

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

Vidalta 15 mg prolonged-release tablets for cats

## **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each prolonged-release tablet contains:

**Active substance:**

Carbimazole 15.0 mg

**Excipients:**

Red ferric oxide (E172) 0.75 mg

For the full list of excipients, see section 6.1

## **3 PHARMACEUTICAL FORM**

Prolonged-release tablet.

Round, dark pink tablet with little spots.

## **4 CLINICAL PARTICULARS**

### **4.1 Target Species**

Cats.

### **4.2 Indications for use, specifying the target species**

Treatment of hyperthyroidism and hyperthyroidism-associated clinical signs in cats.

### **4.3 Contraindications**

Do not use in cats suffering from concurrent systemic diseases, such as severe primary liver disease or diabetes mellitus.

Do not use in cats showing signs of auto-immune diseases and/or altered red or white blood cell counts, such as anaemia, neutropaenia or lymphopaenia.

Do not use in cats with platelet disorders (particularly thrombocytopaenia) or coagulopathies.

Do not use in cats with hypersensitivity to mercaptoimidazoles such as carbimazole or thiamazole (methimazole) or to any of the excipients.

Please refer to section 4.7.

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

Thiamazole (methimazole), the active metabolite of carbimazole, inhibits thyroid hormone production and therefore cessation of treatment with carbimazole will result in a rapid (within 48 hours) return to pre-treatment thyroid hormone levels. Chronic administration is therefore necessary unless surgical or radiation-induced thyroidectomy is performed.

A small proportion of cats with thyroid adenoma may fail to respond or have a poor response to treatment.

Thyroid carcinoma is a rare cause of hyperthyroidism in the cat and medical management alone is not recommended in such cases as it is not curative.

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

##### Special precautions for use in animals

Treatment should be adjusted according to a benefit-risk assessment by the responsible veterinarian in each individual case.

Treatment of hyperthyroidism may result in a reduction in the glomerular filtration rate. This can lead to unmasking of pre-existent renal dysfunction. Treatment of hyperthyroidism may also induce an elevation of liver enzymes or a worsening of pre-existing hepatic disorders. Renal and liver function should therefore be monitored before and during treatment

Due to risk of leucopaenia or haemolytic anaemia, haematology parameters should be monitored on a regular basis before and during treatment, preferably at each visit of the dose adjustment phase and maintenance phase (see section 4.9).

Any animal that suddenly appears unwell during therapy, particularly if they are febrile, should have a blood sample taken for routine haematology and biochemistry. Neutropaenic animals (neutrophil counts  $<2.5 \times 10^9/L$ ) should be treated prophylactically with bactericidal antibiotics and supportive therapy.

Doses above 20 mg have only been trialled in a small number of cats and should be used with caution.

Therefore, careful monitoring is recommended and the dose should be adjusted in individual cases following a benefit-risk assessment by the responsible veterinarian.

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

Wash hands with soap and water after use and when handling litter used by treated animals.

Do not handle this product if you are allergic to antithyroid products. If allergic symptoms develop, such as a skin rash, swelling of the face, lips or eyes or difficulty in breathing, you should seek medical attention immediately and show the package leaflet or label to the doctor.

As carbimazole is a suspected human teratogen, women of child-bearing age should wear gloves when handling litter or vomit of treated cats.

Pregnant women should wear gloves when handling the product.

Do not break or crush tablets.

Do not eat, drink or smoke while handling the tablet or used litter.

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

Carbimazole, as a prodrug of thiamazole (methimazole), may cause vomiting, epigastric distress, headache, fever, arthralgia, pruritus and pancytopenia. Treatment is symptomatic.

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

Treatment of hyperthyroidism may result in a reduction of renal perfusion. Azotaemia has been reported in rare cases; depending on the severity, temporary or permanent discontinuation of treatment may be required. Polydipsia and polyuria have also been reported in rare (polydipsia) or very rare cases (polyuria).

Weight loss, vomiting, lethargy, tachycardia, reduced appetite, diarrhoea and dehydration have been observed in rare cases.

Increased liver enzymes have been reported in rare cases. Severe cases may require temporary or permanent discontinuation of treatment. However, these elevations are usually reversible when treatment is discontinued, although symptomatic therapy (nutritional and fluid support) may be required.

Anaemia, increase or decrease in white blood cell count, neutrophilia, thrombocytopenia, eosinophilia and/or lymphopenia have been reported in rare cases, in particular during the first 4-6 weeks of treatment. Discontinuation of treatment may be required in case of persistent and marked disorder. In most cases, the abnormality will resolve spontaneously within 1 month after the treatment has been discontinued.

Dermatological signs (pruritus, dermatitis, erythema, alopecia) have been reported in rare cases. These clinical signs are usually mild, adequately controlled by symptomatic therapy and do not require discontinuation of treatment. However, if more severe clinical signs occur that do not respond to symptomatic therapy, the dose should be reduced or treatment stopped following a benefit-risk assessment by the responsible veterinarian.

Signs of gastrointestinal bleeding such as bloody vomit, oral haemorrhage or dark faeces have been reported in rare cases.

Ataxia, pyrexia, dyspnoea, disorientation, aggressiveness, and positive antinuclear antibody (ANA) have also been reported in very rare cases.

In cases of serious adverse reactions, mortality, possibly due to the product, might occur if treatment is not discontinued. In many cases adverse reactions are reversible on cessation of treatment.

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**

Laboratory studies in rats and mice have shown evidence of teratogenic and embryotoxic effects of thiamazole (methimazole).

The safety of the product was not assessed in pregnant or lactating cats.

Furthermore, thiamazole crosses the placenta, distributes into milk and reaches approximately the same concentration as in maternal serum.

Do not use in pregnant or lactating animals.

#### **4.8 Interaction with other medicinal products and other forms of interaction**

Concomitant treatment with phenobarbital may reduce the clinical efficacy of carbimazole.

Concomitant use of benzimidazole anthelmintics (fenbendazole or mebendazole) has been shown to reduce the hepatic oxidation of this therapeutic class and may therefore induce an increase in circulating levels. Accordingly, co-administration of carbimazole with a benzimidazole is not recommended.

Thiamazole may display immunomodulating properties. This should be taken into account when considering vaccination of the cat.

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

For oral use only.

Administration with food enhances bioavailability. The timing of treatment and its relation to feeding should be kept consistent from day to day.

Do not break or crush Vidalta tablets as this will affect the sustained release property.

The aim of treatment is to maintain total thyroxine concentrations (TT<sub>4</sub>) in the lower end of the reference range.

The following dose recommendations during the adjustment and maintenance phases are suggested.

Dosing adjustment should primarily be based upon a clinical assessment of the individual cat. Monitoring of TT<sub>4</sub>, full haematology and liver and kidney parameters is recommended at each follow up visit (see sections 4.5 and 4.6).

#### Adjustment phase

The starting dose is a single daily oral administration of one tablet of 15 mg carbimazole per cat. Consideration could be given to a starting dose of one 10 mg tablet daily where the TT<sub>4</sub> concentration is only mildly increased, e.g. between 50 nmol/L and 100 nmol/L.

With the recommended starting dose of one 15 mg tablet once daily, TT<sub>4</sub> may decrease to within the euthyroid range (TT<sub>4</sub><50 nmol/L) shortly after treatment initiation. A dose adjustment may be required as early as 10 days of treatment. Dose adjustment should be also performed 3, 5 and 8 weeks after initiation of treatment, depending on both clinical and hormonal responses to treatment.

#### Maintenance phase

Follow-up visits every 3 to 6 months are recommended. The dose should be adjusted individually based on clinical signs and TT<sub>4</sub>. It is advisable to check TT<sub>4</sub> 10-14 days after dose adjustment.

The therapeutic dose ranges between 10 mg (one 10 mg tablet) and 25 mg (one 10 mg tablet and one 15 mg tablet) once daily.

Some cats require doses of less than 10 mg carbimazole daily. Every other day dosing with 10 mg or 15 mg of carbimazole may be sufficient to control the disease. Dose increases should not be made in increments of greater than 5 mg.

Doses above 20 mg have only been trialled in a small number of cats and should be used with caution.

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

In case of an overdose, adverse effects that may appear include, but are not limited to, weight loss, inappetence, vomiting, lethargy and less frequently signs of gastrointestinal bleeding such as haematemesis, oral haemorrhage or haemorrhage of the intestinal tract. Coat and skin abnormalities (erythema, alopecia), as well as haematological/biochemical changes (eosinophilia, lymphocytosis, neutropaenia, lymphopaenia, slight leucopaenia, agranulocytosis, thrombocytopaenia or haemolytic anaemia) may also appear. Hepatitis and nephritis have been reported. These adverse effects may become severe in case of chronic overdosing. In most cases, adverse effects are reversible upon treatment discontinuation and appropriate veterinary care.

TT<sub>4</sub> below the lower limit of the reference range may be observed during treatment although this is rarely linked to overt clinical signs. Decreasing the dose will lead to

an increase of the TT<sub>4</sub>. Dose adjustment should not be made based on TT<sub>4</sub> only (see section 4.9).

Please also refer to section 4.6

#### **4.11 Withdrawal period(s)**

Not applicable.

### **5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES**

Pharmacotherapeutic group: Systemic hormonal products excl. sex hormones and insulin; thyroid therapy; antithyroid preparations; sulphur-containing imidazole derivatives

ATCvet code: QH03BB01

#### **5.1 Pharmacodynamic properties**

Carbimazole is the prodrug of thiamazole (methimazole). Although carbimazole has inherent antithyroid activity, it is almost totally converted to thiamazole soon after its oral administration *in vivo* in humans and cats.

Thiamazole results in dose-dependent inhibition of the thyroid peroxidase-catalysed reactions involved in thyroid hormone synthesis, including oxidation of iodide and iodination of tyrosyl residues in thyroglobulin, thereby inhibiting neosynthesis of thyroid hormones. Thiamazole also interferes with the coupling of iodotyrosines to iodothyronines via inhibition of thyroid peroxidase or by binding and altering the structure of thyroglobulin, this reaction being more sensitive to inhibition than the formation of iodotyrosines. The inhibitory action of thiamazole is reversible.

Thiamazole does not inhibit the action of thyroid hormones already formed and present in the thyroid glands or bloodstream, or interfere with the effectiveness of administered exogenous thyroid hormone (iatrogenic hyperthyroidism). This explains why the length of the latency period until normalisation of serum concentrations of thyroxine and triiodothyronine, and thus to clinical improvement, differs between individuals.

#### **5.2 Pharmacokinetic particulars**

Carbimazole is rapidly absorbed from the gastrointestinal tract after oral administration and hydrolysed in the gastrointestinal tract (or immediately after entering into the circulation) to the active metabolite thiamazole (methimazole). The absolute bioavailability of thiamazole from carbimazole in Vidalta 15 mg tablets is 88%.

Following oral administration of one tablet of Vidalta 10 mg to healthy fasted cats, maximum thiamazole concentrations are observed 3 – 4 hours after administration, with a mean peak concentration of thiamazole of 0.54 – 0.87 µg/ml.

Following oral administration of one tablet of Vidalta 15 mg to healthy fasted cats, maximum thiamazole concentrations are observed 5 – 7 hours after administration, with a mean peak concentration of thiamazole of 0.72 – 1.13 µg/ml.

For both strengths, the thiamazole concentration/time profile is devoid of pronounced peaks and thiamazole persists in the circulation at least 20 and 24 hours for Vidalta 10 mg and Vidalta 15 mg, respectively.

The presence of food in the gastrointestinal tract at the time of administration has been shown to increase the bioavailability of thiamazole. When tablets are administered with food, both  $C_{max}$  and  $AUC_{last}$  may be increased whereas  $t_{max}$  is not expected to change.

No cumulative effects are observed upon repeated administration.

The tissue distribution of mercaptoimidazoles has not been specifically studied in cats but has been fully described in rodents. Thiamazole is mainly concentrated in the thyroid and adrenal glands, and can be found to a lesser extent in the thymus, diaphragm, kidneys, brain, liver, colon, testes, small intestine, stomach and plasma. Mercaptoimidazoles have also been shown to cross the placental barrier.

In rats, thiamazole is excreted mainly via the urine, and to a lesser extent in the faeces.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Hypromellose  
Microcrystalline cellulose  
Red ferric oxide(E 172)  
Silica, colloidal anhydrous  
Magnesium stearate  
Talc

### **6.2 Major incompatibilities**

Not applicable.

### **6.3 Shelf-life**

Shelf life of the veterinary medicinal products as packaged for sale: 24 months.

Shelf life after first opening the immediate packaging: 100 days

### **6.4 Special precautions for storage**

Do not store above 25 °C.

Store in the original container.

Keep the container tightly closed to protect from moisture.

Do not remove the desiccant.

### **6.5 Nature and composition of immediate packaging**

High density polyethylene container of 30 or 100 tablets closed with polypropylene tamper-evident, child-resistant, screw cap bearing a desiccant.

Packs of 1 or 6 containers.

Not all pack sizes may be marketed.

### **6.6 Special precautions for the disposal of unused veterinary medicinal products 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 Ireland Limited  
Magna Drive  
Magna Business Park, Citywest Road  
Dublin 24  
Ireland

## **8 MARKETING AUTHORISATION NUMBER(S)**

VPA10996/263/002

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 9<sup>th</sup> December 2011

## **10 DATE OF REVISION OF THE TEXT**

March 2018