SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fungiconazol 200 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Active substance:
Ketoconazole 200 mg

Excipients: For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet
Brown spiked, round flavoured tablets, quadrisect.
The tablets can be divided into halves and quarters.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Treatment of dermatomycoses due to the following dermatophytes:
- *Microsporum canis,*
- *Microsporum gypseum,*
- *Trichophyton mentagrophytes.*

4.3 Contraindications

Do not administer to animals with liver failure.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients

4.4 Special warnings for each target species

Although rare, repeated use of ketoconazole may induce cross-resistance to other azoles

4.5 Special precautions for use

Special precautions for use in animals
Treatment with ketoconazole suppresses testosterone concentrations and increases progesterone concentrations and may affect breeding effectiveness in male dogs during and for some weeks after treatment.
Treatment of dermatophytosis should not be limited to treatment of the infected animal(s). It should also include disinfection of the environment, since spores can survive in the environment for long periods of time. Other measures such as frequent vacuuming, disinfection of grooming equipment and removal of all potentially contaminated material that cannot be disinfected will minimize the risk of re-infection or spread of infection.
Combination of systemic and topical treatment is recommended.
In case of long term treatment administration, liver function should be closely monitored. If clinical signs suggestive of liver dysfunction develop, treatment should be discontinued immediately. As the tablets are flavoured, they should be stored in a safe place out of the reach of animals

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Accidental ingestion should be avoided. Keep the blister in the outer carton to prevent access by children. Part (half/quarter) tablets should be stored in the original blister and be used for the next administration. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

People with known hypersensitivity to ketoconazole should avoid contact with the veterinary medicinal product. Wash hands after use.

Other precautions
Dermatophytes mentioned in the indication have zoonotic potential with risk of transmission to humans. Maintain good personal hygiene (washing hands after handling the animal, and avoiding direct contact with animal). If signs of skin lesions occur, contact your physician.

4.6 Adverse reactions (frequency and seriousness)

In rare cases (more than 1 but less than 10 animals in 10,000 animals treated), neurological symptoms (apathy, ataxia, tremors), hepatic toxicity, vomiting, anorexia and/or diarrhoea may be observed at standard doses.
Ketoconazole has transient anti-androgen and anti-glucocorticoid effects; it inhibits the conversion of cholesterol to steroid hormones such as testosterone and cortisol in a dose dependent and time-dependent manner. See also section 4.5.1 for effects in male breeding dogs.

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals have shown evidence of teratogenic and embryotoxic effects.
The safety of the product has not been established in pregnant or lactating bitches.
Use is not recommended during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

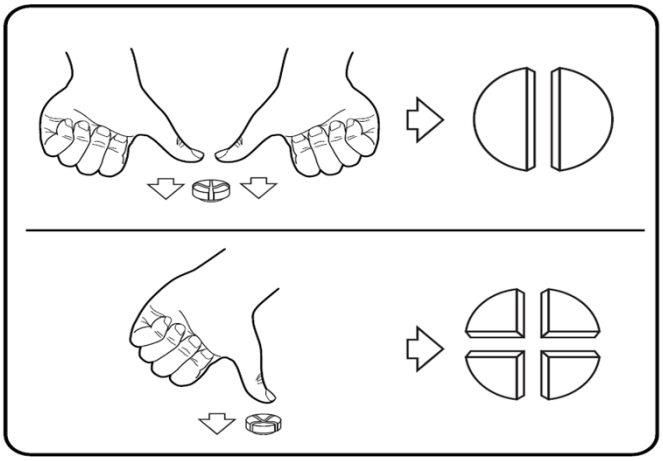
Do not administer with antacids and/or H2-receptor antagonists (cimetidine/rantidine) or proton pump inhibitors (e.g. omeprazole) as the absorption of ketoconazole may be modified (absorption requires an acid environment).

Ketoconazole is a substrate and potent inhibitor of cytochrome P450 3A4 (CYP3A4). It may decrease the elimination of drugs metabolized by CYP3A4, thereby altering their plasma concentrations. This may result in increased plasma concentrations of e.g. cyclosporine, macrocyclic lactones (ivermectin, selamectin, milbemycin), midazolam, cisapride, calcium-channel blocking agents, fentanyl, digoxin, macrolides, methylprednisolone or coumarine anticoagulants. The increased plasma levels of drugs mentioned above can prolong the duration of effects as well as side effects.
On the other hand, inducers of cytochrome P450 may increase the rate of metabolism of ketoconazole, e.g. barbiturates or phenytoin can increase the rate of metabolism of ketoconazole, resulting in a decreased bioavailability, hence a decreased efficacy.
Ketoconazole may decrease theophylline serum concentrations.
Ketoconazole inhibits the conversion of cholesterol to cortisol and may thus affect trilostane / mitotane dosing in dogs concurrently being treated for hyperadrenocorticism.

It is not known to what extent these interactions are relevant for dogs and cats, but in the absence of data, co-administration of the product and these drugs should be avoided.

4.9 Amounts to be administered and administration route

For oral use.
10 mg of ketoconazole per kg body weight daily, by oral administration. This corresponds to 1 tablet per 20 kg body weight daily.
It is recommended to sample the animal once a month during treatment and to stop antifungal administration after two negative cultures. When mycological follow up is not possible, treatment should be continued for an adequate period of time to ensure mycological cure. If lesions persist after 8 weeks of treatment, medication should be re-evaluated by the responsible veterinarian.
To be administered preferably together with food, in order to maximise absorption.
Tablets can be divided into halves or quarters to ensure accurate dosing. Put the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.
Halves: With the tip of the thumbs, exert a slight vertical pressure on both sides of the tablet to break it into halves.
Quarters: With the tip of a thumb, exert a slight vertical pressure on the middle of the tablet to break it into quarters.



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

In cases of overdose the following effects may be seen: anorexia, vomiting, pruritus, alopecia
and increase of hepatic alanine aminotransferase (ALT) and alkaline phosphatase (ALP).

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Systemic antimycotics, imidazole derivatives.
ATCvet code: QJ02AB02

5.1 Pharmacodynamic properties

Ketoconazole is an antifungal agent with a wide spectrum, derived from imidazole-dioxolane, which exerts a fungistatic and sporicidal effect on dermatophytes in dogs.

Ketoconazole widely inhibits the cytochrome P450 system. Ketoconazole modifies the permeability of membranes of fungi, and inhibit specifically the synthesis of ergosterole, which is an essential component of the cellular membrane of fungi, principally by inhibiting the enzyme cytochrome P450 14-alpha-demethylase (P45014DM).

Ketoconazole has anti-androgen and anti-glucocorticoid effects; it inhibits the conversion of cholesterol to steroid hormones such as testosterone and cortisol. It produces this effect through inhibition of cytochrome P450 enzymes involved in the synthesis.

Through inhibition of CYP3A4, metabolism of many drugs is decreased and their *in-vivo* bioavailability increased.

Ketoconazole inhibits p-glycoprotein efflux pumps and may increase the oral absorption and tissue distribution of other medicines, e.g. prednisolone.

5.2 Pharmacokinetic particulars

After oral administration, peak plasma levels of 22 – 49 µg/ml (mean 35 µg/ml) are obtained within 1.5 to 4.0 hours (mean 2.9 hours).

Ketoconazole absorption is enhanced in an acidic environment and drugs that raise gastric pH may lessen absorption. High levels of the drug are found in the liver, adrenals, and pituitary gland, while more moderate levels are found in the kidneys, lungs, bladder, bone marrow, and myocardium. At usual doses (10 mg/kg), drug levels attained are probably inadequate in the brain, testis, and eyes to treat most infections; higher dosages are required. It crosses the placenta (in rats) and is excreted into milk

Ketoconazole is 84% - 99% bound to the albumin fraction of plasma proteins. Ketoconazole is metabolised by the liver into several inactive metabolites. It is excreted predominantly into bile and to a lesser extent into urine. The terminal elimination half-life ranged between 3 and 9 hours (mean 4.6 hours).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Sodium starch glycolate, type A
Sodium laurilsulfate
Dried yeast
Chicken flavour
Colloidal anhydrous silica
Magnesium stearate

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:2 years
In-use shelf life subdivided tablets (quarters/halves): 3 days

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

Carton containing 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 Aluminium/PVC/PE/PVDC blisters, containing 10 tablets each.
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

Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 50406/4027

9. DATE OF FIRST AUTHORISATION

04 November 2014

10. DATE OF REVISION OF THE TEXT

May 2023

Approved 16 May 2023