

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Fungiconazol 400 mg tablets for dogs  
Canizol vet 400 mg tablets for dogs (DK, FI, IS, NO, SE, EE, LT, LV, PL)

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains:

**Active substance:**

Ketoconazole 400 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 equal 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 administer to animals with known hypersensitivity to the active substance or to any of the excipients.

#### **4.4. Special warnings for each target species**

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

#### **4.5. Special precautions for use**

i) Special precautions for use in animals

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.

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

People with known hypersensitivity to the active ingredients should avoid the contact of the skin and mucosae with the veterinary medicinal product.

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

Wash hands after use.

Part (half/quarter) tablets should be stored in the original blister and be used for the next administration. Keep the blister in the outer carton to prevent access by children.

#### **4.6. Adverse reactions (frequency and seriousness)**

In rare cases, neurological symptoms (apathy, ataxia, tremors), hepatic toxicity, vomiting, anorexia and/or diarrhoea may be observed at standard doses.

Ketoconazole has 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 4.4 for effects in male breeding dogs.

#### **4.7. Use during pregnancy, lactation or breeding**

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 H<sub>2</sub>-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. Inducers of cytochrome P450 may increase the rate of metabolism of ketoconazole. Relevant veterinary interactions include cyclosporines, macrocyclic lactones (ivermectin, selamectin, milbemycin), midazolam, cisapride, amlodipine, fentanyl, macrolides (clarithromycin erythromycin), digoxin, anticoagulants and phenobarbital.

Ketoconazole inhibits the conversion of cholesterol to cortisol and may thus affect trilostane / mitotane dosing in dogs concurrently being treated for hyperadrenocorticism.

#### 4.9. Amounts to be administered and administration route

10 mg of ketoconazole per kg body weight daily, by oral administration. This corresponds to 1 tablet per 40 kg body weight daily.

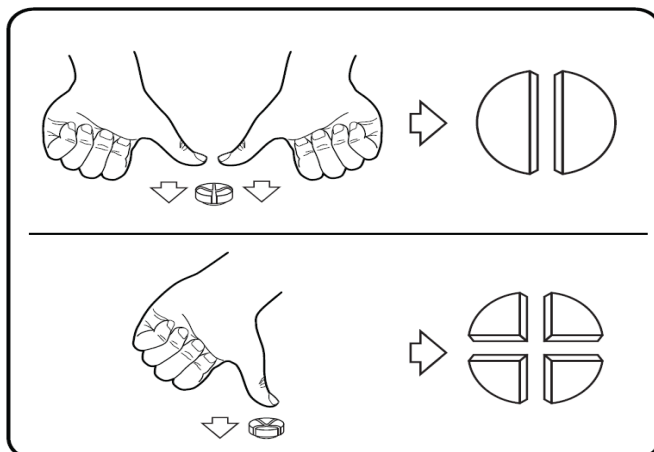
It is recommended to sample the animal once a month during treatment and to stop antifungal administration after two negative cultures. When mycological follow up is not possible, treatment should be continued for an adequate period of time to ensure mycological cure. If lesions persist after 8 weeks 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 equal 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.

Equal Halves: With the tip of the thumbs, exert a slight vertical pressure on both sides of the tablet to break it into halves.

Equal 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**

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 is 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. Incompatibilities**

Not applicable.

### **6.3. Shelf life**

Shelf life of the veterinary medicinal product as packaged for sale: 24 months  
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**

Le Vet Beheer B.V.  
Wilgenweg 7  
3421 TV Oudewater  
The Netherlands

## **8. MARKETING AUTHORISATION NUMBER**


**Vm** 41821/4013

**9. DATE OF FIRST AUTHORISATION**

**Date:** 05 November 2014

**10. DATE OF REVISION OF THE TEXT**

**Date:** November 2014

Approved:  05/11/2014