Proposed European SmPC tracked version

1. NAME OF THE MEDICINAL PRODUCT

[NAME] 600 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 600 mg of prulifloxacin

Excipients with known effect:
each film-coated tablet contains 76 mg of lactose

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet
Yellow, oblong, film-coated tablets.
The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[NAME] is indicated for treatment of infections caused by susceptible strains, in the following conditions:

- Acute uncomplicated infection of lower urinary tract (simple cystitis);
- Complicated lower urinary tract infections;
- Acute exacerbations of chronic bronchitis;
- Acute bacterial rhinosinusitis.

In simple cystitis, acute exacerbations of chronic bronchitis and acute bacterial rhinosinusitis, [NAME] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.

Acute bacterial rhinosinusitis should be adequately diagnosed according to the National or local guidelines on the treatment of respiratory infections. For the treatment of bacterial rhinosinusitis, [NAME] should be used only in patients with a duration of symptoms less than 4 weeks.

Local antibiotic susceptibility pattern should be considered in the treatment of patients with infective diseases.

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

4.2 Posology and method of administration

Posology

The indicative dosage regimen in adults is the following:

- Patients with acute uncomplicated lower urinary tract infections (simple cystitis): only one 600 mg tablet is sufficient.
- Patients with complicated lower urinary tract infections: one 600 mg tablet once a day up to 10-days of maximum treatment.
- Patients with acute exacerbation of chronic bronchitis: one 600 mg tablet once a day up to 10-days of maximum treatment.
- Patients with acute bacterial rhinosinusitis: one 600 mg tablet once a day up to 10-days of maximum treatment.

The duration of treatment for complicated lower urinary tract infections and acute exacerbation of chronic bronchitis, depends on the severity of the disease and on the patient's clinical outcome and should anyway be continued for at least 48-72 hours after remission/ recovery of symptoms.

Paediatric population

[NAME] should not be used in children and adolescent under 18 years of age because of safety concerns (see Sections 4.3 and 5.3).

Method of administration

[NAME] tablets should be swallowed with water and should be taken considering food intake (see Section 4.5).

4.3 Contraindications

- Hypersensitivity to prulifloxacin, to other antibacterial agents from the quinolone-type or to any of the excipients listed in section 6.1.
- Pre-pubertal children or adolescents below the age of 18 years with uncompleted skeletal development.
- Patients with anamnesis of tendon diseases related to the administration of quinolones.
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

The use of prulifloxacin should be avoided in patients who have experienced serious adverse reactions in the past when using quinolone or fluoroquinolone containing products (see section 4.8). Treatment of these patients with prulifloxacin should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment (see also section 4.3).

As for other quinolones, [NAME] should be taken with caution in patients with CNS disorders that may predispose to convulsion or lower the convulsion threshold.

Fluoroquinolones, including prulifloxacin, have neuromuscular blocking activity and may exacerbate muscle weakness in patients with myasthenia gravis. Prulifloxacin is not recommended in patients with a known history of myasthenia gravis.

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. As with other quinolones, exposure to the sun or ultra-violet rays may cause phototoxicity reactions in patients treated with prulifloxacin.

Excessive exposure to the sun or ultra-violet rays should be avoided during treatment with [NAME]; in case of phototoxicity reactions, the treatment should be discontinued.

Patients with latent or known deficiencies for the glucose-6-phosphate dehydrogenase activity, are predisposed to haemolytic reactions when treated with antibacterial agents of the quinolone group and for this reason [NAME] should be administered with caution.

As reported for other quinolones, events of rhabdomyolysis characterized by myalgia, asthenia, increase of CPK and myoglobin in plasma values, and rapid deterioration of the renal function, may

rarely occur. In these cases, patient should be carefully monitored, and appropriate measures must be taken, including the possibility to discontinue the treatment.

The use of quinolones is sometimes correlated to the onset of crystalluria; patients under treatment with this medicinal product belonging to this therapeutic group should maintain an adequate water balance in order to avoid urine concentration.

Tolerability and efficacy of [NAME] in patients with hepatic impairment have not been assessed.

Local and/or national guidelines on the appropriate use of antibacterial drugs should be considered, when prescribing an antibiotic therapy.

Prolonged, disabling and potentially irreversible serious adverse drug reactions

Very 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. prulifloxacin 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.

Tendinitis and tendon rupture

Tendinitis 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 prulifloxacin 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 should be advised also to discontinue treatment in case of myalgia, pain experience or articular inflammation, and to rest the limb or the limbs concerned, until the diagnosis of tendonitis has been excluded.

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 prulifloxacin 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).

Hepatic impairment

Tolerability and efficacy of [NAME] in patients with hepatic impairment have not been assessed. In absence of specific studies, it is not possible to determine the posology in patients with liver impairment. Therefore, for these patients, monitoring of drug plasma levels is the most reliable method for dosage adjustment.

Renal impairment

In absence of specific studies, it is not possible to determine the posology in patients with renal function impairment (patients with creatinine clearance < 60 ml/min) Therefore, for these patients, monitoring of drug plasma levels is the most reliable method for dosage adjustment.

QT prolongation

Some other substances from the fluoroquinolone class have been associated with cases of QT interval prolongation. Prulifloxacin shows a very low potential for inducing QT interval prolongation.

Vision disorders
If vision becomes impaired or any effects on the eyes are experienced, an eye specialist should be consulted immediately.

Clostridium difficile-associated disease
Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment with prulifloxacin (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 prulifloxacin. If CDAD is suspected or confirmed, ongoing treatment with antibacterial agents, including prulifloxacin, should be stopped immediately and appropriate treatment initiated without delay. Anti-peristaltic medicinal products are contraindicated in this clinical situation. Furthermore, appropriate infection control measures should be undertaken to reduce the risk of transmission.

Dysglycaemia

As with all quinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported (see section 4.8), 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.

[NAME] contains lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

[NAME] contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with cimetidine, antacids containing Al and Mg or preparations containing iron and calcium reduces the absorption of [NAME]; therefore, [NAME] should be administered 2 hours before or at least 4 hours after the administration of these compounds.

Concomitant ingestion of prulifloxacin and milk results in decreased area under the concentration-time curve (AUC) and decreased urinary recovery of prulifloxacin, while ingestion of food delays and reduces peak levels. Prulifloxacin urinary excretion decreases when concomitantly administered with probenecid. The concomitant administration of fenbufen with certain quinolones can cause an increased risk of convulsions, the administration of [NAME] and fenbufen must therefore be carefully evaluated.

Quinolones may cause hypoglycemia in diabetic patients taking hypoglycemic drugs.

Concomitant administration of [NAME] and theophylline may cause a slight decrease of theophylline clearance which should have no clinical impact. However, as for other quinolones, theophylline plasma levels should be monitored in patients with metabolic disorders or presenting risk factors.

Quinolones may enhance the effects of oral anticoagulants such as warfarin and its derivatives; when these medicinal products are administered together with [NAME] a close monitoring by prothrombin test or other suitable coagulation tests is recommended.

Preclinical data have shown that nicardipine may potentiate the phototoxicity of prulifloxacin.

No clinically significant interaction has been observed during the clinical development of [NAME] after concomitant administration of other medicinal products commonly employed in patients with the pathologies mentioned in section 4.1.

4.6 Fertility, pregnancy and lactation

Pregnancy

For prulifloxacin no clinical data on exposed pregnancy are available.

Animal studies did not show teratogenicity. Other reproductive toxicity effects were only observed in the presence of maternal toxicity (see section 5.3).

Breastfeeding

In rats, prulifloxacin was found to cross the placenta and to be excreted into maternal milk in high amounts.

As with other quinolones, prulifloxacin has been shown to cause arthropathy in juvenile animals, therefore its use during pregnancy and lactation is contraindicated.

4.7 Effects on ability to drive and use machines

Quinolones may cause dizziness and light-headedness; therefore, patient should know how they react to the drug before driving or using machines or starting in activities which require attention and coordination.

4.8 Undesirable effects

The undesired effects reported hereunder can be traced back to clinical trials carried out on [NAME], except for adverse reactions with not known frequency. Most of the adverse events have been of slight or moderate intensity.

The following rate values have been used: Very common (≥ 1/10), Common (≥ 1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000) and Very rare (<1/10,000), not known (cannot be estimated from the available data).

MedDRA System Organ Class / Frequency	**Adverse reactions**
Metabolism and nutrition disorders	
uncommon	anorexia
rare	appetite lost
not known	hypoglycaemic coma (see section 4.4).
Psychiatric disorders*	
rare	sleep disorder, drowsiness, confusion
Nervous system disorders*	
uncommon	headache, dizziness
rare	psychomotor agitation, taste perversion
Eye disorders*	
rare	ocular hyperaemia
Ear and labyrinth disorders*	
rare	feeling of ear closed
Vascular disorders	
rare	hot flush
Gastrointestinal disorders	
common	epigastralgia
uncommon	abdominal pain, diarrhoea, nausea, gastritis, vomit
rare	abnormal stools, gastrointestinal disorders, eructation, mouth ulcer, angular stomatitis, dyspepsia, flatulence, indigestion, oral cavity discomfort, oral moniliasis, glossitis, gastric dilation
Skin and subcutaneous tissue disorders	
uncommon	pruritus, skin rash, eruption
rare	facial eczema, facial erythema, urticaria

Musculoskeletal and connective tissue disorders*	
rare	generalized joint pains, pain ankle, muscle disorder, muscle twitching
unknown	Exacerbation of myasthenia gravis
General disorders and administration site conditions*	
rare	Fever
Investigations	
rare	albumin increased, alkaline posphatase increased, ALT increased, AST increased, blood calcium increased, blood monocytes increased, lymphocytes raised, WBC increased, γ-GT increased, bilirubin increased

* 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).

The following adverse reactions have been also reported (incidence not known): anaphylactic/anaphylactoid reaction including angioedema, dyspnoea, Stevens-Johnson syndrome, hypoglycemia, hypoesthesia, paraesthesia, tremor, dermatitis due to drugs, rhabdomyolysis, phototoxicity, tachycardia, pseudomembranous colitis.

The treatment with [NAME] may be associated with asymptomatic crystalluria with no change in creatinine levels, with alterations in hepatic function parameters and with eosinophilia. In the observed cases, these alterations were asymptomatic and transient in nature.

During treatment with [NAME], the development of adverse reactions or alterations in laboratory parameters not mentioned above, but reported for other quinolones, cannot be excluded.

Prulifloxacin post-marketing surveillance data show sporadic reports of tendon disorders (see 4.4. Special warning and special precaution for use).

Reporting of suspected adverse reactions

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 the national reporting system listed in Appendix V.

4.9 Overdose

In mice, rats and dogs (males and females), the oral administration of single doses up to 5000 mg/kg had no lethal effects.

No information on overdose in humans are available; [NAME] was tested in healthy volunteers up to 1200 mg/die for 12 days showing a good tolerability.

In the event of acute overdose, the stomach should be emptied by inducing vomiting or by gastric lavage, the patient must be carefully observed and given supportive treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: fluoroquinolones, ATC code: J01MA17

Prulifloxacin is a wide spectrum antibacterial agents belonging to the fluoroquinolone group and provided with high efficacy. After oral administration, prulifloxacin is absorbed by the gastrointestinal tract and immediately turned into ulifloxacin, its active metabolite (see section 5.2).

Mechanism of action. *In vitro*, [NAME] has shown to be active towards a wide range of Gram-positive and Gram-negative strains. Prulifloxacin exerts its antibacterial activity by the selective

inhibition of the DNA-gyrase, an essential enzyme present in bacteria and involved in duplication, transcription and repair of DNA.

Mechanism of resistance. The antibiotic resistance to prulifloxacin (like to the other fluoroquinolones) is commonly due to spontaneous mutations in bacterial DNA-gyrase. Cross-resistance to other fluoroquinolones is observed in vitro.

Due to peculiar mechanisms of resistance of fluoroquinolones, there is no cross-resistance between prulifloxacin and antibiotics of different classes, and [NAME] can therefore prove efficacious even in the presence of bacteria strains resistant to aminoglycosides, penicillins, cephalosporins and tetracyclines.

Breakpoints. They were defined on the basis of NCCLS antibacterial activity data and product pharmacokinetic parameters. The following breakpoints are suggested: Susceptible: MIC ≤ 1 μg/ml, Intermediate: MIC >1 to < 4 μg/ml, Resistant: MIC ≥ 4 μg/ml.

Antibacterial spectrum. It should be considered that the prevalence of acquired 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.

The information reported in table below indicates the antibacterial spectrum of prulifloxacin:

Commonly susceptible species	
Aerobic Gram-positive micro-organisms	*Staphylococcus aureus* (methicillin-susceptible) *Staphylococcus epidermidis* *Streptococcus agalactiae* *Streptococcus pyogenes* *Streptococcus pneumoniae* *
Aerobic Gram-negative micro-organisms	*Campylobacter jejuni* *Citrobacter freundii* *Citrobacter koserii* *Enterobacter aerogenes* *Enterobacter cloacae* *Haemophilus influenzae* *Klebsiella oxytoca* *Klebsiella pneumoniae* *Legionella pneumophila* *Moraxella catarrhalis* *Morganella morganii* *Neisseria gonorrhoeae* *Proteus mirabilis* *Proteus vulgaris* *Providencia rettgeri* *Pseudomonas aeruginosa* *Salmonella* sp. *Shigella* sp. (including *S. flexneri* and *S. sonnei*)
Anaerobic micro-organisms	*Clostridium perfringens* *Peptostreptococcus* sp. *Porphyromonas gingivalis* *Prevotella intermedia*
Species for which acquired resistance may be a problem	
Aerobic Gram-positive micro-organisms	*Enterococcus avium* * *Enterococcus faecalis* * *Enterococcus faecium* *
Aerobic Gram-negative micro-organisms	*Acinetobacter calcoaceticus* * *Escherichia coli* (including enterohemorrhagic and enterotoxic strains) *Serratia marcescens* *
Inherently resistant organisms	
Aerobic Gram-positive micro-organisms	*Enterococcus* vancomycin-resistant *Staphylococcus aureus* methicillin-resistant

Aerobic Gram-negative micro-organisms	*Providencia stuartii*
Anaerobic micro-organisms	*Bacteroides* sp. *Clostridium difficile*

* species that show natural intermediate susceptibility

Other information. In *in-vitro* studies, the antibacterial activity of prulifloxacin has been characterised by a better bacterial penetration and a more prolonged post antibiotic effect compared to the reference fluoroquinolones.

5.2 Pharmacokinetic properties

Prulifloxacin is the pro-drug of the active metabolite, ulifloxacin.

Absorption – Prulifloxacin is rapidly absorbed in humans (T_{max} = about 1h) and turned into ulifloxacin; after a 600 mg single administration, the mean plasma peak of ulifloxacin is 1.6 μg/ml and the AUC is 7.3 μg*h/ml. At the steady-state, which is reached within 2 days from the beginning of treatment after single daily administrations, C_{max} and AUC are 2.0 μg/ml and 7.6 μg*h/ml, respectively.

Ingestion of food delays and slightly reduces the plasma peak concentration of prulifloxacin but does not modify the AUC.

Distribution – In humans, the lung/plasma ratio of [NAME] mean concentration increases with time. After 24 hours, the mean concentrations maintained by the active metabolite ulifloxacin in tissues are 5 times higher than those in plasma, thus confirming the results obtained in animals, where ulifloxacin concentrations in lung and kidney have proved to be higher than in plasma (1.2 – 2.8 times and 3 - 8 times, respectively).

Similarly, tissues penetration data of ulifloxacin in human paranasal sinus showed AUCs ratios between tissues and plasma of 3.0 for ethmoides and 2.4 for turbinates.

In humans, the protein binding assessed both *in vitro* and *ex vivo*, is equal to approx. 50%, regardless of the drug concentration.

The weak ulifloxacin concentration found in the cerebrospinal fluid after i.v. administration in dog and repeated p.o. administration in humans, shows that ulifloxacin hardly crosses the blood-brain barrier.

Biotransformation – The metabolic profile of prulifloxacin in animals and humans is comparable. Studies in animals have shown that the prulifloxacin metabolism begins during the intestinal absorption and is completed with its passing through the liver.

Apart from transformation into ulifloxacin, other minor metabolites have been identified, such as the diolic form and some derivatives as glucuronide, oxo-derivative and ethylendiamine derivatives; the concentration and activity of which are negligible compared to the active substance.

In-vitro studies have not shown significant interactions with the P-450 cytochrome isoenzymes except for a slight inhibition of CYP1A1/2, which results in a small reduction of the theophylline clearance. As methylxanthines, and theophylline in particular, are the main substrate for the isoenzyme CYP1A1/2, the level of interaction with other isoenzyme substrates (see warfarin) may only be considered inferior.

Elimination – The half-life of the active metabolite, ulifloxacin, is about 10 hours, after both single and repeated administration at the steady-state in humans, ranging in animals (rats, dogs and monkeys) between 2 and 12 hours.

In humans, studies with the labelled product have shown that the elimination occurs mainly through the faeces. The radioactivity found in urine and faeces after oral administration of 600 mg, totally amounts to approximately 95%. These results confirm what previously showed by studies carried out in animals (rats, dogs and monkeys).

The quantity of ulifloxacin excreted in urine is equal to 16.7% of the administered dose on a molarity basis and the ulifloxacin renal clearance is about 170 ml/min

The renal elimination of ulifloxacin occurs by glomerular filtration and active secretion.

*Older people*The pharmacokinetic profile of prulifloxacin in elderly patients has been shown to be similar to adults, with no variations due to age, and therefore no dosage modification have been thought necessary in elderly patients.

In patients with mild or moderate renal impairment, after oral administration of [NAME] 600 mg, the mean plasma peak of ulifloxacin reaches values included between 1.30 and 1.62 μg/ml. AUC values range between 13.71 and 23.33 μg*h/ml and the half-life shows to be included between 12.3 and 32.4 hours. Compared to healthy volunteers, the ulifloxacin renal clearance decreases according to the insufficiency level.

5.3 Preclinical safety data

Repeated toxicity. The main target organs in repeated dose toxicity studies were articular cartilage, kidneys, gastro-intestinal tract and liver.

No toxic effects have been observed on articular cartilage (young dogs) up to doses 3 times higher than the therapeutic one; for liver (dogs) and kidney (dogs and rats) no toxic effects have been observed up to doses 6 and 10 and 12 times higher than therapeutic dose, respectively.

The drug did not prolong the QT interval in vivo and did not show inhibiting effects on the retarded rectifying current of potassium (HERG) in vitro.

Reproductive toxicity. Reproductive toxicity studies did not show teratogenicity and effects on fertility or development of embryo and fetus were only observed in association with maternal toxicity.

Mutagenicity. Standard genotoxicity testing with prulifloxacin showed positive effects in some in vitro tests in mammalian cell cultures but was negative in vivo and in bacteria. The effects are considered related to the inhibition of topoisomerase II in high concentrations.

Carcinogenic potential. Prulifloxacin was not carcinogenic in a medium-term initiation-promotion experimental model. Long-term carcinogenicity tests were not performed.

Antigenicity. Prulifloxacin showed to be devoid of antigenic effects.

Phototoxicity. Prulifloxacin has induced phototoxic reactions, although in comparative studies in animals its phototoxic activity has shown to be lower than other fluoroquinolones used (ofloxacin, enoxacin, pefloxacin, nalidixic acid and lomefloxacin). Many quinolones are also photomutagenic/photocarcinogenic, which can not be excluded for prulifloxacin.

Nephrotoxicity. After repeated oral administrations of 3000 mg/kg/die in rats, a far higher dosage than the therapeutic dose in humans, prulifloxacin has caused crystalluria by ulifloxacin precipitation.

Cardiotoxicity. Studies carried out in dogs have shown that prulifloxacin does not cause significant modifications in the electrocardiogram. In particular, no changes in the QTc have been observed, either after single intravenous administration in the anaesthetised dog, or after oral administration for 6 months in the conscious dog, at all the administered doses. *In vitro* studies have confirmed the absence of inhibiting effects on the retarded rectifying currents of potassium (HERG).

Articular toxicity. As other fluoroquinolones, prulifloxacin has caused arthropathy only in young animals.

Ocular toxicity. In monkeys, oral doses of 26.4 or 58.2 mg/kg/die of prulifloxacin once a day for 52 weeks have not caused adverse effects related to the treatment on the ocular function or morphology.

Rhabdomyolytic effect. Ulifloxacin doses up to 10 mg/kg/die administered intravenously once a day for 14 consecutive days have not induced rhabdomyolysis in rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core

lactose monohydrate

microcrystalline cellulose

sodium croscarmellose

povidone

silica, colloidal anhydrous
magnesium stearate

Coating
hypromellose
propylene glycol
titanium dioxide (E171)
talc
ferric oxide (E172).

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Do not store above 30°C.
Store in the original package.

6.5 Nature and contents of container
Cardboard box containing 1 blister of 1, 2, 5 film-coated tablets or 2 blisters of 5 film-coated tablets.
Blister made of thermoformed coupled material (Polyamide/aluminium/PVC) and a lidding material (aluminium/PVC).
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT