SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Thyrasol 5 mg/ml, Oral solution for cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Thiamazole 5.0 mg

Excipients:
Sodium benzoate (E211) 1.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Solution.
Colourless to slightly brownish, turbid, viscous solution.

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 cases of hypersensitivity to the active substance or to any of the excipients.
Do not use during pregnancy or lactation. Please refer to section 4.7.

4.4 Special warnings for each target species

In order to enhance stabilisation of the hyperthyroid patient the same feeding and dosing schedule should be used daily.

4.5 Special precautions for use

Special precautions for use in animals

If more than 10 mg of thiamazole per day is required animals should be monitored particularly carefully.
As thiamazole can cause haemoconcentration, cats should always have access to drinking water.
Use of the product in cats with renal dysfunction should be subject to careful benefit/risk 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 renal impairment may occur.
Haematology must be monitored due to risk of leucopenia or haemolytic anaemia.
Any animal that suddenly appears unwell during therapy, particularly if it is febrile, should have a blood sample taken for routine haematology and biochemistry.
Neutropenic animals (neutrophil counts $<2.5 \times 10^9$/l) should be treated with prophylactic bactericidal antibacterial drugs and supportive therapy, if needed according to the benefit/risk assessment of the prescribing veterinarian.
Please refer to section 4.9 for monitoring instructions.

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

People with known hypersensitivity (allergy) to thiamazole, or one of the excipients, should avoid contact with the veterinary medicinal product. 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.
This product may cause skin and/or eye irritation. Avoid skin and eye contact including hand to eye contact.
In case of accidental skin and/or eye contact, rinse skin and/or eyes immediately with clean running water. If irritation develops, seek medical advice.
Wash hands with soap and water after administration of the product and handling the vomit of or litter used by treated animals.
Thiamazole may cause gastrointestinal disturbances, headache, fever, joint pain, pruritus (itching) and pancytopaenia (decrease in blood cells and platelets).
Avoid oral exposure, including hand-to-mouth contact.
Do not eat, drink or smoke while handling the product or used litter.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Do not leave filled syringes unattended.
Following administration of the product any residual product remaining on the tip of the dosing syringe should be wiped clean with a tissue. The contaminated tissue should be immediately disposed of.
The used syringe should be stored with the product in the original carton.
As thiamazole is a suspected human teratogen, women of child-bearing age must wear non-permeable single-use gloves when administering the product or handling the litter/vomit of treated cats.
If you are pregnant, think you may be pregnant or are attempting to conceive, you should not administer the product or handle the litter/vomit of treated cats.

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, weight-loss, 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.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated- displaying adverse reaction(s))
- 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

Do not use during pregnancy or lactation.
Laboratory studies in rats and mice have shown evidence of teratogenic and embryotoxic effects of thiamazole. The safety of the product has not been assessed in pregnant or lactating cats.

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

Oral use.

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 (= 1 mL of the product) per day.
Wherever possible, the total daily dose should be divided into two and administered morning and evening.
The dose should be administered directly in the mouth using the syringe.
If, for reasons of compliance, once daily dosing is preferable, then this is acceptable although a 2.5 mg dose (= 0.5 mL of the product) given twice daily may be more efficacious in the short term.
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.
Standard 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 of thiamazole/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 of thiamazole/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 of thiamazole 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 period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antithyroid preparations: sulphur-containing imidazole derivatives.
ATCvet 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 2.5-7.8 hours. Peak plasma levels occur 0.5-1 hours after dosing. C_{max} is between 0.8-2.0 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 is eliminated via 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

Sodium benzoate (E211)
Glycerol
Povidone
Hypromellose
Disodium phosphate dihydrate
Sodium dihydrogen phosphate dihydrate
Citric acid
Sodium hydroxide
Sodium cyclamate
Sucralose
Anise flavor
Water, purified

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 24 months.
Shelf life after first opening the immediate packaging: 90 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

Amber type III glass or high density polyethylene (HDPE) screw bottles containing 30 mL, 50 mL and 100 mL product, with child resistant polypropylene (PP) screw cap and low density polyethylene (LDPE) syringe in-lay.
1.5 mL oral dosing syringe graduated in 0.05 mL increments with low density polyethylene (LDPE) body and polystyrene (PS) plunger.

Pack sizes:
Carton box holding 1 vial of 30 mL and 1 graduated syringe of 1.5 mL Carton box holding 1 vial of 50 mL and 1 graduated syringe of 1.5 mL Carton box holding 1 vial of 100 mL and 1 graduated syringe of 1.5 mL

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

CP Pharma Handelsgesellschaft mbH
Ostlandring 13
31303 Burgdorf
Germany

8. MARKETING AUTHORISATION NUMBER

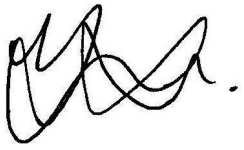
Vm 20916/5004

9. DATE OF FIRST AUTHORISATION

19 December 2022

10. DATE OF REVISION OF THE TEXT

December 2022



Approved: 19 December 2022