PARTICULARS TO APPEAR ON THE OUTER PACKAGE {CARDBOARD BOX}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Phenoleptil 25 mg tablets for dogs

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Active substance:
Phenobarbital 25 mg

3. PACKAGE SIZE

100 tablets
500 tablets

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Return any divided tablets to the opened blister pack and use within 48 hours.

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30°C.
Keep the blister strips in the outer package in order to protect from light.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Dechra Regulatory B.V.
[Company logo]

14. MARKETING AUTHORISATION NUMBERS

Vm 50406/5014

Vm 50406/3012

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS {BLISTER}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Phenoleptil

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Phenobarbital - 25 mg/tablet

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PARTICULARS TO APPEAR ON THE PACKAGE LEAFLET:

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Phenoleptil 25 mg tablets for dogs

2. Composition

Each tablet contains:

Active substance:
Phenobarbital 25 mg

White to off white, circular, convex tablet with brown speckles and a crossed score line on one side (8 mm diameter). The tablets can be divided into two or four equal parts.

3. Target species

Dogs.

4. Indications for use

Prevention of seizures due to generalised epilepsy in dogs.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or any 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 2.5 kg body weight.

6. Special warnings

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.

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.

Special precautions for safe use in the target species:
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.
Caution is recommended in animals with impaired renal function, hypovolemia, anaemia and cardiac or respiratory dysfunction.
Before beginning the treatment monitoring of hepatic parameters should be performed.
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 can 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, so liver function tests are recommended. Increased liver enzyme values may not always require a dose reduction of phenobarbital if the serum bile acids are in the normal range.

In the light of isolated reports describing hepatotoxicity associated with combination anticonvulsant therapy, it is recommended that:
1. Hepatic function is evaluated prior to initiation of therapy (e.g. measurement of serum bile acids).
2. Therapeutic phenobarbital serum concentrations are monitored to enable the lowest effective dose to be used. Typically concentrations of 15-45µg/ml are effective in controlling epilepsy.
3. Hepatic function is re-evaluated on a regular (6 to 12 months) basis.
4. Seizure activity is re-evaluated on a regular basis.

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 medicinal product in its original packaging to avoid accidental ingestion. Each time an unused part-tablet is stored until next use, it should be returned to the open blister space and inserted back into the cardboard box.

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

Other precautions:
Not applicable.

Pregnancy:
The safety of the veterinary medicinal product has not been established during pregnancy.
Use only according to the benefit-risk assessment by the responsible veterinarian.

Studies in laboratory animals have indicated that phenobarbital has an effect during prenatal growth, in particular causing permanent changes in neurological and sexual development. Neonatal bleeding tendencies have been associated with phenobarbital treatment during pregnancy.
Maternal epilepsy may be an additional risk factor for impaired foetal development. Therefore pregnancy should be avoided in epileptic dogs whenever possible. In case of pregnancy, the risk that the medication may cause an increase in the number of congenital defects must be weighed up against the risk of suspending treatment during pregnancy. Discontinuation of treatment is not advised, but the dosage should be kept as low as possible.
Phenobarbital crosses the placenta and, at high doses, (reversible) withdrawal symptoms cannot be ruled out in new-borns.

Lactation:
The safety of the veterinary medicinal product has not been established during lactation.
Use only according to the benefit-risk assessment by the responsible veterinarian.

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 new-borns, an artificial suckling method should be chosen.

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.
Use of phenobarbital tablets in conjunction with primidone is not recommended as primidone is predominantly metabolized to phenobarbital.

Overdose:
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 and give respiratory and cardiovascular support as necessary.

The prime objectives of management are then intensive symptomatic and supportive therapy with particular attention being paid to the maintenance of cardiovascular, respiratory and renal functions and to the maintenance of the electrolyte balance.

There is no specific antidote, but CNS stimulants (like doxapram) may stimulate the respiratory centre.

Special restrictions for use and special conditions for use:
Not applicable.

Major incompatibilities:
Not applicable.

7. Adverse events

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Ataxia (incoordination) [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 (increased urination) [c] Polydipsia (increased thirst) [c], Polyphagia

	(increased appetite) [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.

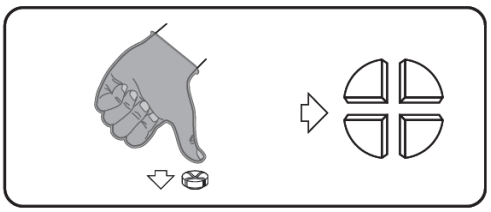
Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system at:
Website: https://www.gov.uk/report-veterinary-medicine-problem/animal-reacts-medicine
e-mail: adverse.events@vmd.gov.uk

8. Dosage for each species, routes and method of administration

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. The required dosage will differ to some extent between individuals and with the nature and severity of the disorder. See also the "Special warnings" section.

9. Advice on correct administration

The crossed score line on one side of the tablet allows division into two (each part of 12.5 mg phenobarbital) or four (each part of 6.25 mg phenobarbital) equal parts.



- Place the tablet with the round side down on a flat surface
- Break the tablet into four equal parts by pressing on the top
with your thumb or finger

The serum phenobarbital concentrations should be measured after steady state has been achieved. Blood samples could be taken at the same time to allow plasma phenobarbital concentration to be determined preferably during trough levels, shortly before the next dose of phenobarbital is due. 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.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 30°C.
Keep the blister strips in the outer package in order to protect from light.
Do not use the veterinary medicinal product after the expiry date stated on the blister and carton after EXP. The expiry date refers to the last day of that month.
Return any divided tablets to the opened blister pack and use within 48 hours.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Vm 50406/5014
Vm 50406/3012

100 tablets in a cardboard carton containing 10 aluminium/PVC blister strips each strip with 10 tablets.
100 tablets in a cardboard carton containing 10 aluminium/PVC/PE/PVdC blister strips each strip with 10 tablets.
500 tablets in a cardboard carton containing 50 aluminium/PVC blister strips each strip with 10 tablets.
500 tablets in a cardboard carton containing 50 aluminium/PVC/PE/PVdC blister strips each strip with 10 tablets.
Not all pack sizes may be marketed.

15. PID LINK (Do not print heading)

[The following statement must be included where reference to the European Union Product Database is included on the product information. This statement is relevant to both UK(GB) and UK(NI) products:]

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

16. Contact details

Marketing authorisation holder:
Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

[Company logo]

Manufacturer responsible for batch release:
LelyPharma B.V.
Zuiveringsweg 42
8243 PZ Lelystad
The Netherlands

Genera d.d.
Svetonedeljska cesta 2, Kalinovica
10436 Rakov Potok
Croatia

Only the site testing and releasing the batches will be mentioned on the printed leaflet.

Local representatives and contact details to report suspected adverse reactions:
Dechra Veterinary Products Limited
Sansaw Business Park
Hadnall
Shrewsbury
Shropshire
SY4 4AS
United Kingdom
Tel: +44 (0)1939 211200

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information

POM-V

Gavin Hall

Approved 19 January 2025