

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Forthyron 200 microgram tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:

200µg levothyroxine sodium per tablet equivalent to 194µg levothyroxine
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet

White to off white round tablets, scored on one side
Tablets divisible into 4 parts

4. CLINICAL PARTICULARS

4.1. Target species

Dogs.

4.2. Indications for use, specifying the target species

For the treatment of hypothyroidism in dogs.

4.3. Contra-indications

Do not use in dogs suffering from uncorrected adrenal insufficiency.

4.4. Special warnings for each target species

The diagnosis hypothyroidism should be confirmed with appropriate tests.

4.5. Special precautions for use

i) Special precautions for use in animals

A sudden increase in demand for oxygen delivery to peripheral tissues, plus the chronotropic effects of levothyroxine sodium, may place undue stress on a poorly functioning heart, causing decompensation and signs of congestive heart failure. Hypothyroid dogs suffering from hypoadrenocorticism have a decreased ability to metabolise levothyroxine sodium and therefore an increased risk of thyrotoxicosis. Dogs with concurrent hypoadrenocorticism and hypothyroidism should be stabilised with glucocorticoid and mineralocorticoid treatment prior to treatment with levothyroxine sodium to avoid precipitating a hypoadrenocortical crisis. After this, thyroid tests should be repeated, then gradual introduction of levothyroxine therapy, starting with 25% of the normal dose, increasing by 25% increments every fortnight until optimal stabilisation is achieved is recommended. Gradual introduction of therapy is also recommended for dogs with other concurrent illnesses; particularly diabetes mellitus and renal or hepatic dysfunction.

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

Wash hands after administering the tablets. Pregnant women should handle the product with caution.

4.6. Adverse reactions (frequency and seriousness)

Restoration of physical activity may unmask or intensify other problems, such as osteoarthritis. Adverse effects of thyroid hormones are generally associated with excessive dosage and correspond to the symptoms of hyperthyroidism. See also section 4.10.

4.7. Use during pregnancy, lactation or lay

The safety of use of the product during pregnancy has not been established through special reproduction studies. However, levothyroxine is an endogenous substance and thyroid hormones are essential for the developing foetus, especially during the first period of gestation. Hypothyroidism during pregnancy may result in major complications such as foetal death and a poor perinatal outcome. Maintenance dose of levothyroxine sodium may need adjustment during pregnancy. Pregnant bitches should therefore be monitored on a regular base from conception until several weeks after delivery.

4.8. Interactions with other medicinal products and other forms of interaction

A variety of drugs may impair plasma or tissue binding of the thyroid hormones or alter thyroid hormone metabolism (eg. barbiturates, antacids, anabolic steroids, diazepam, furosemide, mitotane, phenylbutazone, phenytoin, propranolol, large doses of salicylates, and sulphonamides.). When treating dogs that are receiving concurrent medication the properties of these drugs should be taken into consideration. An increase in the dosage of digitalis may be necessary in a patient that had previously compensated congestive heart failure and that is placed on thyroid hormone

supplementation.

Estrogens may increase thyroid requirements.

Ketamine may cause tachycardia and hypertension when used in patients receiving thyroid hormones. The effect of catecholamines and sympathicomimetics is increased by levothyroxine.

Following treatment of hypothyroidism in dogs with concurrent diabetes, careful monitoring of diabetic control is recommended.

Most dogs on chronic high- dose, daily glucocorticoid therapy will have very low or undetectable serum T₄ concentrations, as well as subnormal T₃ values.

4.9 Amounts to be administered and administration route

The recommended starting dosage of levothyroxine sodium is 10 µg/kg body weight orally every 12 hour. Because of variability in absorption and metabolism, the dosage may require alterations before a complete clinical response is observed. The initial dosage and frequency of administration are merely a starting point. Therapy has to be highly individualised and tailored to the requirements of the individual dog. When initiating dosing of dogs weighing less than 5 kg bodyweight, a quarter of one 200 µg tablet should be administered once daily.

Such cases should be monitored carefully. In the dog, absorption of levothyroxine sodium may be affected by the presence of food. The timing of treatment and its relation to feeding should therefore be kept consistent from day to day. To adequately monitor therapy, trough values (just prior to treatment) and peak values (about three hours after dosing) of plasma T₄ can be measured. In adequately dosed dogs peak plasma concentration of T₄ should be in the high-normal range (approximately 30 to 47 nmol/l) and trough values should be above approximately 19 nmol/l. If T₄ levels are outside this range the levothyroxine dose can be adjusted in 50 to 200 µg increments until the patient is clinically euthyroid and serum T₄ is within the reference range. Plasma T₄ levels can be retested two weeks after change of dosage, but clinical improvement is an equally important factor in determining individual dosage and this will take four to eight weeks. When the optimum replacement dose has been attained, clinical and biochemical monitoring may be performed every 6 – 12 months.

To break a 200 µg tablet accurately and easily, place the tablet score side up and apply pressure with your thumb.



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

Following administration of overdoses thyrotoxicosis could occur. Thyrotoxicosis as a side effect of mild oversupplementation is uncommon in dogs, owing to the canine ability to catabolize and excrete thyroid hormones. In case of accidental intake of large amounts of Forthyron tablets absorption can be decreased by induction of vomiting and oral administration of both activated charcoal and magnesium sulphate once.

Overdoses of three up to six times label recommended starting dose for 4 consecutive weeks in healthy, euthyroid dogs resulted in no significant clinical signs that could be attributed to treatment. Single overdose up to 3-6x the recommended dose does not pose a threat to the dog, and no actions are necessary. However, following chronic over-supplementation, clinical signs of hyperthyroidism such as polydipsia, polyuria, panting, weight loss without anorexia, and either or both tachycardia and nervousness may theoretically occur. The presence of these signs should result in evaluation of T_4 serum concentrations to confirm the diagnosis, and immediate discontinuance of the supplementation. Once the signs have abated (days to weeks), the thyroid dosage has been reviewed, and the animal has fully recovered, a lower dosage may be instituted, with the animal being monitored closely.

4.11. Withdrawal periods

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: synthetic thyroid hormones
ATCvet code: QH03A A 01.

5.1. Pharmacodynamic properties

Pharmacologically levothyroxine is classified as a hormonal preparation that replaces deficient endogenous hormones.

Levothyroxine T_4 is converted to triiodothyronine T_3 . T_3 acts on cellular processes via specific ligand-receptor interactions with the nucleus, the mitochondria, and the plasma membrane. Interaction of T_3 with binding sites leads to augmented transcription of DNA or modulation of RNA, thus influencing protein synthesis and enzyme action.

Thyroid hormones act on many different cellular processes. In developing animals and human beings, they are crucial determinants of normal development, especially in the central nervous system. Thyroid supplementation increases basal cellular metabolism and oxygen consumption thereby affecting the function of virtually all organ systems.

5.2. Pharmacokinetic particulars

Some dogs appeared to consistently either absorb L-thyroxine better and/or eliminate it more slowly than do other dogs. Furthermore absorption and elimination rate is influenced by daily intake of levothyroxine sodium (high absorption/low elimination in case of low intake and vice versa in case of high intake). The variability in pharmacokinetic parameters between individual dogs is considerable and, although the presence of food may affect absorption, it is considered to have a minor effect on the parameters overall. Absorption is relatively slow and incomplete: In most cases T_{max} occurs between 1 to 5 hours after oral administration, mean C_{max} varies more than 3 fold between dogs on the same doses. In adequately dosed dogs the plasma peak approaches or slightly exceeds the upper limit of normal plasma T_4 levels, and by the

end of 12 hours after oral administration, plasma T_4 usually declines to the lower half of the normal range. The rates of disappearance of T_4 from the plasma are slowed in hypothyroidism. A large part of the thyroxine is taken up by the liver. L-thyroxine is bound to plasma-proteins and plasma lipoproteins. Part of a dose of thyroxine is metabolised to the more potent triiodothyronine (T_3) by deiodination. The process of deiodination continues. These further deiodinated metabolic products (other than T_3 and T_4) do not have thyromimetic activity. Other pathways of thyroid hormone metabolism include conjugation to form soluble glucuronides and sulphates for biliary or urinary excretion as well as cleavage of the ether linkage of the iodothyronine molecule. In the dog, over 50% of the T_4 produced each day are lost in the faeces. The extrathyroidal body stores of T_4 are eliminated and replaced in about 1 day.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Calcium hydrogen phosphate dihydrate,
Cellulose, Microcrystalline,
Sodium Starch Glycolate (type A),
Magnesium stearate.

6.2. Incompatibilities

Not applicable

6.3. Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 18 months
Tablet portions can be kept for 4 days in the blister pack.

6.4. Special precautions for storage

Do not store above 25°C.

6.5. Nature and contents of immediate packaging

Blisters, consisting of aluminium foil and a white, opaque PVC/PE/PVDC foil.
10 Tablets per blister, 5, 25, or 50 blisters per carton, 50, 250 or 500 tablets per carton.
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 if appropriate.

Any unused product or waste material should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

Eurovet Animal Health B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 16849/4005

9. DATE OF FIRST AUTHORISATION

Date: 13 April 2005

10. DATE OF REVISION OF THE TEXT

Date: December 2014

APPROVED T. NASH 16/12/14