The following is an English translation of the package insert for the drug sold in Japan (as of February 2013).

Fluoroquinolone Antimicrobial agent for Dogs and Cats
Veterinary Drug
Prescription Legend Drug

Orbifloxacin Tablet 10 mg
Orbifloxacin Tablet 20mg
Orbifloxacin Tablet 40 mg
Orbifloxacin Tablet 80mg

Orbifloxacin Tablet is a tablet preparation for dogs and cats developed by Dainippon Sumitomo Pharma Co., Ltd. It contains the active ingredient orbifloxacin, a fluoroquinolone antimicrobial agent. Orbifloxacin has antibacterial activity against a broad spectrum of gram-negative and gram-positive bacteria. It does not demonstrate cross-resistance with other antimicrobial agents. Orbifloxacin Tablet is well absorbed from the gastrointestinal tract. Its other characteristics include high plasma concentrations, good tissue penetration and minimal *in vivo* metabolism.

■Composition

Orbifloxacin Tablet 10 mg contains 10 mg of orbifloxacin per tablet.
Orbifloxacin Tablet 20 mg contains 20 mg of orbifloxacin per tablet.
Orbifloxacin Tablet 40 mg contains 40 mg of orbifloxacin per tablet.
Orbifloxacin Tablet 80 mg contains 80 mg of orbifloxacin per tablet.

■Indications

Indicated Microorganisms The following bacterial species of susceptible to orbifloxacin
Staphylococcus species, *Streptococcus* species, *Enterococcus* species, *Escherichia coli*, *Klebsiella* species, *Proteus* species, *Pseudomonas aeruginosa*, *Pasteurella multocida*, *Clostridium perfringens*, *Campylobacter jejuni*

Indicated Diseases
Dogs: Bacterial urinary tract infection, bacterial skin infection, bacterial diarrhea, bacterial external otitis
Cats: Bacterial urinary tract infection, bacterial skin infection, bacterial diarrhea

■Dosage and Administration

The dosage in dogs and cats is the following amounts of orbifloxacin per kilogram of body weight administered orally once daily.
Dogs – Bacterial urinary tract infection, bacterial skin infection, bacterial diarrhea:
2.5 to 5.0 mg; bacterial external otitis: 5.0 mg
Cats – Bacterial urinary tract infection, bacterial skin infection, bacterial diarrhea:
2.5 to 5.0 mg

■Precautions

[General Precautions]
(1) Orbifloxacin Tablet is a prescription legend drug dispensed by prescription or order of a veterinarian.
(2) The use of Orbifloxacin Tablet is restricted to animals that have failed standard therapy.
(3) Orbifloxacin Tablet should be used only for the indications listed in the Indications section.
(4) Orbifloxacin Tablet should be used only as indicated.

(5) To prevent the development of resistant bacteria during the use of Orbifloxacin Tablet, susceptibility should be determined and treatment should be discontinued at the minimum time necessary to treat the indication. Treatment should not be continued beyond seven days.

[User Precautions]
Consult a physician immediately in case of accidental ingestion by humans.

[Precautions for Dogs and Cats]
1. Restrictions
(1) Repeated administration of a dose equivalent to five times the recommended maximum dose (25 mg/kg) for 10 days resulted in the formation of vesicles on the articular surface (necropsy finding), without gait abnormality, in some dogs three months of age and younger. Use with caution in dogs three months of age and younger.
(2) Safety has not been established in pregnant dogs and cats.

2. Adverse Reactions
(1) Consult a veterinarian immediately in case of adverse reaction.
(2) Orbifloxacin Tablet may occasionally cause vomiting. Discontinue Victas® S therapy and institute appropriate treatment if abnormalities are noted.

3. Interactions
Rare instances of convulsion have been reported with concurrent administration of NSAIDs, which are analogous compounds.

4. Usage Precautions
Orbifloxacin Tablet must be administered cautiously while closely monitoring the animal's condition.

[Handling Precautions]
Use promptly if Orbifloxacin Tablets must be split prior to use.

[Storage Precautions]
(1) Keep out of the reach of children.
(2) Store Orbifloxacin Tablet away from direct sunlight, high temperatures and high humidity.
(3) To avoid misuse and preserve quality, keep in the original package.

■Therapeutic Efficacy and Pharmacology
1. Antibacterial Activity
(1) Orbifloxacin has a broad antibacterial spectrum. It exhibits potent antibacterial activity against a broad spectrum of bacteria, including gram negative bacteria, gram positive bacteria and mycoplasma.
(2) Orbifloxacin also exhibits antibacterial activity against bacteria that are resistant to such antibiotics as ampicillin, oxytetracycline and kanamycin.

2. Resistance
(1) Inherent bacterial resistance to Orbifloxacin Tablet is uncommon.
(2) This family of drugs inhibits R-plasmid transfer, thereby preventing transfer of R-plasmid-mediated resistance.

3. Mechanism of Action
Orbifloxacin Tablet exhibits bactericidal activity by inhibiting the activity of bacteria-specific DNA gyrase, which prevents DNA replication.

■*In Vivo* Pharmacokinetics

1. Plasma Concentration
Following oral gavage administration of a single dose of 5 mg/kg to dogs and cats, the plasma concentration peaked at 1.1and 1.3 hours respectively (dogs: 3.6 μg/mL, cats: 3.5 μg/mL). The half-life was 8.5 and 8.6 hours respectively. These values are consistent with those obtained with subcutaneous administration, indicating that Orbifloxacin Tablet is well absorbed from the gastrointestinal tract.

2. Tissue Concentration
The active ingredient of Orbifloxacin Tablet, orbifloxacin, is widely distributed in organs and tissues after subcutaneous administration. The concentration is higher than or approximately equivalent to the plasma concentration in nearly all organs and tissues, including the kidneys, liver, lungs and skin, demonstrating good tissue penetration.

3. Metabolism and Excretion
Orbifloxacin is eliminated primarily through the urine following subcutaneous administration. Urinary metabolite analysis has shown that unchanged drug accounts for the majority of urinary recovery (dogs ≥90%, cats ≥80%). Orbifloxacin Tablet therefore has limited in vivo metabolism, indicating that it possesses the antibacterial activity of the unchanged drug as it is distributed in the body.

4. Interactions
Concomitant use with antacids containing the analogous compounds aluminum or magnesium has been reported to cause reduced absorption and reduced efficacy.

■Toxicity

1. Acute toxicity LD_{50} (mg/kg)

Animal Species/Sex \ Administration Route		Intravenous	Intramuscular	Oral
Mouse (CD-1)	Male	250	>500	>2,000
	Female	283	>500	>2,000
Rat (CD)	Male	233	>200	>2,000
	Female	270	>200	>2,000

2. Subacute Toxicity
The NOAEL was 50 mg/kg/day in a 4-week repeated oral gavage study in rats. Increased lymphocyte count, decreased segmented leukocyte ratio and increased cecal weight were observed at the minimal toxic dose of 250 mg/kg/day.

3. Chronic Toxicity
The NOAEL was 50 mg/kg/day in a 13-week oral study in rats. Decreased gamma-globulin ratio and increased cecal weight were observed at the toxic dose of 150 mg/kg/day.

4. Teratogenicity
In studies of oral administration during organogenesis in rats and rabbits, teratogenicity was not observed in rat or rabbit dams at the respective toxic doses of 500 mg/kg/day and 100 mg/kg/day.

■Safety

1. Safety in Dogs
A study evaluating the safety of once daily repeated oral administration of 5 mg (recommended maximum dose), 10 mg (double dose) and 25 mg (quintuple dose) per kilogram of body weight for 10 days was conducted in three-month-old beagles. Neither the upper gastrointestinal damage nor the CNS damage reported with some new quinolone antibiotics was observed. Transient vomiting was, however, observed for one day or two days during the study period (13 days) in one animal each in the 10 mg and 25 mg groups. No significant abnormalities were observed in general condition, body

weight or weight gain profile, hematology or blood chemistry. Although new quinolone drugs have been reported to cause gait disturbance and arthropathy in immature dogs, no gait abnormalities were observed in this study. The results of necropsy of all of the dogs under study three days after the last dose did, however, show the formation of vesicles, without increased synovial fluid, on some of the joints of two of the dogs in the 25 mg group. It can therefore be concluded that no significant safety issues were noted with repeated administration of the recommended dose for 10 days.

2. Safety in Cats
A study evaluating the safety of once daily repeated oral administration of 5 mg (recommended maximum dose), 10 mg (double dose) and 25 mg (quintuple dose) per kilogram of body weight for 10 days was conducted in five- to nine-month-old laboratory mongrel cats. The results showed reduced hemoglobin and hematocrit in males and increased total bilirubin in females in the 10 mg and 25 mg groups. All of the changes were, however, within the normal range and considered insignificant. No other significant changes were observed on examination of general condition, hematology, blood chemistry and necropsy results. It can therefore be concluded that no significant safety issues were noted with repeated administration of the recommended dose for 10 days.

■Description

1. Formulation
Orbifloxacin Tablet 10 mg is a white to yellowish white, scored uncoated tablet.
Orbifloxacin Tablet 20 mg is a white to yellowish white, scored uncoated tablet.
Orbifloxacin Tablet 40 mg is a white to yellowish white, scored uncoated tablet.
Orbifloxacin Tablet 80 mg is a white to yellowish white, scored uncoated tablet.

2. Effective Ingredient
Generic name: Orbifloxacin
Chemical name: 1-cyclopropyl-5, 6, 8-trifluoro-1, 4-dihydro-7-(*cis* -3, 5-dimethyl-1-piperazinyl)-4-oxoquinoline-3-carboxylic acid
Chemical formula: $C_{19}H_{20}F_3N_3O_3$
Molecular weight: 395.38
Melting point: Approximately 263 °C
Description: Orbifloxacin is a white to pale yellow, odorless, crystalline powder, with a bitter taste. It is soluble in acetic acid, very slightly soluble in water, methanol and chloroform and practically insoluble in ethanol and ether. It dissolves in dilute acetic acid and dilute sodium hydroxide reagent.

■Packaging

Orbifloxacin Tablet 10 mg: 100 tablets (10 tablets × 10)
Orbifloxacin Tablet 20 mg: 100 tablets (10 tablets × 10)
Orbifloxacin Tablet 40 mg: 100 tablets (10 tablets × 10)
Orbifloxacin Tablet 80 mg: 60 tablets (10 tablets × 6)

Marketing authorization holder
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