Levofloxacin Combino Pharm 5mg/ml Solution for infusion 100 ml
Levofloxacin

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. WHAT Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml IS AND WHAT IT IS USED FOR

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml belongs to a group of medicines called fluorquinolones, a type of antibacterial agent (antibiotics) with bactericida activity.

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml is used in adults before prescribing~~prscribing~~, this medicine is indicated for the treatment of the following infections when due to levofloxacin-susceptible microorganisms:

- Community-acquired pneumonia.
- Complicated urinary tract infections (dificult to treat) including pyelonephritis (kidney infection).
- Chronic bacterial prostatitis.
- Skin and soft tissue infections.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml

Do not use Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml
- if you are allergic to levofloxacin or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from epilepsy or other nervous system disease that could caused you convulsions (as cranium traumatism, accident cerebrovascular).
- if you have ever had tendon problems (e.g. tendinitis) related to treatment with an antibiotic of the fluoroquinolone class. This is because there is a risk of getting similar problems with levofloxacin, including tendon rupture.
- if you are pregnant or breast-feeding a baby, levofloxacin could harm your baby.

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml is only intended for adults and must not be given to children or growing teenagers. It could harm the cartilage~~cartilague~~ of their growing bones.

If you have any question, tell your doctor o your pharmacist.

Take special care with Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml if

- The risk of getting convulsions (fits) may be increased if in the past you have experienced brain damage (such as stroke or severe brain injury) and are now treated with levofloxacin (you should not be administered Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml if your suffer from epilepsy). Make sure your doctor knows about your medical history, so he can give you appropriate advice.
- Do not stay out in strong sunlight for unnecessarily~~unnecesarily~~ long periods and do not use a sun-lamp or solarium while you are taking Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml. This is because some patients may become more sensitive to light whilst receiving the treatment (sunburn-like reactions).
- Tell your doctor immediately if you have severe, persistent and/or bloody diarrhoea during or after treatment with Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml. This may be a sign of a serious bowel inflammation (pseudomembranous colitis) which may occur following treatment by antibiotics, and it may be necessary to stop treatment and start specific therapy.
- Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml, in rare cases, cause pain and inflammation tendons (tendinitis-affects frequently Achilles'~~achilles~~ tendon) could cause the tendon rupture, particularly in elderly patients or in patients taking corticosteroids (cortisone and similar medicines). If you experience any tendon complains whilst or shortly after receiving levofloxacin, seek medical advice immediately and rest the affected limb to avoid tendon damage. Tell your doctor, it may be necessary to stop treatment.
- Patients with some abnormality of an enzyme called glucose-6-phosphate dehydrogenase (G6-PD) (a rare hereditary disease) may be prone to destruction of red blood cells (hemolysis) when treated with quinolone antibacterial agents, and so levofloxacin should be used with caution in these patients.

Using other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

You should not take Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml with any of the following medicines at the same time:

-Teophylline (medicines used for breathing problems),
-Fenbufen or non-steroidal~~steroideal~~ anti-inflammatory drugs (used for pain and inflammation) due to the possibility to increase convulsion attacks.
-Ciclosporin (used to prevent rejection after organ transplants, to treat psoriasis, rheumatoid arthritis).
-If you are used oral anticoagulant~~anticogulant~~ medicines at the same time (vitamin K antagonist, e.g. warfarin), tell your doctor, coagulation test should be monitored due to the possibility~~posibility~~ to increase the anticoagulants effects.

Pregnancy and breast-feeding
Pregnancy
Ask your doctor or pharmacist for advice before taking any medicine.
Consult with your doctor if you are pregnant or think you may be pregnant. Do not use Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml because the safety of Levofloxacin during~~druring~~ pregnancy has not be established.

Breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.
If you are breast-feeding, do not use Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml, because passes into breast milk.

Driving and using machines

Some side effects like dizzinessdizzeness, drowsiness, visual disturbances may impair your ability to drive or use machinery.

Important information about some of the ingredients of Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml
This medicine contains 354mg of sodium per bottle, it must be taken into account in patients with poor diets of sodium.

3. HOW TO USE Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml

The usual dose is:

Patients with normal renal function
(creatinine clearance> 50 ml/min)

Indication	**Daily dose regimen** *(according to severity)*
Community-acquired pneumonia	500 mg once or twice daily
Complicated urinary tract infections including pyelonephritis	250 mg[1] once daily
Chronic bacterial prostatitis.	500mg once daily
Skin and soft tissue infections	500 mg twice daily

[1]Consideration should be given to increasing the dose in cases of severe infection.

Patients with impaired renal function
(creatinine clearance ≤ 50ml/min)

If your renal function is below normal your doctor will reduce the dose of levofloxacin as shown below:

	250 mg/24 h	**500 mg/24 h**	**500 mg/12 h**
Creatinine clearance	***first dose:*** **250 mg**	***first dose:*** **500 mg**	***first dose:*** **500 mg**
50 - 20 ml/min	***then:*** **125 mg/24 h**	***then:*** **250 mg/24 h**	***then*:** **250 mg/12 h**
19-10 ml/min	***then:*** **125 mg/48 h**	***then:*** **125 mg/24 h**	***then:*** **125 mg/12 h**
< 10 ml/min (including haemodialysis and CAPD) [1]	***then*:** **125 mg/48 h**	***then*:** **125 mg/24 h**	***then*:** **125 mg/24 h**

[1]No additional doses are required after haemodialysis or continuous ambulatory peritoneal dialysis (CAPD).

Elderly patients and patients with impaired liver function (but normal kidney function): should receive the same dosage as normal adult.

Duration of treatment
The duration of therapy varies according to the course of the disease and your response at the treatmenttrearment.
As with antibiotic therapy in general, administration of Levofloxacin Combino Pharm 5 mg/ml solution for infusion 100ml should be continued for a minimum of 2 to 3 days after the patient has become afebrile or evidence of bacterial eradication has been obtained.

Method of administration

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml is ready for use, and should only be administrated by slow infusion into a vein (see section "Instructions for healthcare professionals").

Please inform your doctor or your pharmacist if you estimate that the Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml action is too much intense or weak.

If you received more Levofloxacin Combino Pharm 5 mg/ml solution for infusion 100 ml than you should

Your doctor or nurse will ensure that you will receive the correct dose into the vein. An accidental overdose might result in central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and (convulsive) fits and heart disorders, possibly leading to abnormal heart rhythm. In the event of overdose treatment is according to symptoms. Levofloxacin is not removed from the body by dialysis~~dialisis~~. No specific antidote exits.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml can cause side effects, although not everybody gets them.

General allergic reactions, skin reactions

Common (may occur in 1 to 10 out of 100 patients): itching, rash.
Rare (may occur in 1 to 10 out of 10.000 patients): general allergic reactions (anaphylactic/anaphylactoid reactions) (which may sometimes occur even with the first dose and which may develop during infusion or fast within minutes or hours of infusion) with symptoms such as wheals, irritation and itching (urticaria), and possibly severe breathing problems (dyspnea/bronchospasm~~dypsnea/bronchospam~~).
Very rare (may occur in less than 1 out of 10.000 patients): sudden drop in blood pressure or collapse (shock). Hypersensitivity~~Hipersensitivity~~ skin reactions such as photosensitivity (Sensitivity of the skin to sun and ultraviolet light).
Isolated cases: severe blistering reactions of the skin and mucous membranes (Steven´s Johnson syndrome) with big and multiple blisters, toxic epidermal necrolysis (Lyell syndrome) and erythema exsudativum multiforme.

Gastro-intestinal, metabolism

Common (may occur in 1 to 10 out of 100 patients): nausea, diarrhoea.
Uncommon (may occur in 1 to 10 out of 1.000 patients): loss of appetite (anorexia), stomach upset (dyspepsia), vomiting, pain in the abdominal region.
Rare (may occur in 1 to 10 out of 10.000 patients): diarrhoea which in very rare cases may be indicative of enterocolitis (inflammation of the bowel), including pseudomembranous colitis.
Very rare (may occur in less than 1 out of 10.000 patients): fall of blood sugar to a too low level (hypoglycaemia) which may be of special importance in patients treated for diabetes.

Nervous system

Uncommon (may occur in 1 to 10 out of 1.000 patients): headache, dizziness, drowsiness, sleeping problems.
Rare (may occur in 1 to 10 out of 10.000 patients): feeling like tingling in hands and foots (paraesthesia), trembling, concern (agitation), anxiety, depression, psychotic reactions, "fits" (convulsions) and confusion.
Very rare (may occur in less than 1 out of 10.000 patients): vision and hearing disorders, disturbances of taste and smell, numbness, psychiatric problems including hallucination and depressive changes in the humour. Disorders of movement, including walking difficulties.

Cardiovascular system

Rare (may occur in 1 to 10 out of 10.000 patients): abnormality low blood pressure (hypotension), abnormally rapid beating of the heart (tachycardia).

Very rare (may occur in less than 1 out of 10.000 patients): circulatory collapse (anaphylactic like shock).
Isolated cases: heart disorders, possibly leading to abnormal heart rhythm.

Muscles, tendons and bones

Rare (may occur in 1 to 10 out of 10.000 patients): tendon pain and inflammation (tendinitis) (e.g. Achilles' ~~Achilles´~~tendon), join pain or muscle pain.
Very rare (may occur in less than 1 out of 10.000 patients): tendon rupture (e.g. Achilles'~~Achilles~~ tendon), this side effect may occur within 48 hours of starting treatment and may be bilateral. Muscular weakness, which may be of special importance in patients with myasthenia gravis (a rare disease of the nervous system).
Isolated cases: muscle reactions with muscle cell damage.

Blood~~Bood~~ and lymphatic system

Uncommon (may occur in 1 to 10 out of 1.000 patients): increase or decrease in the number of white blood cells.
Rare (may occur in 1 to 10 out of 10.000 patients): decrease in the number of blood platelets leading to a tendency to bruise and bleed easily.
Very rare (may occur in less than 1 out of 10.000 patients): severe decrease in the number of white blood cells leading to symptoms such as recurrence or persistence of fever, sore throat and feeling more ill again.
Isolated cases: decrease in red blood cells (haemolytic anaemia) due to blood cell damage, decrease in the number of all types of blood cells.

Liver and kidney

Common (may occur in 1 to 10 out of 100 patients): increase in blood levels of liver enzymes.
Uncommon (may occur in 1 to 10 out of 1.000 patients): blood test abnormalities due to liver or kidney problems.
Very rare (may occur in less than 1 out of 10.000 patients): inflammation of the liver. Disturbances of the kidney function and occasional kidney failure which may be due to allergic kidney reactions (interstitial nephritis).

Other reactions:

Uncommon (may occur in 1 to 10 out of 1.000 patients): general weakness.
Very rare (may occur in less than 1 out of 10.000 patients): fever, allergic inflammation of small blood vessels or allergic lung reactions.

Some medicines at the same class to belongs Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml, may trigger attacks of porphyria in patients with porphyria (a very rare metabolic disease). This might therefore also occur with Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml.

The antibacterial treatments destroyed some germs that may caused a disequilibrium~~desequilibrium~~ of the microorganisms (bacterium/fungus) that normally appears in humans. As consequence~~consecuence~~, may be increase others. In rare cases is needed~~nedded~~ treatment.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml contains

Keep this medicine out of the sight and reach of children.

Your doctor or nurse will ensure that Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml is properly stored.

Do not use Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml after the expiry date which is stated on the carton after CAD. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml contains

- The active substance is Levofloxacin (as hemihydrate). Each bottle of 100ml contains levofloxacin hemihydrate, equivalent to 500mg of levofloxacin.
- The other ingredients (excipients) are: sodium chloride, sodium hydroxide, hydrochloric acid and water for injection.

What Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml looks like and contents of the pack

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml is a clear yellowish solution prepared for its use, in a glass bottle of 100ml with a rubber stopper.

The following packs are available:

10 bottles of 100ml.

Marketing Authorisation Holder

Combino Pharm SL
Fructuós Gelabert, 6-8
08970 Sant Joan Despí
Spain

Manufacturer

B.Braun Medical SA
Carretera de Terrassa, 121
08191 Rubí (Barcelona)
Spain

This leaflet was last approved in August 2015.

<u>This information is intended for medical or healthcare professionals only:</u>

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml is a ready to use solution, should only be administered by slow infusion into a vein. The infusion time should not be less than 60 minutes (1 hour) for 500mg (100ml).

WARNINGS:

Infusion time

The infusion time of at least 60 minutes for 500mg of Levofloxacin Combino Pharm (100ml solution for infusion) should be observed. It is known for ofloxacin that during infusion tachycardia and a temporary decrease in blood pressure may develop. In rare cases, as a consequence of a profound drop in blood pressure, circulatory collapse may occur. Should a conspicuous drop in blood pressure occur during infusion of levofloxacin, (I-isomer of ofloxacin) the infusion must be halted immediately.

Storage

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml should be store in the original package in order to protect from light, up to its use. No protection from light is necessary during infusion or before 3 days after extraction of the external packaging if is stored below interior light conditions. The solution should be used immediately (within 3 hours) after perforation of the rubber stopper in order to prevent any bacterial contamination.

Incompatibilities

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml should not be mixed with some solutions as heparin or alkaline solutions (e.g. sodium bicarbonate).

Compatibilities

Levofloxacin Combino Pharm 5mg/ml solution for infusion 100 ml may be administered alone or with the following solutions:

- 0.9% sodium chloride solution, USP
- 5% Glucose, USP
- 2.5% Glucose in Ringer solution.
- Combination solutions for parenteral nutrition (aminoacids, carbohydrates, electrolytes).