SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Orbax Flavoured Oral Suspension 30 mg/ml for Dogs and Cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Orbifloxacin 30 mg

Excipient(s):
Sorbic acid (E200) 1 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension

Brown, smooth viscous suspension

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and cats

4.2 Indications for use, specifying the target species

Dogs:
Treatment of uncomplicated bacterial cystitis due to susceptible strains of *E coli* and *Proteus mirabilis,* and treatment of skin and associated soft tissue infections (wounds and abscesses), associated with bacteria susceptible to orbifloxacin.

Cats:
Treatment of skin and associated soft tissue infections (wounds and abscesses), associated with bacteria susceptible to orbifloxacin.

4.3 Contraindications

Do not use in cases of known hypersensitivity to orbifloxacin, to other fluoroquinolones or to any of the excipients.
Do not use in juvenile dogs during the rapid growth phase (up to 8 month of age in small and medium sized breeds, up to 12 months in large and up to 18 months of age in giant breeds). Quinolones have been shown to cause arthropathy in immature animals, the dog being particularly sensitive to this side-effect.
See also section 4.7.
See also section 4.8

4.4 Special warnings for each target species

Efficacy of the veterinary medicinal product for the treatment of pyoderma has not been investigated.

4.5 Special precautions for use

Special precautions for use in animals

Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population. It is prudent to reserve the fluoroquinolones for the treatment of clinical conditions which have responded poorly to other classes of antimicrobials. Whenever possible, fluoroquinolones should only be used based on susceptibility testing.

Safety has not been established in cats less than 11 weeks of age.

The use of fluoroquinolones in cats has been reported to adversely affect the retina at high doses. These effects can be irreversible and blindness can occur. Such products should be used with caution in cats, and the recommended dose should not be exceeded. The bodyweight should be accurately determined before treatment.

The veterinary medicinal product should be used with caution in animals with hepatic and/or renal impairment and the posology should be adapted if necessary.

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

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

- Avoid skin and eye contact
- In case of accidental contact with skin, rinse affected area with copious amounts of water.
- In case of accidental contact with eyes, rinse with plenty of clean water.
- Do not handle this product if you have known hypersensitivity against substances in this product or to any other (fluoro)quinolones.
- Do not smoke, eat or drink when handling the veterinary medicinal product.
- Wash hands carefully after administering the veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

Mild side effects such as vomiting, soft faeces or diarrhoea may occasionally occur in some dogs and cats. White to yellow faeces was noted in safety studies and was considered to be due to the product. Interruption of treatment is not usually necessary and these effects generally resolve spontaneously without treatment.

Very rare cases of blindness following administration of Orbax have been recorded in cats. Signs may resolve spontaneously but can be permanent.

The frequency of possible adverse effects is defined using the following convention:
Very common (affects more than 1 animal in 10)
Common (affects 1 to 10 animals in 100)

Uncommon (affects 1 to 10 animals in 1,000)
Rare (affects 1 to 10 animals in 10,000)
Very rare (affects less than 1 animal in 10,000)

4.7 Use during pregnancy, lactation or lay

In laboratory animals (rats, rabbits) studies have shown prenatal/postnatal toxicity and developmental effects. The safety of the veterinary medicinal product has not been established during pregnancy and lactation in dogs and cats.
Therefore, the product should not be used during pregnancy and lactation or in animals intended for breeding.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent administration with metal cations such as those contained in antacids made with magnesium hydroxide or aluminium hydroxide, or multivitamins containing iron or zinc, has been reported to dramatically decrease the bioavailability of fluoroquinolones.

The dosage of theophylline should be reduced when used concurrently with fluoroquinolones.

Cimetidine has been shown to interfere with the metabolism of fluoroquinolones and should be used with care when used concurrently.

Concurrent administration of fluoroquinolones may increase the action of oral anticoagulants.

Concurrent use of fluoroquinolones with oral cyclosporine is contraindicated.

4.9 Amounts to be administered and administration route

To ensure correct dosage, body weight should be determined as accurately as possible to avoid over- or under-dosing. Use the provided 3 mL syringe to dose 0.5 mL or more of veterinary medicinal product. In very small animals, a dose of less that 0.5 mL may be required. To dose an amount less than 0.5 mL, a 1 mL syringe should be used to improve dosing accuracy.

BEFORE INITIAL USE, SHAKE VIGOROUSLY for 30 seconds. Remove the cap and inner foil seal and insert the syringe adaptor by pressing firmly into top of bottle.AFTER USE, replace cap, leaving adaptor in the bottle, and rinse the syringe with water.

DOSE ADMINISTRATION
SHAKE WELL BEFORE USE. Insert the syringe tip into the adaptor opening and invert the bottle. Withdraw the required amount of medication. After use, replace cap, leaving adaptor in the bottle, and rinse the syringe with water.
The veterinary medicinal product should be administered directly into the animal’s mouth. The formulation is malt-flavoured and when administered in this fashion in field trials, the medicinal product was accepted by the majority of feline and canine patients.

For the treatment of bacterial cystitis in dogs, the recommended dosage is 2.5 mg/kg bodyweight administered once daily for 10 consecutive days, corresponding to 1 mL of suspension per 12 kg bodyweight.

For the treatment of skin and associated soft tissue infections in dogs or cats, administer 7.5 mg/kg bodyweight administered once daily for 5 to 10 consecutive days, corresponding to 1 mL of suspension per 4 kg bodyweight.

For the treatment of skin and associated soft tissue infections therapy should be continued for at least 2 days beyond cessation of clinical signs. If no improvement is seen within 5 days of starting therapy, the diagnosis should be re-evaluated and a different course of action considered.

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

Dogs:
The effects in dogs of overdose have been investigated following dosing at 3x and 5x the dose level at 3x the intended treatment duration, as well as at 10x the dose level for the intended treatment duration. Symptoms observed include gastrointestinal signs such as discolouration of the faeces (white/yellow), emesis, soft and/or mucoid faeces, and at high doses, hypersalivation, reduced food consumption, mild weight loss, glucosuria and lower urine pH. Symptomatic treatment and/or discontinuation of therapy should be considered if intolerance is observed.

Cats:
The effects in cats of overdose have been investigated following dosing at 2x, 3x, 5x, 6x and 10x the dose level at 3x the intended treatment duration. Symptoms observed at the highest dose level included mild gastrointestinal effects such as increased incidence of emesis, salivation, and soft, mucoid, and/or watery feces. A slight decrease in food consumption has been observed. Symptomatic treatment and/or discontinuation of therapy should be considered if intolerance is observed.

Particular attention was paid to ocular safety assessment. There were no electroretinographic changes and no visual deficits observed in any cat. At the exaggerated doses of 45.0 and 75.0 mg/kg/day, minimal ophthalmic changes were noted which consisted of tapetal hyperreflectivity, which correlated histopathologically with swelling of photoreceptor cells. Electron microscopy revealed swollen rod cells with disorganized disc material in the outer photoreceptor segments. If a visual deficit is suspected, discontinue use immediately.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for systemic use, fluoroquinolones
ATCvet code: QJ01MA95

5.1 Pharmacodynamic properties

Orbifloxacin is a synthetic, broad spectrum antibacterial agent from the class of fluoroquinolone carboxylic acid derivatives.

Orbifloxacin is bactericidal with activity against mainly Gram-negative bacteria but also against some Gram-positive bacteria. The mode of action of the fluoroquinolones is through interference with the bacterial enzyme DNA gyrase which is needed for the synthesis of bacterial DNA.

Orbifloxacin has been shown to be effective against strains of *E.coli* and *P.mirabilis* in treating urinary tract infection in dogs.

Clinical trials have shown the veterinary medicinal product to be effective against the following pathogens indicated in causing skin infections in dogs: *E.coli, Staphylococcus intermedius, Staphylococcus aureus,* and *Klebsiella pneumoniae*.
Clinical trials have shown the veterinary medicinal product to be effective against the following pathogens indicated in causing skin infections in cats: *Staphylococcus intermedius, Staphylococcus aureus, Pasteurella multocida, Klebsiella pneumoniae, Streptococcus haemolyticus G, and Enterococcus spp.*

The *in vitro* activity of orbifloxacin against pathogens isolated from clinical cases of canine skin infections in an EU field trial conducted in 2000 was:

Minimum Inhibitory Concentrations vs. Orbifloxacin – Summary

Pathogen	**N**	**Min**	**Max**	**MIC_{50}**	**MIC_{90}**
Escherichia coli	21	0.012	1	0.12	1
Enterobacter agglomerans	13	0.03	8	0.25	2
Klebsiella pneumoniae	14	0.12	2	0.25	2
Pasteurella multocida	16	0.015	2	0.06	0.5
Pseudomonas aeruginosa	10	0.25	8	2	8
Staphylococcus aureus	27	0.015	4	0.5	2
Staphylococcus intermedius	69	0.015	8	0.5	1
Streptococcus haemolyticus	22	0.015	4	1	4

The distribution of the *in vitro* activity of orbifloxacin against canine urinary tract infections is bimodal with most isolates of *Escherichia coli* having an MIC of 0.25 micrograms/mL or less and most isolates of Proteus mirabilis having an MIC of 2 micrograms/mL or less. A separate population of these organisms have an MIC of 16 micrograms/mL or greater. A culture and sensitivity should be taken prior to initiating therapy.

The in vitro activity of orbifloxacin against pathogens isolated from clinical cases of feline skin infections in an EU field trial conducted in 2000 and from clinical isolates obtained from 2002 to 2007 was:

Minimum Inhibitory Concentrations vs. Orbifloxacin – Summary

Pathogen	**N**	**Min**	**Max**	**MIC_{50}**	**MIC_{90}**
Pasteurella multocida	94	0.015	4	0.03	0.5
Staphylococcus spp.	105	0.03	16	0.5	2

Bacterial resistance to the fluoroquinolones may occur through alterations in bacterial cell wall permeability, activation of an efflux pump or alteration in the 4-quinolone molecule's

binding site via mutation of DNA gyrase or topoisomerase IV. Resistance to one fluoroquinolone frequently results in resistance to all (cross-resistance). Some mutations that can confer resistance to the fluoroquinolones can also confer resistance to other classes of antibiotics such as the cephalosporins and tetracyclines. Resistance to fluoroquinolones may induce resistance to imipenem. As a class, fluoroquinolones may exert additive or synergistic effects when combined with other antibiotic classes such as beta-lactams and clindamycin.

5.2 Pharmacokinetic particulars

Orbifloxacin is widely distributed to the tissues of dogs and cats. Orbifloxacin undergoes limited metabolism in both the dog and cat and in both species undergoes both renal and hepatic elimination.

Dogs:

The oral bioavailability of orbifloxacin in dogs is approximately 100%. Maximum plasma concentrations (C_{max}) of approximately 2.3 μg/mL are achieved within one hour after a 2.5 mg/kg oral dose. After single dose administration to dogs at 7.5 mg/kg bodyweight, a C_{max} of approximately 5.8 μg/mL is achieved within two hours. The plasma elimination half life is approximately 6 hours. The accumulation between doses given at 24 hour intervals is negligible. Approximately 50% of an orally administered dose is excreted in the urine as unchanged drug. After a 2.5 mg/kg dose, urine concentrations of orbifloxacin are approximately 100 μg/mL for approximately 12 hours after dosing. By 24 hours, urine concentrations of orbifloxacin are approximately 40 μg/mL. Plasma protein binding of orbifloxacin is low in the dog.

Cats:
After single dose administration to cats at 7.5 mg/kg bodyweight, maximum plasma concentrations (C_{max}) of approximately 3.4 μg/mL are achieved in approximately 2 hours. The plasma half-life ($T_{1/2}$) is approximately 8 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbic acid
Water for Injection
Lactic acid
Methacrylic Acid divinylbenzene copolymer
Sodium hydroxide
Propylene glycol
Colloidal silicon dioxide
Malt extract

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years

Shelf-life after first opening the immediate packaging: 30 days

6.4. Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions. Store upright.
Keep the container in the outer carton.

6.5 Nature and composition of immediate packaging

The veterinary medicinal product (20 mL) is supplied in Amber type 1 glass bottles of nominal volume 25 mL with white polypropylene cap containing 20 mL suspension. A low density polyethylene press in bottle adapter and a 3 mL oral syringe composed of polypropylene with graduations of 0.1 mL are included. The contents are packaged within a partitioned folding carton which houses the bottle and package insert on one side and the PIBA and syringe on the other side.

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

Intervet UK Ltd.
Walton Manor
Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

8. MARKETING AUTHORISATION NUMBER

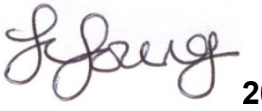
Vm 01708/4602

9. DATE OF FIRST AUTHORISATION

Date: 20 January 2009

10. DATE OF REVISION OF THE TEXT

Date: December 2013

Approved:  **20/12/2013**