1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Veraflox 15 mg tablets for dogs and cats
Veraflox 60 mg tablets for dogs
Veraflox 120 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Pradofloxacin	15 mg
Pradofloxacin	60 mg
Pradofloxacin	120 mg

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

Brownish single-scored tablets with “P15” on one side
Brownish single-scored tablets with “P60” on one side
Brownish single-scored tablets with “P120” on one side
The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs, cats

4.2 Indications for use, specifying the target species

Dogs:

Treatment of:
- wound infections caused by susceptible strains of the *Staphylococcus intermedius* group (including *S. pseudintermedius*),
- superficial and deep pyoderma caused by susceptible strains of the *Staphylococcus intermedius* group (including *S. pseudintermedius*),
- acute urinary tract infections caused by susceptible strains of *Escherichia coli* and the *Staphylococcus intermedius* group (including *S. pseudintermedius*) and
- as adjunctive treatment to mechanical or surgical periodontal therapy in the treatment of severe infections of the gingiva and periodontal tissues caused by susceptible strains of anaerobic organisms, for example *Porphyromonas* spp. and *Prevotella* spp. (see section 4.5).

Cats:

Treatment of acute infections of the upper respiratory tract caused by susceptible strains of *Pasteurella multocida*, *Escherichia coli* and the *Staphylococcus intermedius* group (including *S. pseudintermedius*).

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

Dogs:

Do not use in dogs during the period of growth as developing articular cartilage may be affected. The period of growth depends on the breed. For the majority of breeds, pradofloxacin-containing veterinary medicinal products must not be used in dogs of less than 12 months of age and in giant breeds less than 18 months.

Do not use in dogs with persisting articular cartilage lesions, since lesions may worsen during treatment with fluoroquinolones.

Do not use in dogs with central nervous system (CNS) disorders, such as epilepsy, as fluoroquinolones could possibly cause seizures in predisposed animals.

Do not use in dogs during pregnancy and lactation (see section 4.7).

Cats:

Due to the lack of data, pradofloxacin should not be used in kittens aged less than 6 weeks.

Pradofloxacin has no effects on the developing cartilage of kittens of 6 weeks of age and older. However, the product must not be used in cats with persisting articular cartilage lesions, as these lesions may worsen during treatment with fluoroquinolones.

Do not use in cats with central nervous system (CNS) disorders, such as epilepsy, as fluoroquinolones could potentially cause seizures in predisposed animals.

Do not use in cats during pregnancy and lactation (see section 4.7).

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Whenever possible, the veterinary medicinal product should only be used based on susceptibility testing.

Official and local antimicrobial policies should be taken into account when the veterinary medicinal product is used.

Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials.

Use of the veterinary medicinal product deviating from instructions given in the summary of product characteristics (SPC) may increase the prevalence of bacteria resistant to the fluoroquinolones and

may decrease the effectiveness of treatment with other fluoroquinolones due to the potential for cross-resistance.

Pyoderma occurs mostly secondary to an underlying disease, thus, it is advisable to determine the underlying cause and to treat the animal accordingly.

This veterinary medicinal product should only be used in severe cases of periodontal disease. Mechanical cleaning of teeth and removal of plaque and calculus or extraction of teeth are prerequisites for a persistent therapeutic effect. In case of gingivitis and periodontitis, the veterinary medicinal product should only be used as an adjunct to mechanical or surgical periodontal therapy. Only those dogs for which periodontal treatment goals cannot be achieved by mechanical treatment alone should be treated with this veterinary medicinal product.

Pradofloxacin may increase sensitivity of the skin to sunlight. During treatment, animals should therefore not be exposed to excessive sunlight.

Excretion via kidneys is an important elimination route for pradofloxacin in dogs. As for other fluoroquinolones, the renal excretion rate of pradofloxacin may be decreased in dogs with impaired kidney function and, therefore, pradofloxacin should be used with caution in such animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Due to potential harmful effects, the tablets must be kept out of the sight and reach of children.

People with known hypersensitivity to quinolones should avoid any contact with the veterinary medicinal product.

Avoid skin and eye contact with the veterinary medicinal product. Wash hands after use.

Do not eat, drink or smoke while handling the veterinary medicinal product.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Mild transient gastro-intestinal disturbances including vomiting have been observed in rare cases in dogs and cats.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reactions)
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated-)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety of this veterinary medicinal product has not been established during pregnancy and lactation in cats and dogs.

Pregnancy:
Do not use during pregnancy. Pradofloxacin induced eye malformations at foetal and maternal toxic doses in rats.

Lactation:
Do not use during lactation. Laboratory studies in puppies have shown evidence of arthropathy after systemic administration of fluoroquinolones. Fluoroquinolones are known to cross the placenta and to be distributed into milk.

Fertility:
Pradofloxacin has been shown to have no effects on fertility in breeding animals.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent administration with metal cations such as those contained in antacids or sucralfate made with magnesium hydroxide or aluminium hydroxide, or multivitamins containing iron or zinc, and dairy products containing calcium, has been reported to decrease the bioavailability of fluoroquinolones. Therefore, Veraflox should not be administered concurrently with antacids, sucralfate, multivitamins or dairy products, as absorption of Veraflox may be decreased. Further, fluoroquinolones should not be used in combination with non-steroidal anti-inflammatory drugs (NSAIDs) in animals with a history of seizures because of potential pharmacodynamic interactions in the CNS. The combination of fluoroquinolones with theophylline could increase the plasma levels of theophylline by altering its metabolism and thus should be avoided. The combined use of fluoroquinolones with digoxin should also be avoided because of potentially increased oral bioavailability of digoxin.

4.9 Amounts to be administered and administration route

Oral use.

Doses

The recommended dose is 3 mg/kg bodyweight of pradofloxacin once daily. Due to the available tablet sizes the resulting dose range is 3 to 4.5 mg/kg bodyweight according to the following tables.

To ensure a correct dose, bodyweight should be determined as accurately as possible to avoid under dosing. When the dose requires a half tablet to be used the remaining portion should be given at the next administration.

Dogs:

Bodyweight of Dog (kg)	**Number of tablets**			**Pradofloxacin dose (mg/kg bw)**
	15 mg	**60 mg**	**120 mg**	
>3.4 – 5	1			3 – 4.4
5 – 7.5	1½			3 – 4.5
7.5 – 10	2			3 – 4
10 – 15	3			3 – 4.5
15 – 20		1		3 – 4
20 – 30		1½		3 – 4.5
30 – 40			1	3 – 4
40 – 60			1½	3 – 4.5
60 – 80			2	3 – 4

Cats:

Bodyweight of Cat	**Number of tablets**	**Pradofloxacin dose**

(kg)	15 mg	(mg/kg bw)
>3.4 – 5	1	3 – 4.4
5 – 7.5	1½	3 – 4.5
7.5 – 10	2	3 – 4

Duration of treatment

The duration of the treatment depends on the nature and severity of the infection and on the response to treatment. For most infections the following treatment courses will be sufficient:

Dogs:

Indication	Duration of treatment (days)
Infections of the skin:	
Superficial pyoderma	14 – 21
Deep pyoderma	14 – 35
Wound infections	7
Acute infections of the urinary tract	7 – 21
Severe infections of the gingiva and periodontal tissues	7

The treatment should be re-considered if no improvement of the clinical conditions is observed within 3 days, or in cases of superficial pyoderma 7 days, and in cases of deep pyoderma 14 days, after starting the treatment.

Cats:

Indication	Duration of treatment (days)
Acute infections of the upper respiratory tract	5

The treatment should be re-considered if no improvement of the clinical condition is observed within 3 days after starting the treatment.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No specific antidotes for pradofloxacin (or other fluoroquinolones) are known, therefore, in case of overdose, symptomatic treatment should be given.

Intermittent vomiting and soft faeces were observed in dogs after repeated oral administration of 2.7 times the maximum recommended dose.

Infrequent vomiting was observed in cats after repeated oral administration of 2.7 times the maximum recommended dose.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, fluoroquinolones.
ATCvet code: QJ01MA97

5.1 Pharmacodynamic properties

Mode of Action
The primary mode of action of the fluoroquinolones involves interaction with enzymes essential for major DNA functions such as replication, transcription and recombination. The primary targets for pradofloxacin are the bacterial DNA gyrase and topoisomerase IV enzymes. Reversible association between pradofloxacin and DNA gyrase or DNA topoisomerase IV in the target bacteria results in inhibition of these enzymes and rapid death of the bacterial cell. The rapidity and extent of bacterial killing are directly proportional to the drug concentration.

Antibacterial Spectrum
Although pradofloxacin has *in-vitro* activity against a wide range of Gram-positive and Gram-negative organisms, including anaerobic bacteria, this veterinary medicinal product should only be used for the approved indications (see section 4.2) and in accordance with the prudent use recommendations in section 4.5 of this SPC.

MIC-Data

Dogs:

Bacterial species	Number of strains	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)	MIC range (µg/ml)
Staphylococcus intermedius group (including *S. pseudintermedius*)	1097	0.062	0.062	0.002-4
Escherichia coli	173	0.031	0.062	0.008-16
Porphyromonas spp.	310	0.062	0.125	≤ 0.016-0.5
Prevotella spp.	320	0.062	0.25	≤ 0.016-1

The bacteria were isolated between 2001 and 2007 from clinical cases in Belgium, France, Germany, Hungary, Italy, Poland, Sweden and UK.

Cats:

Bacterial species	Number of strains	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)	MIC range (µg/ml)
Pasteurella multocida	323	0.016	0.016	0.002-0.062
Escherichia coli	135	0.016	4	0.008-8
Staphylococcus intermedius group (including *S. pseudintermedius*)	184	0.062	0.125	0.016-8

The bacteria were isolated between 2001 and 2007 from clinical cases in Belgium, France, Germany, Hungary, Poland, Sweden and UK.

Types and Mechanisms of Resistance
Resistance to fluoroquinolones has been reported to arise from five sources, (i) point mutations in the genes encoding for DNA gyrase and/or topoisomerase IV leading to alterations of the respective enzyme, (ii) alterations of drug permeability in Gram-negative bacteria, (iii) efflux mechanisms, (iv) plasmid mediated resistance and (v) gyrase protecting proteins. All mechanisms lead to a reduced susceptibility of the bacteria to fluoroquinolones. Cross-resistance within the fluoroquinolone class of antimicrobials is common.

5.2 Pharmacokinetic particulars

In laboratory studies the bioavailability of pradofloxacin was reduced in fed dogs and cats compared to fasted animals. However in the clinical studies feeding did not reveal any impact on the treatment effect.

Dogs:

After oral administration of the therapeutic dose to dogs, pradofloxacin is rapidly (T_{max} of 2 hours) and almost completely (approximately 100%) absorbed reaching peak concentrations of 1.6 mg/l.

A linear relationship between pradofloxacin serum concentrations and the administered dose is observed in dogs within a tested dose range of 1 to 9 mg/kg body weight. Long-term daily treatment has no impact on the pharmacokinetic profile, with an accumulation index of 1.1. *In vitro* plasma protein binding is low (35%). The high volume of distribution (V_d) >2 l/kg bodyweight indicates good tissue penetration. Pradofloxacin concentrations in skin homogenates of dogs exceed those in serum by up to seven times.

Pradofloxacin is eliminated from serum with a terminal half-life of 7 hours. Major elimination pathways are glucuronidation as well as renal excretion. Pradofloxacin is cleared from the body at 0.24 l/h/kg. Approximately 40% of the administered product is excreted unchanged via the kidneys.

Cats:

In cats, absorption of orally administered pradofloxacin at the therapeutic dose is rapid reaching peak concentrations of 1.2 mg/l within 0.5 hours. The bioavailability of the tablet is at least 70%. Repeated dosing shows no impact on the pharmacokinetic profile (accumulation index = 1.0). *In vitro* plasma protein binding is low (30%). The high volume of distribution (V_d) >4 l/kg body weight indicates good tissue penetration.

Pradofloxacin is eliminated from serum with a terminal half-life of 9 hours. The major elimination pathway in cats is glucuronidation. Pradofloxacin is cleared from the body at 0.28 l/h/kg.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Cellulose, microcrystalline
Povidone
Magnesium stearate
Silica, colloidal anhydrous
Artificial beef flavour
Croscarmellose sodium

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Folding cartons containing aluminium blister packs. One blister contains 7 tablets.

The following pack sizes are available:

- 7 tablets
- 21 tablets
- 70 tablets
- 140 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bayer Animal Health GmbH
D-51368 Leverkusen
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/10/107/001-012

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12/04/2011
Date of last renewal: 07/01/2016

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.