Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Kelevo 800 µg tablets for dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Levothyroxine sodium	800 µg
(equivalent to levothyroxine	778 µg)

Excipients:
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.
White to off white, round and convex tablet with brown spots and a cross-shaped break line on one side. The tablets can be divided into 2 or 4 equal parts.

4 CLINICAL PARTICULARS

4.1 Target Species

Dogs.

4.2 Indications for use, specifying the target species

Treatment of primary and secondary hypothyroidism.

4.3 Contraindications

Do not use in dogs suffering from uncorrected adrenal insufficiency.
Do not use in cases of known hypersensitivity to levothyroxine sodium or to any of the excipients.

4.4 Special warnings for each target species

The diagnosis of hypothyroidism should be confirmed with appropriate tests.

4.5 Special precautions for use

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 animals with concurrent hypoadrenocorticism have a decreased ability to metabolise levothyroxine sodium and therefore an increased risk of thyrotoxicosis. These animals 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 is recommended (starting with 25 % of the normal dose and increasing by 25% increments every fortnight until optimal stabilisation is achieved). Gradual introduction of therapy is also recommended for animals with other concurrent illnesses; particularly in animals with cardiac disease, diabetes mellitus and renal or hepatic dysfunction.

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

This product contains a high concentration of levothyroxine sodium and may be harmful when ingested, particularly for children. Pregnant women should handle this veterinary medicinal product with caution. Any unused tablet portion(s) should be returned to the open blister, inserted back into the outer packaging and stored out of the sight and reach of children and always be used at the next administration.

In the case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. Wash hands after handling the tablets.

4.6 Adverse reactions (frequency and seriousness)

Initially an exacerbation of skin symptoms can occur with increased pruritus by shedding of the old epithelial cells.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established in pregnant or lactating bitches and therefore use of the product in these animals should be based on a benefit-risk assessment by the responsible veterinarian. 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 basis from conception until several weeks after delivery.

4.8 Interaction with other medicinal products and other forms of interactions

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 animals that are receiving concurrent medication the properties of these drugs should be taken into consideration.

Oestrogens may increase thyroid requirements.

Ketamine may cause tachycardia and hypertension when used in patients receiving thyroid hormones.

The effect of catecholamines and sympathomimetics is increased by levothyroxine.

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

Most patients 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

Oral use.

The recommended starting dose for dogs is 20 µg levothyroxine sodium per kg body weight per day given as a single daily dose or in two equally divided doses.

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 animal especially for small dogs, in accordance with monitoring by the veterinarian.

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.

Information for the treating veterinarian

For small dogs, it is recommended to use the lower strength 200 µg tablet when commencing therapy and for subsequent dose adjustments given that more accurate dosing and dose titration is possible.

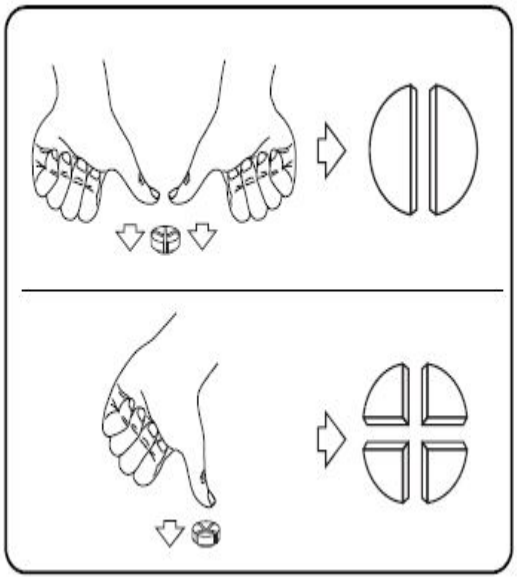
Therapeutic monitoring

The dose should be adjusted based on clinical response and plasma thyroxine levels.

To adequately monitor therapy, trough values (just prior to treatment) and peak values (about four hours after dosing) of plasma T4 can be measured. In adequately dosed animals 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 sodium 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.

Tablets can be divided into 2 or 4 equal parts to ensure accurate dosing. Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.



Halves: press down with your thumbs on both sides of the tablet.
Quarters: press down with your thumb in the middle of the tablet.

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

Following administration of overdoses thyrotoxicosis could occur. Thyrotoxicosis as a side effect of mild over-supplementation is uncommon in dogs, owing to the ability of this species to catabolise and excrete thyroid hormones. In case of accidental intake of large amounts of the veterinary medicinal product absorption can be decreased by induction of vomiting and oral administration of both activated charcoal and magnesium sulphate once.
In an acute overdose situation in dogs, the clinical signs are extensions of the hormone's physiological effects. Acute overdose of levothyroxine may produce vomiting, diarrhoea, hyperactivity, hypertension, lethargy, tachycardia, tachypnoea, dyspnoea, and abnormal pupillary light reflexes.
Following chronic over-supplementation in dogs, 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 T4 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 period(s)

Not applicable

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group:Thyroid hormones
ATCvet code:QH03AA01

5.1 Pharmacodynamic properties

Levothyroxine is a synthetic homologue of the naturally occurring thyroid hormone, thyroxine (T4). It is converted to the more biologically active triiodothyronine (T3). T3 binds via specific receptors within the plasma membrane, mitochondria and chromatin resulting in changes in DNA transcription and protein synthesis. Onset of action is therefore slow.
Levothyroxine sodium affects the metabolism of carbohydrates, proteins, fats, vitamins, nucleic acids and ions. Levothyroxine sodium stimulates the consumption of oxygen and causes an increased metabolic activity by increasing the number of mitochondria. Protein synthesis is stimulated, and the consumption of carbohydrates increases. The fat metabolism is stimulated.

5.2 Pharmacokinetic particulars

After oral intake the gastrointestinal absorption is 10 to 50 % in dogs and C_{max} is reached in 4-12 hours after administration. After administration of 20 micrograms per kg of active ingredient to
57 hypothyroid dogs, the plasma thyroxine (T4) levels increased in the majority of cases to normal values (20-46 nmol). After absorption into the circulation T4 is deiodinated to T3 in the peripheral tissues. In the dog, over 50 % of the T4 produced each day are lost in the faeces. The serum half-life in normal dogs is 10 to 16 hours. In hypothyroid dogs this takes longer.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate dihydrate
Magnesium stearate
Cellulose, microcrystalline
Croscarmellose sodium
Yeast flavour

6.2 Major incompatibilities

Not applicable

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale:2 years.

Shelf-life of the divided tablets: 4 days

6.4 Special precautions for storage

Do not store above 30°C.
Return unused tablet portion(s) to the open blister and always use at the next administration.

6.5 Nature and composition of immediate packaging

PVC / PE / PVDC - Aluminium blister each with 10 or 25 tablets.

Package sizes:
Cardboard box with 50 tablets.
Cardboard box with 100 tablets.
Cardboard box with 250 tablets.

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

LIVISTO Int'l, S.L.
Av. Universitat Autònoma, 29
08290 Cerdanyola del Vallès
Barcelona
Spain

8 MARKETING AUTHORISATION NUMBER(S)

VPA10425/018/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 June 2021

10 DATE OF REVISION OF THE TEXT

January 2022