SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Leventa 1 mg/ml Oral Solution for Dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Levothyroxine sodium (as multihydrate) 1 milligram
(equivalent to 0.97 milligram levothyroxine)

Excipients:
Ethanol 96 % 0.15 ml

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.
Clear, slight reddish coloured solution.

4. CLINICAL PARTICULARS

4.1 Target Species

Dogs.

4.2 Indications for use, specifying the target species

Treatment of hypothyroidism in dogs.

4.3 Contraindications

Do not use in dogs with hyperthyroidism or uncorrected adrenal insufficiency (hypoadrenocorticism).
Do not use in case of hypersensitivity to levothyroxine sodium or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i) Special precautions for use in animals
The product should be used with caution in dogs with cardiac disease, diabetes mellitus or treated adrenal insufficiency (hypoadrenocorticism). For these dogs, gradual introduction of levothyroxine therapy, starting with 25 % of the normal

dose and increasing by 25 % increments every two weeks until optimal stabilisation is achieved is recommended.
The clinical diagnosis of hypothyroidism should be confirmed by laboratory tests.

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

In the case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. Note: this product contains a high concentration of L-thyroxine sodium and may present a risk to humans if ingested.
Wash hands after use.
In case of eye contact, flush immediately with water.

4.6 Adverse reactions (frequency and seriousness)

Adverse reactions associated with treatment with L-thyroxine sodium are primarily those of hyperthyroidism due to therapeutic overdose. They include body weight loss, hyperactivity, tachycardia, polydipsia, polyuria, polyphagia, vomiting and diarrhoea. Transient, self-resolving skin reactions such as mild to moderate scale formation may occur.
See also section 4.10.

4.7 Use during pregnancy, lactation or lay

The safety of use in pregnant bitches has not been evaluated. However, thyroxine is essential for normal foetal development. Hypothyroidism during pregnancy may be associated with impaired cognitive development and increased foetal mortality. During pregnancy, maternal thyroid hormone requirements may increase. Pregnant bitches receiving treatment should therefore be monitored on a regular basis from conception until several weeks after delivery, as dose requirements may change during pregnancy and lactation.
Use in lactating bitches or animals intended for future breeding has not been evaluated

4.8 Interaction with other medicinal products and other forms of interaction

L-thyroxine absorption may be impaired by the concomitant administration of antacids, e.g. aluminium or magnesium salts or calcium carbonate, or ferrous sulphate, and sucralfate. Therefore, concomitant administration of Leventa with the above mentioned compounds should be avoided. At least 2 hours should elapse between administration of Leventa and such products.
The therapeutic response to Leventa may be altered by any compound that influences thyroid hormone metabolism and disposition (e.g. drugs displacing protein-binding site, modifying serum thyroxine-binding globulin concentration, or altering hepatic degradation of thyroxine or peripheral conversion of thyroxine to triiodothyronine). Thus, in case of concomitant administration of Leventa with a compound exhibiting one of these properties, it is recommended to recheck that thyroid hormone concentrations are appropriate and to adjust the dose of Leventa accordingly if needed.
Conversely, L-thyroxine supplementation may affect the pharmacokinetics and activity of concurrent therapies. In diabetic dogs treated with insulin, L-thyroxine

supplementation may alter insulin requirements. In dogs with cardiac insufficiency, therapeutic response to cardiac glycosides may be decreased by L-thyroxine supplementation. Therefore, if treated with any of these compounds, dogs should be monitored carefully during initiation of treatment with Leventa.

4.9 Amounts to be administered and administration route

For oral use only.

In thyroid hormone replacement therapy with L-thyroxine, the dose rate and regime have to be tailored individually to each dog. A starting dose rate of 20 microgram L-thyroxine sodium/kg once daily is recommended; this corresponds to 0.2 ml of the product per 10 kg bodyweight.

At re-examination four weeks later, dose adjustments should be performed based on the clinical response to treatment and thyroid hormone concentration evaluated 4-6 hours after administration of the product. Further assessment of hormonal responses and dose adjustment may be repeated at 4 week intervals if required.

A maintenance dose rate between 10 and 40 microgram/kg body weight once daily is generally sufficient to control the clinical signs of hypothyroidism and to restore thyroid hormone concentrations to within the reference range. Depending on the dose rate determined as suitable for the dog and on its body weight, the volume (in ml) of the product to be administered once daily can be estimated using the following table:

Body weight (kg)	**Dosage (microgram/kg)**			
	10	**20**	**30**	**40**
	Volume of the product (ml)			
5	0.05	0.10	0.15	0.20
10	0.10	0.20	0.30	0.40
15	0.15	0.30	0.45	0.60
20	0.20	0.40	0.60	0.80
25	0.25	0.50	0.75	1.00
30	0.30	0.60	0.90	1.20
35	0.35	0.70	1.05	1.40
40	0.40	0.80	1.20	1.60
45	0.45	0.90	1.35	1.80
50	0.50	1.00	1.50	2.00

Once a suitable dose rate and regime have been established, it is recommended to recheck every 6 months that thyroid hormone concentrations are appropriate.

The improvement in clinical signs occurs differentially following the onset of treatment with L-thyroxine: whilst metabolic signs improve within two weeks after the onset of treatment, dermatological signs may require 6 weeks or more of treatment before improvement is seen.

The product should be administered at the same time every day. The absorption of L-thyroxine is influenced by food.

In order to achieve consistent absorption of L-thyroxine, it is recommended to administer L-thyroxine 2 – 3 hours prior to feeding, which will maximise the degree of absorption and minimize variation in absorption (see also section 5.2).
If L-thyroxine is administered less than 2 hours before feeding, at or after feeding, the feed given (type and amount) should be standardized.

Instruction for use of the oral syringe:
Open the bottle. Attach the dosing syringe to the bottle by gently pushing the end of the syringe onto the insert in the bottle. Turn the bottle/syringe upside down and draw the solution into the syringe by pulling the plunger out until the edge of the ring on the end of the plunger coincides with the expected volume or body weight in kilograms. Turn the bottle/syringe right way up and remove the syringe from the insert. After administering the product, clean the syringe by flushing with clean water and allow to dry naturally.

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

Clinical signs of overdose with L-thyroxine are identical to those of hyperthyroidism and include body weight loss, hyperactivity, tachycardia, polydipsia, polyuria, polyphagia and diarrhoea. These signs are generally mild and fully reversible.
Overdose may be accompanied by reversible changes in blood biochemistry, e.g. elevated glucose, inorganic phosphorus and albumin:globulin ratio, and reduced total protein and cholesterol.
In a tolerance study, healthy dogs treated with the product at 40 µg/kg body weight once daily during 91 consecutive days did not present any relevant clinical sign. At dose rates of 120 and 200 µg/kg body weight, dogs did not exhibit signs other than those of hyperthyroidism, mainly body weight loss. These signs were mild and reversible, with recovery occurring within 5 weeks after cessation of treatment.

Standard measures should be taken to remove non-absorbed drug from the gastro-intestinal tract.
If chronic overdosage is suspected, the dose should be re-evaluated.

4.11 Withdrawal Period(s)

Not applicable.

5. PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: thyroid hormones
ATCvet code: QH03AA01.

5.1 Pharmacodynamic properties

L-thyroxine is identical in structure and mode of action to the thyroxine (T4) secreted physiologically and present in mammals with a normally functioning

thyroid gland. Thyroxine is metabolised mainly to tri-iodothyronine (T3). T4 and T3 have a large variety of biological effects throughout the body. They are essential for the regulation of basal metabolism, cardiac function and blood flow, lipid and carbohydrate metabolism. They are also essential for the normal growth and development of the neurological and skeletal systems.

5.2 Pharmacokinetic properties

There is considerable variation in the pharmacokinetics between individual dogs. After oral administration of the product to euthyroid, fasted dogs, t_{max} occurred at approximately 2.5 – 3 hours. The serum half-life of L-thyroxine was approximately 7 hours. Bioavailability was 22 %.
After repeated oral administration over 14 consecutive days at a dose rate of 40 µg/kg/day, there was no accumulation of L-thyroxine in serum. Concomitant administration of food with the product delays absorption and reduces the extent of absorption of L-thyroxine from the gastrointestinal tract by approximately 50 %. L-thyroxine is highly protein bound.

The major site of thyroxine (T4) metabolism is the liver. The main pathway for the metabolism of T4 is its conversion, by deiodination, to the active metabolite triiodothyronine (T3). Further deiodination of T4 and T3 leads to production of inactive compounds.

Excretion is mainly observed via biliary and, to a lesser extent, urinary routes.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol 96 %
Hydroxypropylbetadex
Sodium hydrogen carbonate
Sodium hydroxide
Hydrochloric acid
Purified Water

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 6 months.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Store in the original container.

6.5 Nature and composition of immediate packaging

30 ml amber glass bottle with a transparent LDPE insert and with a white HDPE child-resistant cap with tamper-proof closure in a printed carton.
A 1 ml oral syringe graduated in 0.05 ml increments is supplied with the product.

Pack sizes: 1 x 30 ml, 6 x 30 ml and 12 x 30 ml. Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

MSD Animal Health UK Limited
Walton Manor
Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

8. MARKETING AUTHORISATION NUMBER

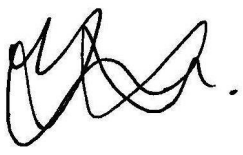
Vm 01708/4527

9. DATE OF FIRST AUTHORISATION

23 April 2007

10. DATE OF REVISION OF THE TEXT

August 2020



Approved: 14 August 2020