Felimazole®
Treatment of feline hyperthyroidism

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Treat hypertension if present:
see ISFM Consensus Guidelines on diagnosis and management of hypertension (Taylor *et al*, 2017)

Hyperthyroidism diagnosed

- Measure systolic blood pressure (doppler or oscillometric)
- Measure urea/creatinine pre-treatment
- Full physical examination for comorbidities
- Nutritional assessment including weight, body condition score (BCS) and muscle condition score (MCS) (Freeman *et al*, 2011)*
- Advise owner on diet and how much to feed according to body weight/BCS/MCS
- Discuss preferred formulation with owner

Support owners to give medication and monitor for adverse effects

- Provide advice on giving chosen formulation
- Demonstrate administration
- Follow up phone call/nurse clinic to assist with compliance after 1-2 weeks
- Encourage owner to report problems openly

Non-azotaemic pre-treatment of hyperthyroidism

- Azotaemia may still develop with treatment
- Renal function should be monitored closely after starting treatment
- Start Felimazole at **either** 0.5 ml of oral solution twice daily **or** one 2.5 mg Felimazole tablet twice daily
- If, for reasons of compliance, once daily dosing is preferable, then this is acceptable, although the twice-daily dose may be more efficacious in the short term

Azotaemic pre-treatment for hyperthyroidism

- In most cases, hyperthyroidism should still be treated to avoid negative effects of hyperthyroidism (however an individual risk: benefit assessment should be completed)
- Renal function should be monitored closely after starting treatment
- Gradually introduce Felimazole starting at lowest possible dose
- Stage and manage CKD according to IRIS Guidelines (http://www.iris-kidney.com/) including use of renal diet e.g. SPECIFIC™ FKD/FKW Kidney Support

Development of azotaemia on treatment

- Ensure total T4 not below reference interval, aim for T4 in lower half of reference interval but accept upper half of reference interval if appropriate
- Stage and manage CKD according to IRIS Guidelines (http://www.iris-kidney.com/) including use of renal diet e.g. SPECIFIC™ FKD/FKW Kidney Support
- Ensure appropriate nutrition and maintain BCS/MCS

After 3 weeks of Felimazole treatment

- Obtain history from owner (adverse medication effects, appetite, compliance to medication, improvement in clinical signs)
- Record weight, BCS, MCS
- Re-check systolic blood pressure (hypertension can develop during treatment for hyperthyroidism)
- Blood sample to assess Total T4, haematology and biochemistry
- Aim for Total T4 concentration in mid to lower half of reference interval but avoid iatrogenic hypothyroidism (for cats azotaemic before treatment accept T4 in upper reference interval and monitor for worsening azotaemia)
- Timing of sampling not important

Total T4 below reference interval

- Reduce Felimazole dose by 1.25-2.5 mg per day

Total T4 in lower half of reference interval

- If non-azotaemic maintain current dose
- If stable azotaemic and clinical signs of hyperthyroidism controlled, consider maintaining dose
- If azotaemia worsened/developed or unstable consider reducing Felimazole dose by 1.25-2.5 mg per day

Total T4 in upper half of reference interval

- If azotaemic and clinical signs of hyperthyroidism controlled consider maintaining dose
- If considerable improvement in clinical signs and lowering of total T4 from diagnosis, consider maintaining dose and re-assess in 3 weeks
- If non-azotaemic (+/- ongoing clinical signs of hyperthyroidism) check owner compliance. If no issues, then increase Felimazole dose by 1.25-2.5 mg per day

Total T4 above reference interval

- Check owner compliance to medication (repeat demonstrations on how to give Felimazole)
- If non-azotaemic (+/- ongoing clinical signs of hyperthyroidism) increase Felimazole dose by 1.25-2.5 mg per day
- If azotaemic increase dose cautiously and re-check Total T4 and urea/creatinine in 2-3 weeks **OR**
- If azotaemic and Total T4 has lowered considerably and clinical signs of hyperthyroidism improving, maintain dose and re-check Total T4 and urea/creatinine in 2-3 weeks

Continue to monitor as per datasheet recommendations

- Measure Total T4, haematology and biochemistry at 6 weeks, 10 weeks, 20 weeks and every 3 months thereafter
- Support owners through nursing clinics between assessments
- Make dose adjustments as needed
- Maintain appropriate Total T4 concentration using lowest possible dose of Felimazole
- Monitor for comorbidities (e.g. osteoarthritis)
- Pay particular attention to systolic blood pressure for development of hypertension
- Monitor nutritional status (appetite, food intake, body weight, BCS and MCS) and adjust diet if necessary
- Continue to support owner in administration of medication

References

*See the SPECIFIC™ Diets Guide on Nutritional support of the hyperthyroid cat for more information (add link and QR code)

FELIMAZOLE®
A problem precisely answered

Dechra

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Felimazole 2.5 mg Coated Tablets for Cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Thiamazole	2.5 mg

Excipients:

Titanium Dioxide (E171)	1.12 mg
Erythrosine (E127)	0.01 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablet.

Pink sugar-coated biconvex tablets, 5.5 mm diameter.

4. CLINICAL PARTICULARS

4.1 Target species

Cats.

4.2 Indications for use, specifying the target species

For the stabilisation of hyperthyroidism in cats prior to surgical thyroidectomy.

For the long-term treatment of feline hyperthyroidism.

4.3 Contraindications

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

Do not use in cats showing signs of autoimmune disease.

Do not use in animals with disorders of white blood cells, such as neutropenia and lymphopenia.

Do not use in animals with platelet disorders and coagulopathies (particularly thrombocytopenia).

Do not use in cats with hypersensitivity to thiamazole or the excipient, polyethylene glycol.

Do not use in pregnant or lactating females.

Please refer to section 4.7.

4.4 Special warnings

As thiamazole can cause haemoconcentration, cats should always have access to drinking water.

4.5 Special precautions for use

i.Special precautions for use in animals

If more than 10 mg per day is required animals should be monitored particularly carefully.

Use of the product in cats with renal dysfunction should be subject to careful risk : benefit assessment by the clinician. Due to the effect thiamazole can have on reducing the glomerular filtration rate, the effect of therapy on renal function should be monitored closely as deterioration of an underlying condition may occur.

Haematology must be monitored due to risk of leucopenia or haemolytic anaemia.

Any animal that suddenly appears unwell during therapy, particularly if they are febrile, should have a blood sample taken for routine haematology and biochemistry.

Neutropenic animals (neutrophil counts <2.5 x 109/l) should be treated with prophylactic bactericidal antibacterial drugs and supportive therapy.

Please refer to section 4.9 for monitoring instructions.

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

Wash hands after use.

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

Thiamazole may cause vomiting, epigastric distress, headache, fever, arthralgia, pruritus and pancytopaenia. Treatment is symptomatic.

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

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

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.

Do not break or crush tablets.

As thiamazole is a suspected human teratogen, women of child-bearing age and pregnant women should wear gloves when handling litter of treated cats.

Pregnant women should wear gloves when handling the product.

4.6 Adverse reactions (frequency and seriousness)

Adverse reactions have been reported following long term control of hyperthyroidism. In many cases, signs may be mild and transitory and not a reason for withdrawal of treatment. The more serious effects are mainly reversible when medication is stopped.

Adverse reactions are uncommon. The most common clinical side effects that are reported include vomiting, inappetance/anorexia, lethargy, severe pruritus and excoriations of the head and neck, bleeding diathesis and icterus associated with hepatopathy, and haematological abnormalities (eosinophilia, lymphocytosis, neutropenia, lymphopenia, slight leucopenia, agranulocytosis, thrombocytopenia or haemolytic anaemia). These side effects resolve within 7-45 days after cessation of thiamazole therapy.

Possible immunological side effects include anaemia, with rare side effects including thrombocytopenia and serum anti-nuclear antibodies, and, very rarely, lymphadenopathy can occur. Treatment should be stopped immediately and alternative therapy considered following a suitable period for recovery.

Following long-term treatment with thiamazole in rodents, an increased risk of neoplasia in the thyroid gland has been shown to occur, but no evidence is available in cats.

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and mice have shown evidence of teratogenic and embryotoxic effects of thiamazole. The safety of the product was not assessed in pregnant or lactating cats. Do not use in pregnant or lactating females.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent treatment with phenobarbital may reduce the clinical efficacy of thiamazole.

Thiamazole is known to reduce the hepatic oxidation of benzimidazole wormers and may lead to increases in their plasma concentrations when given concurrently.

Thiamazole is immunomodulatory, therefore this should be taken into account when considering vaccination programmes.

4.9 Amounts to be administered and administration route

For oral administration only.

For the stabilisation of feline hyperthyroidism prior to surgical thyroidectomy and for the long term treatment of feline hyperthyroidism, the recommended starting dose is 5 mg per day. Wherever possible, the total daily dose should be divided into two and administered morning and evening. Tablets should not be split.

If, for reasons of compliance, once daily dosing with a 5 mg tablet is preferable, then this is acceptable although the 2.5 mg tablet given twice daily may be more efficacious in the short term. The 5 mg tablet is also suitable for cats requiring higher dose rates.

Haematology, biochemistry and serum total T4 should be assessed before initiating treatment and after 3 weeks, 6 weeks, 10 weeks, 20 weeks, and thereafter every 3 months. At each of the recommended monitoring intervals, the dose should be titrated to effect according to the total T4 and to clinical response to treatment. Dose adjustments should be made in increments of 2.5 mg and the aim should be to achieve the lowest possible dose rate.

If more than 10 mg per day is required animals should be monitored particularly carefully.

The dose administered should not exceed 20 mg/day.

For long term treatment of hyperthyroidism the animal should be treated for life.

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

In tolerance studies in young healthy cats, the following dose-related clinical signs occurred at doses of up to 30 mg/animal/day: anorexia, vomiting, lethargy, pruritus and haematological and biochemical abnormalities such as neutropenia, lymphopenia, reduced serum potassium and phosphorus levels, increased magnesium and creatinine levels and the occurrence of anti-nuclear antibodies. At a dose of 30 mg/day some cats showed signs of haemolytic anaemia and severe clinical deterioration. Some of these signs may also occur in hyperthyroid cats treated at doses of up to 20 mg per day.

Excessive doses in hyperthyroid cats may result in signs of hypothyroidism. This is however unlikely, as hypothyroidism is usually corrected by negative feedback mechanisms. Please refer to Section 4.6 Adverse reactions.

If overdosage occurs, stop treatment and give symptomatic and supportive care.

4.11 Withdrawal periods

Not applicable.

5. PHARMACOLOGICAL PARTICULARS

Pharmacotherapeutic group: antithyroid preparations: sulphur-containing imidazole derivatives.

ATC Vet Code: QH03BB02.

5.1 Pharmacodynamic properties

Thiamazole acts by blocking the biosynthesis of thyroid hormone in vivo. The primary action is to inhibit binding of iodide to the enzyme thyroid peroxidase, thereby preventing the catalysed iodination of thyroglobulin and T3 and T4 synthesis.

5.2 Pharmacokinetic particulars

Following oral dosing in healthy cats, thiamazole is rapidly and completely absorbed with a bioavailability of >75%. However, there is a considerable variation between animals. Elimination of the drug from cat plasma is rapid with a half life of 3.5-4.0 hours. Peak plasma levels occur approximately 1-2 hours after dosing. Cmax is approximately 0.8 µg/ml.

In rats thiamazole has been shown to be poorly bound to plasma protein (5 %); 40 % was bound to red blood cells. The metabolism of thiamazole in cats has not been investigated, however, in rats thiamazole is rapidly metabolised in the thyroid gland. About 64 % of the administered dose being eliminated in the urine and only 7.8 % excreted in faeces. This is in contrast with man where the liver is important for the metabolic degradation of the compound. The drug residence time in the thyroid gland is assumed to be longer than in the plasma.

From man and rats it is known that the drug can cross the placenta and concentrates in the foetal thyroid gland. There is also a high rate of transfer into breast milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Lactose monohydrate, Povidone, Sodium starch glycolate, Magnesium stearate

Coating:

Sucrose, Povidone, Erythrosine, Macrogol, Purified talc, White beeswax, Carnauba wax, Shellac, Titanium dioxide (E171), Sodium methyl, parahydroxybenzoate (E219)

6.2 Incompatibilities None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Do not store above 25ºC.

Keep the container tightly closed in order to protect from moisture.

Keep the container in the outer carton.

6.5 Nature and contents of immediate packaging

White polypropylene tub with white low density polyethylene tamper evident lid containing 100 tablets.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Dechra Limited, Dechra House, Jamage Industrial Estate, Talke Pits, Stoke-on-Trent, Staffordshire, ST7 1XW, UK

8. MARKETING AUTHORISATION NUMBERS

UK: Vm 10434/4050

IE: VPA 10799/15/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

UK: 19/11/2004

IE: 20/02/2009

10. DATE OF ANY REVISION OF THE TEXT

April 2012

DVP1036

Felimazole: Felimazole contains Thiamazole

Dechra Veterinary Products A/S, Mekuvej 9, 7171 Uldum, Denmark.

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