Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tarivid IV 2 mg/ml Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of 100ml contains 220mg Ofloxacin Hydrochloride equivalent to 200mg Ofloxacin. (2mg/ml Ofloxacin).

Excipients: Contains 354mg of Sodium

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
A colourless, Type I, Ph. Eur., glass vial, sealed with a chlorobutyl stopper, containing a clear greenish yellow aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ofloxacin is a synthetic 4-fluoroquinolone antibacterial agent.

Tarivid solution for infusion is indicated in adults for the treatment of the following bacterial infections (see sections 4.4 and 5.1):
- Pyelonephritis and complicated urinary tract infections
- Prostatitis, epididymo-orchitis
- Pelvic inflammatory disease, in combination treatment
- Sepsis due to above-mentioned genito-urinary infections

The treatment of acute and chronic infections of respiratory tract due to Gram-positive and Gram-negative micro organisms sensitive to ofloxacin.

Skin and soft tissue infections.

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

4.2 Posology and method of administration

The dose of ofloxacin is determined by the type and severity of the infection.

The usual recommended dosages of Tarivid IV in adults are:

Respiratory tract infection: 200mg twice daily.
Skin and soft tissue infections: 400mg twice a day.

Indication	Daily dose regimen (according to severity)	Duration of treatment (according to severity)
Complicated UTI	200 mg twice daily (can be increased to 400 mg twice daily)	7-21 days
Pyelonephritis	200 mg twice daily (can be increased to 400 mg twice daily)	7-10 days (can be extended to 14 days)
Acute prostatitis	200 mg twice daily (can be increased to 400 mg twice daily)	2- 4 weeks *

Chronic prostatitis		4-8 weeks *
Epididymo-orchitis	200 mg twice daily (can be increased to 400 mg twice daily)	14 days
Pelvic inflammatory disease	400 mg twice daily	14 days

* for prostatitis longer duration of treatment may be considered after careful re-examination of the patient.

Tarivid tablets may also be used to complete a course of therapy in patients who have shown improvement during initial treatment with intravenous ofloxacin.

The infusion time for Tarivid IV should not be less than 30 minutes.
Daily doses of more than 400mg must be divided into two separate doses and be given at approximately equal intervals.
Ofloxacin solution is only intended for slow intravenous infusion: it is administered once or twice daily. The infusion time must be at least 30 minutes for 200mg of ofloxacin solution. This is of particular importance when ofloxacin is administered concomitantly with drugs that can lead to a reduction in blood pressure or with barbiturate-containing anaesthetics.

The duration of treatment is determined according to the response of the causative organisms and the clinical picture. As with all antibacterial agents, treatments for both Tarivid tablets and Tarivid IV should be continued for at least 3 days after the body temperature has returned to normal and the symptoms have subsided.

In most cases of acute infection a course of treatment lasting 7 to 10 days is sufficient. For infections with β-haemolytic streptococci, treatment should be continued for at least 10 days. Until further experience has been obtained, the duration of treatment should not exceed 2 months.

Impaired renal function: The dosage of Tarivid should be adjusted according to the degree of renal impairment.

Dosage in adults with renal insufficiency:
In patients with impaired renal function, the following oral or IV dosages are recommended:

Creatinine Clearance	Unit Dose mg*	Number / 24h	Intervals h
50 – 20 ml/min	100 – 200	1	24
<20 ml/min** or haemodialysis or peritoneal dialysis	100 or 200	1 1	24 48

* According to indication or dose interval.
** The serum concentration of ofloxacin should be monitored in patients with severe renal impairment and dialysis patients.

Impaired liver function: The excretion of ofloxacin may be reduced in patients with severe liver function disorders (e.g. cirrhosis of the liver with ascites). A maximum daily dose of 400mg ofloxacin should therefore not be exceeded.

Children: Contra-indicated in children and growing adolescents.

Elderly: Dosage may need to be reduced in accordance with renal or hepatic function. (See section 4.4 QT interval prolongation).

4.3 Contraindications

Ofloxacin must not be used:

- In patients hypersensitive to ofloxacin, other quinolones, or 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 adolescents in the growth phase.*
- During pregnancy*
- In breast-feeding women*
- Patients with pre-existing CNS lesions involving a lowered convulsion threshold

* Because judging from animal experiments, a risk of damage to the growth-plate cartilage in the growing organism cannot be entirely excluded.

4.4 Special warnings and precautions for use

- The use of ofloxacin should be avoided in patients who have experienced serious adverse reactions in the past when using quinolone or fluoroquinolones containing products (see section 4.8). Treatment of these patients with ofloxacin should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment (see also section 4.3).
- Prolonged, disabling and potentially irreversible serious adverse drug reactionVery rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving quinolones and fluoroquinolones irrespective of their age and pre-existing risk factors. Ofloxacin should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their prescriber for advice.
- Methicillin-resistant S. aureus are very likely to possess co-resistance to fluoroquinolones, including ofloxacin. Therefore ofloxacin is not recommended for the treatment of known or suspected MRSA infections unless laboratory results have confirmed susceptibility of the organism to ofloxacin (and commonly recommended antibacterial agents for the treatment of MRSA-infections are considered inappropriate).
- Neisseria gonorrhoeae infectionsDue to increase in resistance to N. gonorrhoeae, ofloxacin should not be used as empirical treatment option in suspected urethral gonococcal infection (urethral gonococcal infection, pelvic inflammatory disease and epididymo-orchitis), unless the pathogen has been identified and confirmed as susceptible to ofloxacin. If clinical improvement is not achieved after 3 days of treatment, the therapy should be reconsidered.
- Pelvic inflammatory disease For pelvic inflammatory disease, ofloxacin should only be considered in combination with anaerobe coverage.
- Escherichia coli infection 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.

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

- Hypersensitivity and allergic reactions have been reported for fluoroquinolones after first administration. Anaphylactic and anaphylactoid reactions can progress to life-threatening shock, even after the first administration. In these cases ofloxacin should be discontinued and suitable treatment (e.g. treatment for shock) should be initiated.
- *Clostridium difficile* – associated diseaseDiarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with ofloxacin (including several weeks after treatment), may be symptomatic of pseudo-membranous colitis (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 ofloxacin. If pseudo-membranous colitis is suspected, ofloxacin must be stopped immediately.Appropriate specific antibiotic therapy must be started without delay (e.g. oral vancomycin, oral teicoplanin or metronidazole). Products inhibiting the peristalsis are contraindicated in this clinical situation.
- Patients predisposed to seizuresQuinolones may lower the seizure threshold and may trigger seizures. Ofloxacin is contraindicated in patients with a history of epilepsy (see section 4.3) and, as with other quinolones, ofloxacin should be used with extreme caution in patients predisposed to seizures. Such patients may be patients with pre-existing central nervous system lesions, concomitant treatment with fenbufen and similar non-steroidal anti-inflammatory drugs or with drugs which lower the cerebral seizure threshold, such as theophylline (see section 4.5: Interactions). If seizure develops, treatment with ofloxacin should be discontinued.
- Tendinitis and tendon ruptureTendinitis and tendon rupture (especially but not limited to Achilles tendon), sometimes bilateral, may occur as early as within 48 hours of starting treatment with quinolones and

fluoroquinolones and have been reported to occur even up to several months after discontinuation of treatment. The risk of tendinitis and tendon rupture is increased in older patients, patients with renal impairment, patients with solid organ transplants, and those treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided.At the first sign of tendinitis (e.g. painful swelling, inflammation) the treatment with ofloxacin should be discontinued and alternative treatment should be considered. The affected limb(s) should be appropriately treated (e.g. immobilisation). Corticosteroids should not be used if signs of tendinopathy occur.

- Patients with renal impairmentSince ofloxacin is mainly excreted by the kidneys, the dose of ofloxacin should be adjusted in patients with renal impairment. (See section 4.2 Posology and method of administration).
- Patients with history of psychotic disorder Psychotic reactions including suicidal ideation/attempt (see Section 11) have been reported in patients receiving fluoroquinolones sometimes only after a single dose. In some cases these have progressed to suicidal thoughts or self-endangering behaviour including suicide attempt, sometimes after a single dose of ofloxacin (see section 4.8). In the event that a patient develops these reactions, ofloxacin should be discontinued immediately at the first signs or symptoms of these reactions and patients should be advised to contact their prescriber for advice. Alternative nonfluoroquinolone antibacterial therapy should be considered, and appropriate measures instituted. Ofloxacin should be used with caution in patients with a history of psychotic disorder or in patients with psychiatric disorder.
- Patients with impaired liver function

Ofloxacin should be used with caution in patients with impaired liver function, as liver damage may occur. Cases of fulminant hepatitis potentially leading to liver failure (including fatal cases) have been reported with fluoroquinolones. 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, pruritis or tender abdomen (see section 4.8: Undesirable effects).

- Patients treated with vitamin K antagonists

Due to possible increase in coagulation tests (PT/INR) and/or bleeding in patients treated with fluoroquinolones, including ofloxacin, 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).

- Risks of resistance

The prevalence of acquired resistance may vary geographically and over time for selected species. Therefore, local information on resistance is required; microbiological diagnosis with isolation of the pathogen and demonstration of its susceptibility should be sought, especially for severe infections or failure to respond to treatment.

- Myasthenia gravis

Fluoroquinolones, including ofloxacin, 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. Ofloxacin is not recommended in patients with a known history of myasthenia gravis

- Prevention of photosensitization

Photosensitization has been reported with ofloxacin (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.

- Superinfection

As with other antibiotics, the use of ofloxacin, especially if prolonged, may result in the overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If secondary infection occurs during therapy, appropriate measures should be taken.

- QT interval prolongation

Cases of QT interval prolongation have been reported in patients taking fluoroquinolones including ofloxacin.

Caution should be taken when using fluoroquinolones, including ofloxacin, 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 ofloxacin, in these populations.(See section 4.2 *Elderly*, section 4.5, section 4.8, section 4.9).

- Dysglycaemia

Disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported with fluoroquinolones including ofloxacin and occur more frequently in the elderly. 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).

Tarivid treatment should be stopped immediately if a patient reports blood glucose disturbance and alternative nonfluoroquinolone antibacterial therapy should be considered.

- Peripheral neuropathy

Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypaesthesia, dysesthesia, or weakness have been reported in patients receiving quinolones and fluoroquinolones. Patients under treatment with ofloxacin should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of potentially irreversible condition. (see section 4.8)

- Patients with glucose-6-phosphate-dehydrogenase deficiency

Patients with a latent or diagnosed glucose-6-phosphate dehydrogenase deficiency may be predisposed to haemolytic reactions if they are treated with quinolones. Therefore, if ofloxacin has to be used in these patients, potential occurrence of haemolysis should be monitored.

- 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).

- Interference with laboratory tests

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

- Tarivid IV contains sodium

This medicinal product contains 354 mg sodium per dose, equivalent to 18% of the WHO recommended maximum daily intake for sodium. The maximum daily dose of this product is equivalent to 71% of the WHO recommended maximum daily intake for sodium. Tarivid IV is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

- Aortic Aneurysm and Dissection

Epidemiologic studies report an increased risk of aortic aneurysm and dissection after intake of fluoroquinolones, particularly in the older population.

Therefore, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease, or in patients diagnosed with pre-existing aortic aneurysm and/or aortic dissection, or in presence of other risk factors or conditions predisposing for aortic aneurysm and dissection (e.g. Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet's disease, hypertension, known atherosclerosis).

In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.

4.5 Interaction with other medicinal products and other forms of interactions

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

No pharmacokinetic interactions of ofloxacin 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 drugs, which lower the seizure threshold.

● Vitamin K antagonists

Increased coagulation tests (PT/INR) and/or bleeding, which may be severe, have been reported in patients treated with ofloxacin in combination with a vitamin K antagonist (e.g. warfarin). Coagulation tests, therefore, should be monitored in patients treated with Vitamin K antagonists because of a possible increase in the effect of coumarin derivatives.

● Probenecid, cimetidine, furosemide or methotrexate

Probenecid decreased the total clearance of ofloxacin by 24%, and increased AUC by 16%. The proposed mechanism is a competition or inhibition for active transport at the renal tubular excretion. Caution should be exercised when ofloxacin is coadministered with drugs that affect the tubular renal secretion (such as probencid, cimetidine, furosemide or methotrexate).

Sudden reductions in blood pressure may occur when Tarivid IV is administered with hypotensive agents. In such cases, or if the drug is given concomitantly with barbiturate anaesthetics, cardiovascular function should be monitored.
● Drugs known to prolong QT interval

Ofloxacin, 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).

Concurrent administration of anticoagulant therapy may require adjustment of the dose of the latter as prolongation of bleeding time has been reported. In a study with phencourmarin no interactions were noted.

Glibenclamide

Ofloxacin may cause a slight increase in serum concentrations of glibenclamide administered concurrently; it is therefore recommended that patients treated concomitantly with this combination should be closely monitored.

Concomitant use with some phenylpropionic acid derived non-steroidal anti-inflammatory drugs may lead to toxicity possibly because of renal effects.

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

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

4.6 Fertility, pregnancy and lactation

Pregnancy
Based on a limited amount of human data, the use of fluoroquinolones in the first trimester of pregnancy has not been associated with an increased risk of major malformations or other adverse effects on pregnancy outcome. Animal studies have shown damage to the joint cartilage in immature animals but no teratogenic effects. Therefore Ofloxacin must not be prescribed in pregnancy or in women at risk of pregnancy. (See section 4.3 Contraindications).

Breast-feeding
Ofloxacin is excreted into human breast milk in small amounts. Because of the potential for arthropathy and other serious toxicity in the nursing infant, breast feeding should be discontinued during treatment with ofloxacin (See 4.3 Contraindications).

4.7 Effects on ability to drive and use machines

Some adverse reactions (e.g. dizziness/vertigo, drowsiness, visual disturbance) 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 and on extensive post marketing experience.

System organ class	**Common (≥1/100 to <1/10)**	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Very rare (< 1/10,000)**	**Not known (cannot be estimated from available data)***
Infections and infestations		Fungal infection, Pathogen resistance			
Blood and the lymphatic system disorders				Anaemia Haemolytic anaemia, Leukopenia, Eosinophilia, Thrombo-cyto penia	Agranulocytosis, Bone marrow failure
Immune system disorders			Anaphylactic reaction*, Anaphylactoid reaction*, Angioedema*	Anaphylactic shock*, Anaphylactoid shock*	
Metabolism and Nutrition disorders			Anorexia, Hypoglycaemic coma (see section 4.4)		Hypoglycaemia in diabetics treated with hypoglycaemic agents (see Section 4.4) Hyperglycaemia
Psychiatric disorders**		Agitation, Sleep disorder, Insomnia	Psychotic disorder (for e.g. hallucination), Anxiety, Confusional state, Nightmares, Depression, Delirium, Memory impairment		Psychotic disorder and depression with self-endangering behaviour including suicidal ideation or suicide attempt (see Section 4.4) Nervousness
Nervous system disorders**		Dizziness, Headache	Somnolence, Paraesthesia,	Peripheral sensory	Tremor Dyskinesia Ageusia Syncope, Benign intracranial hypertension

			Dysgeusia, Parosmia	neuropathy* Peripheral sensory motor neuropathy* Convulsion*, Extra-pyramidal symptoms or other disorders of muscular coordination	
Eye disorders**		Eye irritation	Visual disturbance		Uveitis
Ear and labyrinth disorders**		Vertigo		Tinnitus, Hearing loss	Hearing impaired
Cardiac disorders			Tachycardia		Ventricular arrhythmias, torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged (see section 4.4 and 4.9)
Vascular disorders	Phlebitis		Hypotension		During infusion of ofloxacin, tachycardia and hypotension may occur. Such a decrease in blood pressure may, in very rare cases, be severe.
Respiratory, thoracic and mediastinal disorders	-	Cough, Naso-pharyngitis	Dyspnoea, Bronchospasm		Allergic pneumonitis, Severe dyspnoea
Gastro-intestinal disorders		Abdominal pain, Diarrhoea, Nausea, Vomiting	Enterocolitis,which may sometimes haemorrhagic	Pseudo-membranous colitis*	Dyspepsia Flatulence Constipation Pancreatitis, stomatitis
Hepato-bilary disorders			Hepatic enzymes increased (ALAT, ASAT, LDH, gamma-GT and/or alkaline phosphatase) Blood bilirubin increased	Jaundice cholestatic	Hepatitis, which may be severe* **Severe liver injury, including cases with acute liver failure, sometimes fatal, have been reported with ofloxacin, primarily in patients with underlying liver disorders (see section 4.4).**
Skin and subcutaneous tissue disorders		Pruritus, Rash	Urticaria, Hot flushes, Hyperhidrosis Pustular rash	Erythema multiforme, Toxic epidermal necrolysis, Photo-sensitivity reaction*, Drug eruption Vascular purpura, Vasculitis, which can lead in exceptional cases to skin necrosis	Stevens-Johnson syndrome; Acute generalized exanthemous pustulosis; drug rash, Exfoliative dermatitis
Musculoskeletal			Tendonitis	Arthralgia,	Rhabdomyolysis and/or Myopathy,

and Connective tissue disorders**				Myalgia, Tendon rupture (e.g. Achilles tendon) which may occur within 48 hours of treatment start and may be bilateral.	Muscular weakness which may be of special importance in patients with myasthenia gravis, Muscle tear, muscle rupture, Ligament rupture, Arthritis
Renal and Urinary disorders			Bloodcreatinine increased	Acute renal failure	Acute interstitial nephritis
Congenital and familial/genetic disorders					Attacks of porphyria in patients with porphyria
General disorders and administration site conditions**	Infusion site reaction (pain, reddening)				Asthenia Pyrexia Pain (including pain in back, chest, and extremities)

* postmarketing experience

**Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendonitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impairment of hearing, vision, taste and smell) have been reported in association with the use of quinolones and fluoroquinolones in some cases irrespective of pre-existing risk factors (see Section 4.4).

Reporting of suspected adverse events

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance. Website: www.hpra.ie

4.9 Overdose

The most important signs to be expected following acute overdose are CNS symptoms such as confusion, dizziness, impairment of consciousness and seizures, increase in QT interval, as well as gastrointestinal reactions such as nausea and mucosal erosions.
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. Antacids may be used for protection of gastric mucosa. A fraction of ofloxacin may be removed from the body with haemodialysis. Peritoneal dialysis and CAPD are not effective in removing ofloxacin from the body. No specific antidote exists.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ofloxacin is a quinolone-carbolic acid derivative with a wide range of antibacterial activity against both gram negative and gram positive organisms.It inhibits bacterial DNA replication by blocking DNA topo-isomerases, in particular DNA gyrase.

Therapeutic doses of ofloxacin are devoid of pharmacological effects on the voluntary or autonomic nervous systems.

The ATC code is J01 MA01.

Fluoroquinolones have a concentration-dependent bactericidal activity, with a moderate post antibiotic effect. For this class of antimicrobials, the ratio between AUC and MIC or Cmax and MIC is predictive of clinical success.

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.

Resistance to ofloxacin 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 ofloxacin.

5.2 Pharmacokinetic properties

An oxoquinolone anti-infective, widely distributed, with a protein binding capacity of 25%, slightly metabolised in liver to inactive metabolites and excreted via the kidney with T ½ of 5 hours. Ofloxacin concentrations in the urine and at the site of urinary tract infections exceed those measured in serum by 5 to 100-fold.

5.3 Preclinical safety data

Toxicological studies have shown that administration of oxoquinolone antibacterial agents at doses higher than the therapeutic range can produce erosion of the cartilage in weight-bearing joints in immature animals of some species. No such lesions have been shown to occur in man to date. This product should not be prescribed for children.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

6.2 Incompatibilities

This medicical product should not be mixed with other medicinal products except those mentioned in section 6.6. Heparin should not be administered in the same intravenous infusion fluid because of the risk of precipitation.

6.3 Shelf life

Unopened: 3 years.
Once opened, use immediately and discard any unused contents.

6.4 Special precautions for storage

Do not store above 30°C. Store in the original container, protected from light.

6.5 Nature and contents of container

Pack size: 1 vial of 100 ml.
A colourless Type I (Ph. Eur.) glass vial, sealed with a chlorobutyl stopper.

6.6 Special precautions for disposal and other handling

Tarivid IV should be administered alone unless compatibility with other infusion fluids has been demonstrated. Compatible infusion solutions include isotonic sodium chloride, ringers solution and 5% glucose solution.

For single use only. Discard remaining contents.

7 MARKETING AUTHORISATION HOLDER

Sanofi-Aventis Ireland Ltd. T/A SANOFI
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0540/076/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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