Annex III

Summary of product characteristics, labelling and package leaflets

Note:

These SmPCs, labelling and packages leaflets are the version valid at the time of Commission decision.

After the Commission decision the Member State competent authorities, in liaison with the reference Member State, will update the product information as required. Therefore, these SmPCs, labelling and package leaflets may not necessarily represent the current text.

SUMMARY OF PRODUCT CHARACTERISTICS

Highlighted in grey: Applies to 500 mg (100 ml) bottle only

1 NAME OF THE MEDICINAL PRODUCT

Tavanic 5 mg/ml solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

50 ml of solution for infusion contains 250 mg of levofloxacin as levofloxacin hemihydrate.
100 ml of solution for infusion contains 500 mg of levofloxacin as levofloxacin hemihydrate .

Excipients with known effect:
50 ml of solution for infusion contain 7.9 mmol (181 mg) sodium.
100 ml of solution for infusion contain 15.8 mmol (363 mg) sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

Clear greenish-yellow isotonic solution with pH of 4.3 to 5.3 and osmolarity of 282 - 322 mOsm/litre.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Tavanic solution for infusion is indicated in adults for the treatment of the following infections (see sections 4.4 and 5.1):

• Community-acquired pneumonia
• Complicated skin and soft tissue infections

For the above-mentioned infections Tavanic should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections.

• Pyelonephritis and complicated urinary tract infections (see section 4.4)
• Chronic bacterial prostatitis
• Inhalation Anthrax: postexposure prophylaxis and curative treatment (see section 4.4).

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Tavanic solution for infusion is administered by slow intravenous infusion once or twice daily. The dosage depends on the type and severity of the infection and the susceptibility of the presumed causative pathogen. Treatment with Tavanic after initial use of the intravenous preparation may be completed with an appropriate oral presentation according to the SPC for the film-coated tablets and as considered appropriate for the individual patient. Given the bioequivalence of the parenteral and oral forms, the same dosage can be used.

Posology

The following dose recommendations can be given for Tavanic:

Dosage in patients with normal renal function (creatinine clearance > 50 ml/min)

Indication	**Daily dose regimen** *(according to severity)*	**Total duration of treatment**[1] *(according to severity)*
Community-acquired pneumonia	500 mg once or twice daily	7 - 14 days
Pyelonephritis	500 mg once daily	7 - 10 days
Complicated urinary tract infections	500 mg once daily	7 - 14 days
Chronic bacterial prostatitis	500 mg once daily	28 days
Complicated skin and soft tissue infections	500 mg once or twice daily	7 - 14 days
Inhalation anthrax	500 mg once daily	8 weeks

[1] Treatment duration includes intravenous plus oral treatment. The time to switch from intravenous to oral treatment depends on the clinical situation but is normally 2 to 4 days.

Special populations

Impaired renal function (creatinine clearance ≤50 ml/min)

	Dose regimen		
	250 mg/24h	**500 mg/24h**	**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).

Impaired liver function

No adjustment of dose is required since levofloxacin is not metabolised to any relevant extent by the liver and is mainly excreted by the kidneys.

Elderly population

No adjustment of dose is required in the elderly, other than that imposed by consideration of renal function (see section 4.4 “Tendinitis and tendon rupture” and “QT interval prolongation”).

Paediatric population

Tavanic is contraindicated in children and growing adolescents (see section 4.3).

Method of administration

Tavanic solution for infusion is only intended for slow intravenous infusion; it is administered once or twice daily. The infusion time must be at least 30 minutes for 250 mg or 60 minutes for 500 mg Tavanic solution for infusion (see section 4.4).

For incompatibilities see section 6.2 and compatibility with other infusion solutions see section 6.6.

4.3 Contraindications

Levofloxacin solution for infusion must not be used:

- in patients hypersensitive to levofloxacin or any other quinolone and any of the excipients listed in section 6.1,
- in patients with epilepsy,
- in patients with history of tendon disorders related to fluoroquinolone administration,
- in children or growing adolescents,
- during pregnancy,
- in breast-feeding women.

4.4 Special warnings and precautions for use

Methicillin-resistant *S. aureus* are very likely to possess co-resistance to fluoroquinolones, including levofloxacin. Therefore levofloxacin is not recommended for the treatment of known or suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to levofloxacin (and commonly recommended antibacterial agents for the treatment of MRSA-infections are considered inappropriate).

Resistance to fluoroquinolones of *E. coli* – the most common pathogen involved in urinary tract infections – varies across the European Union. Prescribers are advised to take into account the local prevalence of resistance in *E. coli* to fluoroquinolones.

Inhalation Anthrax: Use in humans is based on *in vitro Bacillus anthracis* susceptibility data and on animal experimental data together with limited human data. Treating physicians should refer to national and/or international consensus documents regarding the treatment of anthrax.

Infusion Time

The recommended infusion time of at least 30 minutes for 250 mg or 60 minutes for 500 mg Tavanic 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, (*l*-isomer of ofloxacin) the infusion must be halted immediately.

Sodium content

This medicinal product contains 7.8 mmol (181 mg) sodium per 50 ml dose and 15.8 mmol (363 mg) per 100 ml dose. To be taken into consideration by patients on a controlled sodium diet.

Tendinitis and tendon rupture

Tendinitis may rarely occur. It most frequently involves the Achilles tendon and may lead to tendon rupture. Tendinitis and tendon rupture, sometimes bilateral, may occur within 48 hours of starting treatment with levofloxacin and have been reported up to several months after discontinuation of treatment. The risk of tendinitis and tendon rupture is increased in patients aged over 60 years, inpatients receiving daily doses of 1000 mg and in patients using corticosteroids. The daily dose should be adjusted in elderly patients based on creatinine clearance (see section 4.2). Close monitoring of these patients is therefore necessary if they are prescribed levofloxacin. All patients should consult their physician if they experience symptoms of tendinitis. If tendinitis is suspected, treatment with levofloxacin must be halted immediately, and appropriate treatment (e.g. immobilisation) must be initiated for the affected tendon (see sections 4.3 and 4.8).

Clostridium difficile-associated disease

Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with levofloxacin (including several weeks after treatment), may be symptomatic of *Clostridium difficile*-associated disease (CDAD). CDAD may range in severity from mild to life threatening, the most severe form of which is pseudomembranous colitis (see section 4.8). It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with levofloxacin. If CDAD is suspected or confirmed, levofloxacin should be stopped immediately and appropriate treatment initiated without delay. Anti-peristaltic medicinal products are contraindicated in this clinical situation.

Patients predisposed to seizures

Quinolones may lower the seizure threshold and may trigger seizures. Levofloxacin is contraindicated in patients with a history of epilepsy (see section 4.3) and, as with other quinolones, should be used with extreme caution in patients predisposed to seizures or concomitant treatment with active substances that lower the cerebral seizure threshold, such as theophylline (see section 4.5). In case of convulsive seizures (see section 4.8), treatment with levofloxacin should be discontinued.

Patients with G-6- phosphate dehydrogenase deficiency

Patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity may be prone to haemolytic reactions when treated with quinolone antibacterial agents. Therefore, if levofloxacin has to be used in these patients, potential occurrence of haemolysis should be monitored.

Patients with renal impairment

Since levofloxacin is excreted mainly by the kidneys, the dose of Tavanic should be adjusted in patients with renal impairment (see section 4.2).

Hypersensitivity reactions

Levofloxacin can cause serious, potentially fatal hypersensitivity reactions (e.g. angioedema up to anaphylactic shock), occasionally following the initial dose (see section 4.8). Patients should discontinue treatment immediately and contact their physician or an emergency physician, who will initiate appropriate emergency measures.

Severe bullous reactions

Cases of severe bullous skin reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported with levofloxacin (see section 4.8). Patients should be advised to contact their doctor immediately prior to continuing treatment if skin and/or mucosal reactions occur.

Dysglycaemia

As with all quinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g., glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose is recommended (see section 4.8).

Prevention of photosensitisation

Photosensitisation has been reported with levofloxacin (see section 4.8). It is recommended that patients should not expose themselves unnecessarily to strong sunlight or to artificial UV rays (e.g. sunray lamp, solarium), during treatment and for 48 hours following treatment discontinuation in order to prevent photosensitisation.

Patients treated with Vitamin K antagonists

Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with levofloxacin in combination with a vitamin K antagonist (e.g. warfarin), coagulation tests should be monitored when these drugs are given concomitantly (see section 4.5).

Psychotic reactions

Psychotic reactions have been reported in patients receiving quinolones, including levofloxacin. In very rare cases these have progressed to suicidal thoughts and self-endangering behaviour- sometimes after only a single dose of levofloxacin (see section 4.8). In the event that the patient develops these reactions, levofloxacin should be discontinued and appropriate measures instituted. Caution is recommended if levofloxacin is to be used in psychotic patients or in patients with history of psychiatric disease.

QT interval prolongation

Caution should be taken when using fluoroquinolones, including levofloxacin, in patients with known risk factors for prolongation of the QT interval such as, for example:
- congenital long QT syndrome
- concomitant use of drugs that are known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics).
- uncorrected electrolyte imbalance (e.g. hypokalemia, hypomagnesemia)
- cardiac disease (e.g. heart failure, myocardial infarction, bradycardia).

Elderly patients and women may be more sensitive to QTc-prolonging medications. Therefore, caution should be taken when using fluoroquinolones, including levofloxacin, in these populations.
(See sections 4.2 *Elderly*, 4.5, 4.8, and 4.9).

Peripheral neuropathy

Peripheral sensory neuropathy and peripheral sensory motor neuropathy have been reported in patients receiving fluoroquinolones, including levofloxacin, which can be rapid in its onset (see section 4.8). Levofloxacin should be discontinued if the patient experiences symptoms of neuropathy in order to prevent the development of an irreversible condition.

Hepatobiliary disorders

Cases of hepatic necrosis up to fatal hepatic failure have been reported with levofloxacin, primarily in patients with severe underlying diseases, e.g. sepsis (see section 4.8). Patients should be advised to stop treatment and contact their doctor if signs and symptoms of hepatic disease develop such as anorexia, jaundice, dark urine, pruritus or tender abdomen.

Exacerbation of myasthenia gravis

Fluoroquinolones, including levofloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Postmarketing serious adverse reactions, including deaths and the requirement for respiratory support, have been associated with fluoroquinolone use in patients with myasthenia gravis. Levofloxacin is not recommended in patients with a known history of myasthenia gravis.

Vision disorders

If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately (see sections 4.7 and 4.8).

Superinfection

The use of levofloxacin, especially if prolonged, may result in overgrowth of non-susceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.

Interference with laboratory test

In patients treated with levofloxacin, determination of opiates in urine may give false-positive results. It may be necessary to confirm positive opiate screens by more specific method.

Levofloxacin may inhibit the growth of *Mycobacterium tuberculosis* and, therefore, may give false-negative results in the bacteriological diagnosis of tuberculosis.

4.5 Interactions with other medicinal products and other forms of interaction

Effect of other medicinal products on Tavanic

Theophylline, fenbufen or similar non-steroidal anti-inflammatory drugs

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, non-steroidal anti-inflammatory drugs, or other agents which lower the seizure threshold.
Levofloxacin concentrations were about 13% higher in the presence of fenbufen than when administered alone.

Probenecid and cimetidine

Probenecid and cimetidine had a statistically significant effect on the elimination of levofloxacin. The renal clearance of levofloxacin was reduced by cimetidine (24%) and probenecid (34%). This is because both drugs are capable of blocking the renal tubular secretion of levofloxacin. However, at the tested doses in the study, the statistically significant kinetic differences are unlikely to be of clinical relevance. Caution should be exercised when levofloxacin is coadministered with drugs that affect the tubular renal secretion such as probenecid and cimetidine, especially in renally impaired patients.

Other relevant information

Clinical pharmacology studies have shown that the pharmacokinetics of levofloxacin were not affected to any clinically relevant extent when levofloxacin was administered together with the following drugs: calcium carbonate, digoxin, glibenclamide, ranitidine.

Effect of Tavanic on other medicinal products

Ciclosporin

The half-life of ciclosporin was increased by 33% when coadministered with levofloxacin.

Vitamin K antagonists

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 (see section 4.4)

Drugs known to prolong QT interval

Levofloxacin, like other fluoroquinolones, should be used with caution in patients receiving drugs known to prolong the QT interval (e.g. Class IA and III antiarrhythmics, tricyclic antidepressants, macrolides, antipsychotics) (see section 4.4 QT interval prolongation).

Other relevant information

In a pharmacokinetic interaction study, levofloxacin did not affect the pharmacokinetics of theophylline (which is a probe substrate for CYP1A2), indicating that levofloxacin is not a CYP1A2 inhibitor.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited amount of data from the use of levofloxacin in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

However in the absence of human data and due to that experimental data suggest a risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism, levofloxacin must not be used in pregnant women (see sections 4.3 and 5.3).

Breast-feeding

Tavanic is contraindicated in breast-feeding women. There is insufficient information on the excretion of levofloxacin in human milk; however other fluoroquinolones are excreted in breast milk. In the absence of human data and due to that experimental data suggest a risk of damage by fluoroquinolones to the weight-bearing cartilage of the growing organism, levofloxacin must not be used in breast-feeding women (see sections 4.3 and 5.3).

Fertility

Levofloxacin caused no impairment of fertility or reproductive performance in rats.

4.7 Effects on ability to drive and use machines

Some undesirable effects (e.g. dizziness/vertigo, drowsiness, visual disturbances) may impair the patient's ability to concentrate and react, and therefore may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

4.8 Undesirable effects

The information given below is based on data from clinical studies in more than 8300 patients and on extensive post marketing experience.

Frequencies in this table are defined using the following convention: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10000, <1/1000), very rare (<1/10000), not known (cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System organ class	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Not known (cannot be estimated from available data)**
Infections and infestations		Fungal infection including Candida infection Pathogen resistance		
Blood and the lymphatic system disorders		Leukopenia Eosinophilia	Thrombocytopenia Neutropenia	Pancytopenia Agranulocytosis Haemolytic anaemia
Immune system disorders			Angioedema Hypersensitivity (see section 4.4)	Anaphylactic shock [a] Anaphylactoid shock [a] (see section 4.4)

System organ class	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)	Not known (cannot be estimated from available data)
Metabolism and nutrition disorders		Anorexia	Hypoglycaemia particularly in diabetic patients (see section 4.4)	Hyperglycaemia Hypoglycaemic coma (see section 4.4)
Psychiatric disorders	Insomnia	Anxiety Confusional state Nervousness	Psychotic reactions (with e.g. hallucination, paranoia) Depression Agitation Abnormal dreams Nightmares	Psychotic disorders with self-endangering behaviour including suicidal ideation or suicide attempt (see section 4.4)
Nervous system disorders	Headache Dizziness	Somnolence Tremor Dysgeusia	Convulsion (see sections 4.3 and 4.4) Paraesthesia	Peripheral sensory neuropathy (see section 4.4) Peripheral sensory motor neuropathy (see section 4.4) Parosmia including anosmia Dyskinesia Extrapyramidal disorder Ageusia Syncope Benign intracranial hypertension
Eye disorders			Visual disturbances such as blurred vision (see section 4.4)	Transient vision loss (see section 4.4)
Ear and Labyrinth disorders		Vertigo	Tinnitus	Hearing loss Hearing impaired
Cardiac disorders			Tachycardia, Palpitation	Ventricular tachycardia, which may result in cardiac arrest Ventricular arrhythmia and torsade de pointes (reported predominantly in patients with risk factors of QT prolongation), electrocardiogram QT prolonged (see sections 4.4 and 4.9)
Vascular disorders	*Applies to iv form only:* Phlebitis		Hypotension	
Respiratory, thoracic and mediastinal disorders		Dyspnoea		Bronchospasm Pneumonitis allergic

System organ class	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)	Not known (cannot be estimated from available data)
Gastro-intestinal disorders	Diarrhoea Vomiting Nausea	Abdominal pain Dyspepsia Flatulence Constipation		Diarrhoea – haemorrhagic which in very rare cases may be indicative of enterocolitis, including pseudomembranous colitis (see section 4.4) Pancreatitis
Hepatobiliary disorders	Hepatic enzyme increased (ALT/AST, alkaline phosphatase, GGT)	Blood bilirubin increased		Jaundice and severe liver injury, including fatal cases with acute liver failure, primarily in patients with severe underlying diseases (see section 4.4) Hepatitis
Skin and subcutaneous tissue disorders [b]		Rash Pruritus Urticaria Hyperhidrosis		Toxic epidermal necrolysis Stevens-Johnson syndrome Erythema multiforme Photosensitivity reaction (see section 4.4) Leukocytoclastic vasculitis Stomatitis
Musculoskeletal and connective tissue disorders		Arthralgia Myalgia	Tendon disorders (see sections 4.3 and 4.4) including tendinitis (e.g. Achilles tendon) Muscular weakness which may be of special importance in patients with myasthenia gravis (see section 4.4)	Rhabdomyolysis Tendon rupture (e.g. Achilles tendon) (see sections 4.3 and 4.4) Ligament rupture Muscle rupture Arthritis
Renal and Urinary disorders		Blood creatinine increased	Renal failure acute (e.g. due to interstitial nephritis)	
General disorders and administration site conditions	*Applies to iv form only:* Infusion site reaction (pain, reddening)	Asthenia	Pyrexia	Pain (including pain in back, chest, and extremities)

[a] *Anaphylactic and anaphylactoid reactions may sometimes occur even after the first dose.*

[b] Mucocutaneous reactions may sometimes occur even after the first dose

Other undesirable effects which have been associated with fluoroquinolone administration include:

- attacks of porphyria in patients with porphyria

4.9 Overdose

According to toxicity studies in animals or clinical pharmacology studies performed with supra-therapeutic doses, the most important signs to be expected following acute overdose of Tavanic solution for infusion are central nervous system symptoms such as confusion, dizziness, impairment of consciousness, and convulsive seizures, increases in QT interval.

CNS effects including confusional state, convulsion, hallucination, and tremor have been observed in post marketing experience.

In the event of overdose, symptomatic treatment should be implemented. ECG monitoring should be undertaken, because of the possibility of QT interval prolongation. Haemodialysis, including peritoneal dialysis and CAPD, are not effective in removing levofloxacin from the body. No specific antidote exists.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: quinolone antibacterials, fluoroquinolones, ATC code: J01MA12
Levofloxacin is a synthetic antibacterial agent of the fluoroquinolone class and is the S (-) enantiomer of the racemic active substance ofloxacin.

Mechanism of action

As a fluoroquinolone antibacterial agent, levofloxacin acts on the DNA-DNA-gyrase complex and topoisomerase IV.

PK/PD relationship

The degree of the bactericidal activity of levofloxacin depends on the ratio of the maximum concentration in serum (Cmax) or the area under the curve (AUC) and the minimal inhibitory concentration (MIC).

Mechanism of resistance

Resistance to levofloxacin is acquired through a stepwise process by target site mutations in both type II topoisomerases, DNA gyrase and topoisomerase IV. Other resistance mechanisms such as permeation barriers (common in *Pseudomonas aeruginosa*) and efflux mechanisms may also affect susceptibility to levofloxacin.

Cross-resistance between levofloxacin and other fluoroquinolones is observed. Due to the mechanism of action, there is generally no cross-resistance between levofloxacin and other classes of antibacterial agents.

Breakpoints

The EUCAST recommended MIC breakpoints for levofloxacin, separating susceptible from intermediately susceptible organisms and intermediately susceptible from resistant organisms are presented in the below table for MIC testing (mg/l).

EUCAST clinical MIC breakpoints for levofloxacin (version 2.0, 2012-01-01):

Pathogen	**Susceptible**	**Resistant**
Enterobacteriacae	≤1 mg/l	>2 mg/l
Pseudomonas spp.	≤1 mg/l	>2 mg/l
Acinetobacter spp.	≤1 mg/l	>2 mg/l
Staphylococcus spp.	≤1 mg/l	>2 mg/l

S. pneumoniae [1]	≤2 mg/l	>2 mg/l
Streptococcus A, B, C, G	≤1 mg/l	>2 mg/l
H. influenzae [2, 3]	≤1 mg/l	>1 mg/l
M. catarrhalis [3]	≤1 mg/l	>1 mg/l
Non-species related breakpoints [4]	≤1 mg/l	>2 mg/l

1. The breakpoints for levofloxacin relate to high dose therapy.
2. Low-level fluoroquinolone resistance (ciprofloxacin MICs of 0.12-0.5 mg/l) may occur but there is no evidence that this resistance is of clinical importance in respiratory tract infections with *H. influenzae*.
3. Strains with MIC values above the susceptible breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate must be sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC above the current resistant breakpoint they should be reported resistant.
4. Breakpoints apply to an oral dose of 500 mg x 1 to 500 mg x 2 and an intravenous dose of 500 mg x 1 to 500 mg x 2.

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Commonly susceptible species

Aerobic Gram-positive bacteria
Bacillus anthracis
Staphylococcus aureus methicillin-susceptible
Staphylococcus saprophyticus
Streptococci, group C and G
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

Aerobic Gram-negative bacteria
Eikenella corrodens
Haemophilus influenzae
Haemophilus para-influenzae
Klebsiella oxytoca
Moraxella catarrhalis
Pasteurella multocida
Proteus vulgaris
Providencia rettgeri

Anaerobic bacteria
Peptostreptococcus

Other
Chlamydophila pneumoniae
Chlamydophila psittaci
Chlamydia trachomatis

Legionella pneumophila

Mycoplasma pneumoniae

Mycoplasma hominis *Ureaplasma urealyticum*

Species for which acquired resistance may be a problem

Aerobic Gram-positive bacteria
Enterococcus faecalis
Staphylococcus aureus methicillin-resistant[#]
Coagulase negative *Staphylococcus spp*

Aerobic Gram-negative bacteria
Acinetobacter baumannii
Citrobacter freundii
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Klebsiella pneumoniae
Morganella morganii
Proteus mirabilis
Providencia stuartii
Pseudomonas aeruginosa
Serratia marcescens

Anaerobic bacteria
Bacteroides fragilis

Inherently Resistant Strains

Aerobic Gram-positive bacteria
Enterococcus faecium

[#] Methicillin-resistant *S. aureus* are very likely to possess co-resistance to fluoroquinolones, including levofloxacin.

5.2 Pharmacokinetic properties

Absorption

Orally administered levofloxacin is rapidly and almost completely absorbed with peak plasma concentrations being obtained within 1 - 2 h. The absolute bioavailability is 99 - 100%.

Food has little effect on the absorption of levofloxacin.

Steady state conditions are reached within 48 hours following a 500 mg once or twice daily dosage regimen.

Distribution

Approximately 30 - 40% of levofloxacin is bound to serum protein.

The mean volume of distribution of levofloxacin is approximately 100 l after single and repeated 500 mg doses, indicating widespread distribution into body tissues.

Penetration into tissues and body fluids:

Levofloxacin has been shown to penetrate into bronchial mucosa, epithelial lining fluid, alveolar macrophages, lung tissue, skin (blister fluid), prostatic tissue and urine. However, levofloxacin has poor penetration intro cerebro-spinal fluid.

Biotransformation

Levofloxacin is metabolised to a very small extent, the metabolites being desmethyl-levofloxacin and levofloxacin N-oxide. These metabolites account for <5% of the dose and are excreted in urine. Levofloxacin is stereochemically stable and does not undergo chiral inversion.

Elimination

Following oral and intravenous administration of levofloxacin, it is eliminated relatively slowly from the plasma ($t_{½}$: 6 - 8 h). Excretion is primarily by the renal route (>85% of the administered dose).

The mean apparent total body clearance of levofloxacin following a 500 mg single dose was 175 +/-29.2 ml/min.

There are no major differences in the pharmacokinetics of levofloxacin following intravenous and oral administration, suggesting that the oral and intravenous routes are interchangeable.

Linearity

Levofloxacin obeys linear pharmacokinetics over a range of 50 to 1000 mg.

Special populations

Subjects with renal insufficiency

The pharmacokinetics of levofloxacin are affected by renal impairment. With decreasing renal function renal elimination and clearance are decreased, and elimination half-lives increased as shown in the table below:

Pharmacokinetics in renal insufficiency following single oral 500 mg dose

Cl_{cr} [ml/min]	<20	20 - 49	50 – 80
Cl_R [ml/min]	13	26	57
$t_{1/2}$ [h]	35	27	9

Elderly subjects

There are no significant differences in levofloxacin pharmacokinetics between young and elderly subjects, except those associated with differences in creatinine clearance.

Gender differences

Separate analysis for male and female subjects showed small to marginal gender differences in levofloxacin pharmacokinetics. There is no evidence that these gender differences are of clinical relevance.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of single dose toxicity, repeated dose toxicity, carcinogenic potential and toxicity to reproduction and development.

Levofloxacin caused no impairment of fertility or reproductive performance in rats and its only effect on fetuses was delayed maturation as a result of maternal toxicity.

Levofloxacin did not induce gene mutations in bacterial or mammalian cells but did induce chromosome aberrations in Chinese hamster lung cells *in vitro*. These effects can be attributed to inhibition of topoisomerase II. *In vivo* tests (micronucleus, sister chromatid exchange, unscheduled DNA synthesis, dominant lethal tests) did not show any genotoxic potential.
Studies in the mouse showed levofloxacin to have phototoxic activity only at very high doses. Levofloxacin did not show any genotoxic potential in a photomutagenicity assay, and it reduced tumour development in a photocarcinogenity study.

In common with other fluoroquinolones, levofloxacin showed effects on cartilage (blistering and cavities) in rats and dogs. These findings were more marked in young animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)
Water for injection

6.2 Incompatibilities

This medicinal product must not be mixed with heparin or alkaline solutions (e.g. sodium bicarbonate).
This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years

Shelf life after perforation of the rubber stopper: immediate use (see section 6.6).

From a microbiological point of view, the solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Keep the bottle in the outer carton in order to protect from light.
Inspect visually prior to use. Only clear solutions without particles should be used.

6.5 Nature and contents of container

50 ml type I glass bottle with flanged aluminium cap, chlorobutyl rubber stopper and tear-off polypropylene lid. Each bottle contains 50 ml solution for infusion. Pack sizes of 1 and 5 bottles.

100 ml type I glass bottle with flanged aluminium cap, chlorobutyl rubber stopper and tear-off polypropylene lid. Each bottle contains 100 ml solution for infusion. Pack sizes of 1, 5 and 20 bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Tavanic solution for infusion should be used immediately (within 3 hours) after perforation of the rubber stopper in order to prevent any bacterial contamination. No protection from light is necessary during infusion.
This medicinal product is for single use only.
The solution should be visually inspected prior to use. It must only be used if the solution is clear, greenish-yellow solution, practically free from particles.
As for all medicines, any unused medicinal product should be disposed of accordingly and in compliance with local environmental regulations.

Mixture with other solutions for infusion:

Tavanic solution for infusion is compatible with the following solutions for infusion:

- 0.9% sodium chloride solution.
- 5% glucose injection.
- 2.5% glucose in Ringer solution.
- Combination solutions for parenteral nutrition (amino acids, glucose, electrolytes).

See section 6.2 for incompatibilities.

7 MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8 MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: [To be completed nationally]

Date of last renewal: [To be completed nationally]

10 DATE OF REVISION OF THE TEXT

[To be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARDBOARD / BOTTLE OF 50 ML
LABEL / BOTTLE OF 50 ML

CARDBOARD / BOTTLE OF 100 ML
LABEL / BOTTLE OF 100 ML

1. NAME OF THE MEDICINAL PRODUCT

Tavanic 5 mg/ml solution for infusion
levofloxacin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each bottle of 50 ml solution for infusion contains 250 mg levofloxacin as levofloxacin hemihydrate
Each bottle of 100 ml solution for infusion contains 500 mg levofloxacin as levofloxacin hemihydrate

3. LIST OF EXCIPIENTS

Also contains: sodium chloride, sodium hydroxide, hydrochloric acid and water for injection. See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion
For 50 ml bottle:
1 bottle of 50 ml
5 bottles of 50 ml

For 100 ml bottle:
1 bottle of 100 ml
5 bottles of 100 ml
20 bottles of 100 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Single use only
Read the package leaflet before use
Intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use as directed by your doctor.

8. EXPIRY DATE

EXP
Should be used within 3 hours after perforation of the rubber stopper

9. SPECIAL STORAGE CONDITIONS

Keep the bottle in the outer carton in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Discard any unused contents

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[To be completed nationally]
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12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

[To be completed nationally]

16. INFORMATION IN BRAILLE

[To be completed nationally]

PACKAGE LEAFLET

Package leaflet: Information for the user

Tavanic 5 mg/ml solution for infusion

levofloxacin

Read all of this leaflet carefully before you are given 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, nurse or pharmacist.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Tavanic solution for infusion is and what it is used for

The name of your medicine is Tavanic solution for infusion. Tavanic solution for infusion contains a medicine called levofloxacin. This belongs to a group of medicines called antibiotics. Levofloxacin is a 'quinolone' antibiotic. It works by killing the bacteria that cause infections in your body.

Tavanic solution for infusion can be used to treat infections of the:

- Lungs, in people with pneumonia
- Urinary tract, including your kidneys or bladder
- Prostate gland, where you have a long lasting infection
- Skin and underneath the skin, including muscles. This is sometimes called 'soft tissue'

In some special situations, Tavanic solution for infusion may be used to lessen the chances of getting a pulmonary disease named anthrax or worsening of the disease after you are exposed to the bacteria causing anthrax.

2. What you need to know before you are given Tavanic solution for infusion

Do not have this medicine and tell your doctor if:
- You are allergic to levofloxacin, any other quinolone antibiotic such as moxifloxacin, ciprofloxacin or ofloxacin or any of the other ingredients of this medicine (listed in section 6)
  Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
- You have ever had epilepsy
- You have ever had a problem with your tendons such as tendonitis that was related to treatment with a 'quinolone antibiotic'. A tendon is the cord that joins your muscle to your skeleton

- You are a child or a growing teenager
- You are pregnant, might become pregnant, or think you may be pregnant
- You are breast-feeding

Do not have this medicine if any of the above applies to you. If you are not sure, talk to your doctor, nurse or pharmacist before you are given Tavanic.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before you have your medicine if:

- You are 60 years of age or older
- You are using corticosteroids, sometimes called steroids (see section ”Other medicines and Tavanic”)
- You have ever had a fit (seizure)
- You have had damage to your brain due to a stroke or other brain injury
- You have kidney problems
- You have something known as ‘glucose – 6 – phosphate dehydrogenase deficiency’. You are more likely to have serious problems with your blood when taking this medicine
- You have ever had mental health problems
- You have ever had heart problems: caution should be taken when using this kind of medicine, if you were born with or have family history of prolonged QT interval (seen on ECG, electrical recording of the heart), have salt imbalance in the blood (especially low level of potassium or magnesium in the blood), have a very slow heart rhythm (called ‘bradycardia’), have a weak heart (heart failure), have a history of heart attack (myocardial infarction), you are female or elderly or you are taking other medicines that result in abnormal ECG changes (see section “Other medicines and Tavanic”).
- You are diabetic
- You have ever had liver problems
- You have myasthenia gravis.

If you are not sure if any of the above applies to you, talk to your doctor, nurse or pharmacist before being given Tavanic.

Other medicines and Tavanic

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Tavanic can affect the way some other medicines work. Also some medicines can affect the way Tavanic work.

In particular, tell your doctor if you are taking any of the following medicines. This is because it can increase the chance of you getting side effects, when taken with Tavanic:

- Corticosteroids, sometimes called steroids – used for inflammation. You may be more likely to have inflammation and/or rupture of your tendons.
- Warfarin - used to thin the blood. You may be more likely to have a bleed. Your doctor may need to take regular blood tests to check how well your blood can clot.
- Theophylline - used for breathing problems. You are more likely to have a fit (seizure) if taken with Tavanic.
- Non-steroidal anti-inflammatory drugs (NSAIDS) - used for pain and inflammation such as aspirin, ibuprofen, fenbufen, ketoprofen, indomethacin. You are more likely to have a fit (seizure) if taken with Tavanic.
- Ciclosporin - used after organ transplants. You may be more likely to get the side effects of ciclosporin.
- Medicines known to affect the way your heart beats. This includes medicines used for abnormal heart rhythm (antiarrhythmics such as quinidine, hydroquinidine, disopyramide, sotalol, dofetilide, ibutilide and amiodarone), for depression (tricyclic antidepressants such as amitriptyline and imipramine), for psychiatric disorders (antipsychotics), and for bacterial infections (‘macrolide’ antibiotics such as erythromycin, azithromycine and clarithromycin).

- Probenecid – used for gout and cimetidine – used for ulcers and heartburn. Special care should be taken when taking either of these medicines with Tavanic. If you have kidney problems, your doctor may want to give you a lower dose.

Urine tests for opiates
Urine tests may show 'false-positive' results for strong painkillers called 'opiates' in people having Tavanic. If your doctor has prescribed a urine test, tell your doctor you are having Tavanic.

Tuberculosis tests
This medicine may cause "false negative" results for some tests used in laboratory to search for the bacteria causing tuberculosis.

Pregnancy and breast-feeding
Do not have this medicine if:
- You are pregnant, might become pregnant or think you may be pregnant
- You are breast-feeding or planning to breast-feed

Driving and using machines

You may get side effects after being given this medicine, including feeling dizzy, sleepy, a spinning feeling (vertigo) or changes to your eyesight. Some of these side effects can affect you being able to concentrate and your reaction speed. If this happens, do not drive or carry out any work that requires a high level of attention.

Tavanic solution for infusion contains sodium
This medicine contains181 mg of sodium per 250 mg dose. This should be taken into consideration by patients on a controlled sodium diet.

3. How Tavanic solution for infusion is given

How Tavanic solution for infusion is given
- Tavanic solution for infusion is a medicine for use in hospitals
- It will be given to you by a doctor or nurse as an injection. The injection will be into one of your veins and be given over a period of time (this is called an intravenous infusion)
- For 250 mg Tavanic solution for infusion, the infusion time should be 30 minutes or more
- For 500 mg Tavanic solution for infusion, the infusion time should be 60 minutes or more
- Your heart rate and blood pressure should be closely monitored. This is because an unusual fast beating of the heart and a temporary lowering of blood pressure are possible side effects that have been seen during the infusion of a similar antibiotic. If your blood pressure drops noticeably while you are being given the infusion, it will be stopped straight away.

How much Tavanic solution for infusion is given
If you are not sure why you are being given Tavanic or have any questions about how much Tavanic is being given to you, speak to your doctor, nurse or pharmacist.
- Your doctor will decide on how much Tavanic you should have
- The dose will depend on the type of infection you have and where the infection is in your body
- The length of your treatment will depend on how serious your infection is

Adults and the elderly
- Pneumonia: 500 mg once or twice daily
- Infection of urinary tract, including your kidneys or bladder: 500 mg once daily
- Prostate gland infection: 500 mg once daily

- Infection of skin and underneath the skin, including muscles: 500 mg once or twice daily

Adults and the elderly with kidney problems
Your doctor may need to give you a lower dose.

Children and Teenagers
This medicine must not be given to children or teenagers.

Protect your skin from sunlight
Keep out of direct sunlight while having this medicine and for 2 days after you stop having it. This is because your skin will become much more sensitive to the sun and may burn, tingle or severely blister if you do not take the following precautions:
- Make sure you use high factor sun cream
- Always wear a hat and clothes which cover your arms and legs
- Avoid sun beds

If you have more Tavanic solution for infusion than you should
It is unlikely that your doctor or nurse will give you too much medicine. Your doctor and nurse will monitor your progress, and check the medicine you are given. Always ask if you are not sure why you are getting a dose of medicine.
Having too much Tavanic may cause the following effects to happen: convulsive fits (seizures), feeling confused, dizzy, less conscious, having tremor and heart problems - leading to uneven heart beats as well as feeling sick (nausea).

If you miss a dose of Tavanic solution for infusion
Your doctor or nurse will have instructions on when to give you this medicine. It is unlikely that you will not be given the medicine as it has been prescribed. However, if you do think you have missed a dose, tell your doctor or nurse.

If you stop having Tavanic solution for infusion
Your doctor or nurse will continue giving you Tavanic, even if you feel better. If it is stopped too soon, your condition may get worse or the bacteria may become resistant to the medicine. After a few days treatment with the solution for infusion, your doctor may decide to switch you to the tablet form of this medicine to complete your course of treatment.

If you have any further questions on the use of this medicine, ask your doctor, nurse, or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. These effects are normally mild or moderate and often disappear after a short time.

Stop having Tavanic and tell a doctor or nurse straight away if you notice the following side effect:

Very rare (may affect up to 1 in 10,000 people)
- You have an allergic reaction. The signs may include: a rash, swallowing or breathing problems, swelling of your lips, face, throat, or tongue.

Stop having Tavanic and tell a doctor or nurse straight away if you notice any of the following serious side effects - you may need urgent medical treatment:

Rare (may affect up to 1 in 1,000 people)
- Watery diarrhoea which may have blood in it, possibly with stomach cramps and a high temperature. These could be signs of a severe bowel problem

- Pain and inflammation in your tendons or ligaments which could lead to rupture. The Achilles tendon is affected most often
- Fits (convulsions)

Very rare (may affect up to 1 in 10,000 people)
- Burning, tingling, pain, or numbness. These may be signs of something called 'neuropathy'

Other:
- Severe skin rashes which may include blistering or peeling of the skin around your lips, eyes, mouth, nose and genitals
- Loss of appetite, skin and eyes becoming yellow in colour, dark-coloured urine, itching, or tender stomach (abdomen). These may be signs of liver problems which may include a fatal failure of the liver

If your eyesight becomes impaired or if you have any other eye disturbances whilst taking Tavanic, consult an eye specialist immediately.

Tell your doctor if any of the following side effects gets serious or lasts longer than a few days:

Common (may affect up to 1 in 10 people)
- Sleeping problems
- Headache, feeling dizzy
- Feeling sick (nausea, vomiting) and diarrhoea
- Increase in the level of some liver enzymes in your blood
- Reactions at the site of infusion
- Inflammation of a vein

Uncommon (may affect up to 1 in 100 people)
- Changes in the number of other bacteria or fungi, infection by fungi named Candida, which may need to be treated
- Changes in the number of white blood cells shown up in the results of some blood tests (leukopenia, eosinophilia)
- Feeling stressed (anxiety), feeling confused, feeling nervous, feeling sleepy, trembling, a spinning feeling (vertigo)
- Shortness of breath (dyspnoea)
- Changes in the way things taste, loss of appetite, stomach upset or indigestion (dyspepsia), pain in your stomach area, feeling bloated (flatulence) or constipation
- Itching and skin rash, severe itching or hives (urticaria), sweating too much (hyperhidrosis)
- Joint pain or muscle pain
- Blood tests may show unusual results due to liver (bilirubin increased) or kidney (creatinine increased) problems
- General weakness

Rare (may affect up to 1 in 1,000 people)
- Bruising and bleeding easily due to a lowering in the number of blood platelets (thrombocytopenia)
- Low number of white blood cells (neutropenia)
- Exaggerated immune response (hypersensitivity)
- Lowering of your blood sugar levels (hypoglycaemia). This is important for people that have diabetes.
- Seeing or hearing things that are not there (hallucinations, paranoia), change in your opinion and thoughts (psychotic reactions) with a risk of having suicidal thoughts or actions
- Feeling depressed, mental problems, feeling restless (agitation), abnormal dreams or nightmares
- Tingly feeling in your hands and feet (paraesthesia)

- Problems with your hearing (tinnitus) or eyesight (blurred vision)
- Unusual fast beating of your heart (tachycardia) or low blood pressure (hypotension)
- Muscle weakness. This is important in people with myasthenia gravis (a rare disease of the nervous system).
- Changes in the way your kidney works and occasional kidney failure which may be due to an allergic kidney reaction called interstitial nephritis.
- Fever

Other side effects include:
- Lowering in red blood cells (anemia): this can make the skin pale or yellow due to damage of the red blood cells; lowering in the number of all types of blood cells (pancytopenia)
- Fever, sore throat and a general feeling of being unwell that does not go away. This may be due to a lowering in the number of white blood cells (agranulocytosis).
- Loss of circulation (anaphylactic like shock)
- Increase of your blood sugar levels (hyperglycaemia) or lowering of your blood sugar levels leading to coma (hypoglycaemic coma). This is important for people that have diabetes.
- Changes in the way things smell, loss of smell or taste (parosmia, anosmia, ageusia)
- Problems moving and walking (dyskinesia, extrapyramidal disorders)
- Temporary loss of consciousness or posture (syncope)
- Temporary loss of vision
- Impairment or loss of hearing
- Abnormal fast heart rhythm, life-threatening irregular heart rhythm including cardiac arrest, alteration of the heart rhythm (called 'prolongation of QT interval', seen on ECG, electrical activity of the heart)
- Difficulty breathing or wheezing (bronchospasm)
- Allergic lung reactions
- Pancreatitis
- Inflammation of the liver (hepatitis)
- Increased sensitivity of your skin to sun and ultraviolet light (photosensitivity)
- Inflammation of the vessels that carry blood around your body due to an allergic reaction (vasculitis)
- Inflammation of the tissue inside the mouth (stomatitis)
- Muscle rupture and muscle destruction (rhabdomyolysis)
- Joint redness and swelling (arthritis)
- Pain, including pain in the back, chest and extremities
- Attacks of porphyria in people who already have porphyria (a very rare metabolic disease)
- Persistent headache with or without blurred vision (benign intracranial hypertension)

If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet.

5. How to store Tavanic solution for infusion

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

Keep the bottle in the outer carton in order to protect from light. No protection from light is required during the infusion.

Once the infusion bottle has been opened (rubber stopper perforated) the solution should be used immediately (within 3 hours) in order to prevent any bacterial contamination.

Do not use this medicine after the expiry date which is stated on the carton and the bottle after EXP. The expiry date refers to the last day of that month.

Do not use this medicine if you notice that the solution is not clear, greenish-yellow solution and/or has particles in it.

Do not throw away any medicines via wastewater or household waste. Ask your nurse or pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Tavanic solution for infusion contains
The active substance is levofloxacin. Tavanic solution for infusion is available in two presentations: 250 mg in a 50 ml glass bottle and 500 mg in a 100 ml glass bottle. One ml of solution for infusion contains 5 mg of levofloxacin.

The other ingredients are: sodium chloride, sodium hydroxide, hydrochloric acid and water for injection.

What Tavanic solution for infusion looks like and contents of the pack
Tavanic solution for infusion is a clear solution, greenish-yellow, without particles. It is presented in glass bottle.

- The 50 ml bottle is available in packs of 1 and 5
- The 100 ml bottle is available in packs of 1, 5 and 20

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
[To be completed nationally]

Manufacturer

[To be completed nationally]

This medicine is authorised in the Member States of the EEA under the following name:
Tavanic

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

This leaflet was last revised in MM/YYYY
[To be completed nationally]