SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Phenoleptil 12.5 mg tablets for dogs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Phenobarbital 12.5 mg

Excipients:

Qualitative composition of excipients and other constituents
Yeast (dried)
Chicken flavour
Lactose Monohydrate
Microcrystalline Cellulose
Sodium Starch Glycolate (Type A)
Silica, Colloidal Anhydrous
Magnesium Stearate

White to off white, circular, biconvex tablet with brown speckles and a score line on one side (6 mm diameter). The tablets cannot be divided.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Prevention of seizures due to generalised epilepsy in dogs.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to other barbiturates or to any of the excipients.
Do not use in animals with serious impaired hepatic function.
Do not use in animals with serious renal or cardiovascular disorders.
Do not use in dogs weighing less than 5 kg body weight.

3.4 Special warnings

The decision to start antiepileptic drug therapy with phenobarbital should be evaluated for each individual case and depends on number, frequency, duration and severity of seizures in dogs.
General recommendations for initiating therapy include a single seizure occurring more than once every 4-6 weeks, cluster seizure activity (i.e. more than one seizure within 24 h) or status epilepticus regardless of frequency.
To achieve successful therapy, administration of tablets must be at the same time each day.
Withdrawal or transition from other types of antiepileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures.
Some of the dogs are free of epileptic seizures during the treatment, but some of the dogs show only a seizure reduction, and some of the dogs are considered to be non-responders.

3.5 Special precautions for use

Special precautions for safe use in the target species:
These tablets should not be divided. Doses for smaller dogs cannot be adjusted in accordance with the recommended 20% regime, and therefore special care should be taken in monitoring these animals. Also see “Administration routes and dosages” section 3.9.
Caution is recommended in animals with impaired hepatic and renal function, hypovolemia, anaemia and cardiac or respiratory dysfunction.
The chance of hepatotoxic side effects can be diminished or delayed using an effective dose that is as low as possible. Monitoring of hepatic parameters is recommended in case of a prolonged therapy
It is recommended to assess the clinical pathology of the patient 2-3 weeks after start of treatment and afterwards every 4-6 months, e.g. measurement of hepatic enzymes and serum bile acids. It is important to know that the effects of hypoxia etc. do cause increased levels of hepatic enzymes after a seizure.
Phenobarbital may increase the activity of serum alkaline phosphatase and transaminases. These may demonstrate non-pathological changes, but could also represent hepatotoxicity. Therefore, in the case of suspected hepatotoxicity, liver function tests are recommended. Increased liver enzyme values do not require a dose reduction of phenobarbital if the serum bile acids are in the normal range.
The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Barbiturates can cause hypersensitivity. People with known hypersensitivity to barbiturates should avoid contact with the veterinary medicinal product. Administer the veterinary medicinal product with caution. It is advisable to wear disposable gloves during administration of the veterinary medicinal product to reduce skin contact. Wash hands thoroughly after use.

Accidental ingestion may cause intoxication and could be fatal, particularly for children. Take utmost care that children do not come in contact with the product. In case of accidental ingestion, seek medical attention immediately, advising medical services of barbiturate poisoning; show the package leaflet or the label to the physician. If

possible, the physician should be informed about the time and amount of ingestion, as this information may help to ensure that appropriate treatment is given.

Phenobarbital is teratogenic and may be toxic to unborn and breastfeeding children; it may affect the developing brain and lead to cognitive disorders. Phenobarbital is excreted in breast milk. Pregnant women, women of childbearing age and women who are breastfeeding should avoid accidental ingestion and prolonged skin contact with the product.

Keep this veterinary medical product in its original packaging to avoid accidental ingestion.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Ataxia [a,d], Dizziness [a] Lethargy [a]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Sleepiness – Neurologival disorder [a], Sedation [d] Hyperexcitation [b] Polyuria [c] Polydipsia [c], Polyphagia [c] Hepatic toxicosis [e] Pancytopenia [f, g], Neutropenia [g], Low thyroxine [h]

[a] During start of the therapy. These effects are usually transitory and disappear in most, but not all, patients with continued medication.
[b] Paradoxical, particularly after first starting therapy. As this hyperexcitability is not linked to overdosage, no reduction of dosage is needed.
[c] At average or higher therapeutic active serum concentrations; these effects can be diminished by limiting intake of both food and water.
[d] Often become significant concerns as serum levels reach the higher ends of the therapeutic range.
[e] Associated with high plasma concentrations.
[f] Immunotoxic.
[g] Consequences of deleterious effects of phenobarbital on stem cells from bone marrow. These reactions disappear after the treatment's withdrawal.
[h] This may not be an indication of hypothyroidism. Treatment with thyroid hormone replacement should only be started if there are clinical signs of the disease.

If adverse effects are severe, a decrease in the administered phenobarbital dose is recommended.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
Pregnancy and lactation:
Use only according to the benefit-risk assessment by the responsible veterinarian.
Phenobarbital crosses the placental barrier and at higher doses (reversible) withdrawal symptoms in newborns cannot be excluded.
Studies in laboratory animals have shown evidence of action of phenobarbital on prenatal growth, especially concerning sexual development. Neonatal bleeding tendencies have been associated with phenobarbital treatment during pregnancy. Administration of Vitamin K to the dam for 10 days before parturition may help to minimize these effects on the foetus.
The benefits of treatment may be greater than the potential risks associated with epileptic seizures on the foetus (hypoxia and acidosis). Therefore, in case of pregnancy, termination of antiepileptic treatment is not recommended; however, the dose should be as low as possible.
Phenobarbital is excreted in small amounts in breast milk and during nursing pups should be monitored carefully for undesired sedative effects. Weaning early may be an option. If somnolence/sedative effects (that could interfere with suckling) appear in nursing newborns, an artificial suckling method should be chosen.

3.8 Interaction with other medicinal products and other forms of interaction

A therapeutic dose of phenobarbital for antiepileptic therapy can significantly induce plasma protein (such as α1acid glycoprotein, AGP), which bind drugs. Therefore special attention must be paid to the pharmacokinetics and doses of drugs simultaneously administered.
The plasmatic concentration of cyclosporine, thyroid hormones and theophylline is decreased in the case of concurrent administration of phenobarbital. The effectiveness of these substances is diminished too.
Cimetidine and ketoconazole are inhibitors of hepatic enzymes: concurrent use with phenobarbital can induce an increase of serum concentration of phenobarbital.
Concurrent use with potassium bromide increases the risk of pancreatitis.
Concurrent use with other drugs having a central depressive action like narcotic analgesics, morphinic derivates, phenothiazines, antihistamines, clomipramine and chloramphenicol can increase the effect of phenobarbital.
Phenobarbital may enhance the metabolism of, and therefore decrease the effect of, antiepileptics, chloramphenicol, corticosteroids, doxycycline, beta blockers and metronidazole.
The reliability of oral contraceptives is lower.
Phenobarbital may decrease the absorption of griseofulvin.
The following drugs can decrease the convulsive threshold: quinolones, high doses of β-lactam antibiotic, theophyllin, aminophyllin, cyclosporine and propofol for example).
Medications which may alter the seizure threshold should only be used if really necessary and when no safer alternative exists.

3.9 Administration routes and dosage

Oral use.
Amounts to be administered:

The recommended initial dosage is 2.5 mg phenobarbital per kg body weight twice daily.
Tablets must be given at the same time each day to achieve successful therapy.
Eventual adjustments of this dosage should be made on the basis of clinical efficacy, blood levels and the occurrence of undesirable side effects. Also see the “Special precautions for safe use in the target species” section 3.5).
The serum phenobarbital concentrations should be measured after steady state has been achieved. The ideal therapeutic range for serum phenobarbital concentration is between 15 and 40 µg/ml. If serum phenobarbital concentration is less than 15 µg/ml or the seizures are not controlled the dose may be increased by 20% at a time, with associated monitoring of serum phenobarbital levels up to a maximum serum concentration 45 µg/ml. The ultimate doses may vary considerably (ranging from 1 mg to 15 mg per kg body weight twice daily) because of the differences in phenobarbital excretion and differences in sensitivity among patients.
If the seizures are not being satisfactorily controlled and if the maximum level concentration is about 40µg/ml, then the diagnosis should be reconsidered and/or a second antiepileptic veterinary medicinal product (such as bromides) should be added to the treatment protocol.
In stabilised epileptic patients, it is not recommended to switch this tablet formulation for another phenobarbital formulation. However, if this cannot be avoided then additional caution should be taken. It is recommended to try to achieve as similar dosages as possible compared with the previous formulation used, taking into consideration current plasma concentration measurements. Monitoring for increased side effects and for hepatic dysfunction should be conducted more regularly until stabilisation is confirmed. Stabilisation protocols as for initiating treatments should be followed.. Withdrawal of therapy with Phenobarbital formulations should be made gradually to avoid precipitating an increase in the frequency of seizures.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Symptoms of overdose are:
- depression of the central nervous system demonstrated by signs ranging from sleep to coma,
- respiratory problems,
- cardiovascular problems, hypotension and shock leading to renal failure and death.

In case of overdose remove ingested veterinary medicinal product from the stomach, for example by lavage. Activated charcoal may be given. Offer respiratory support.

There is no specific antidote, but CNS stimulants (like Doxapram) may stimulate the respiratory centre. Give oxygen support.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QN03AA02.

4.2 Pharmacodynamics

The antiepileptic effects of phenobarbital are probably the result of at least two mechanisms, being decreased monosynaptic transmission, which presumably results in reduced neuronal excitability and an increase in the motor cortex's threshold for electrical stimulation.

4.3 Pharmacokinetics

After oral administration of phenobarbital to dogs, the drug is rapidly absorbed and Maximal plasma concentrations are reached within 4-8 hours. Bioavailability is between 86%-96%, apparent volume of distribution is 0,75 l/kg and a steady state serum concentration is reached 2-3 weeks after start of therapy.

About 45% of the plasma concentration is protein bound. Metabolism is by aromatic hydroxylation of the phenyl group in the para position (p-hydroxyphenobarbital), and about 25% of the drug is excreted unchanged in the urine. Elimination half-lives vary considerably between individuals and range from about 40-90 hours.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

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

5.3 Special precautions for storage

Keep the blister strips in the outer carton in order to protect from light.
This veterinary medicinal product does not require any special temperature storage conditions.

5.4 Nature and composition of immediate packaging

Aluminium/PVC strips with 10 tablets packed in cardboard boxes with 5, 10, 25, 50 or 100 strips.
Aluminium/PVC/PE/PVdC strips with 10 tablets packed in cardboard boxes with 5, 10, 25, 50 or 100 strips.
Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Dechra Regulatory B.V.

7. MARKETING AUTHORISATION NUMBER(S)

Vm 50406/5012
Vm 50406/3010

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 04 March 2010

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

September 2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

Gavin Hall

Approved 19 January 2025