SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PHENOLEPTIL 50 mg tablets for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 320 mg tablet contains:

Active substances:
Phenobarbital 50 mg

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

3. PHARMACEUTICAL FORM

Tablet.
White to off white, circular, biconvex tablets with brown speckles and a score line on one side (9 mm diameter). The tablet can be divided into two equal parts.

4. CLINICAL PARTICULARS

4.1 Target species

Dog

4.2 Indications for use, specifying the target species

Prevention of seizures due to generalised epilepsy in dogs.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to other barbiturates.
Do not use in animals with serious impaired hepatic function.
Do not use in animals with serious renal or cardiovascular disorders.

4.4 Special warnings for each target species

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.

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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.

4.5 Special precautions for use

Special precautions for use in animals

Caution is recommended in animals with impaired hepatic and renal function, hypovolemia, anemia 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.
In stabilised epileptic patients, it is not recommended to switch from other phenobarbital formulations to Phenoleptil 12.5 mg or 50 mg Tablets. However, if this can not be avoided then additional caution should be taken. This includes more frequent plasma concentration sampling to ensure that therapeutic levels are maintained. Monitoring for increased side effects and for hepatic dysfunction should be conducted more regularly until stabilisation is confirmed.
Withdrawal of therapy with Phenobarbital formulations should be made gradually to avoid precipitating an increase in the frequency of seizures.

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

People with known hypersensitivity to barbiturates should avoid contact with the veterinary medicinal product. Wash hands after use.
Take utmost care that children do not come into contact with the product. Children are particularly at risk of intoxication which may prove fatal.
In case of accidental ingestion, seek medical advice immediately and 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.

4.6 Adverse reactions (frequency and seriousness)

During start of therapy ataxia, sleepiness, slackness and dizziness can occur but these effects are usually transitory and disappear in most, but not all, patients with continued medication.
Some animals can demonstrate a paradoxical hyperexcitability, particularly after first starting therapy.

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As this hyperexcitability is not linked to overdosage, no reduction of dosage is needed.
Polyuria, polydipsia and polyphagia can occur at average or higher therapeutic active serum concentrations; these effects can be diminished by limiting intake of both food and water.
Sedation and ataxia often become significant concerns as serum levels reach the higher ends of the therapeutic range.
High plasma concentrations may be associated with hepatotoxicity.
Phenobarbital can have deleterious effects on stem cells from bone marrow. Consequences are immunotoxic pancytopenia and/or neutropenia. These reactions disappear after the treatment's withdrawal.
Treating dogs with phenobarbital may lower their TT4 or FT4 serum levels, however 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, the decrease in the administered dose is recommended.

4.7 Use during pregnancy, lactation or lay

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 fetus.
The safety of the veterinary medicinal product has not been established during pregnancy of dogs. The benefits of treatment may be greater than the potential risks associated with epileptic seizures on the fetus (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.
Use during pregnancy and lactation only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 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.

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Concurrent use with other drugs having a central depressive action like narcotic analgesics, morphinic derivates, phenothiazines, antihistamines, clomipramine and chloramphenicol can decrease 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.

4.9 Amounts to be administered and administration route

Administration route
Oral.
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 under section 4.5i).
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 product (such as bromides) should be added to the treatment protocol.
In stabilised epileptic patients, it is not recommended to switch from other phenobarbital formulations to Phenoleptil 12.5 mg or 50 mg Tablets. However, if this can not 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. Stabilisation protocols as for initiating treatments should be followed. Also see section 4.5i).
For accuracy of dosing, dogs under 10 kg should commence therapy with Phenoleptil 12.5 mg Tablet.

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

Symptoms of overdose are:
- depression of the central nervous system demonstrated by signs ranging from sleep to coma,
- respiratory problems,

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- cardiovascular problems, hypotension and shock leading to renal failure and death.

In case of overdose remove ingested 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.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antiepileptics/barbiturates and derivates.
ATCvet code: QN03AA02

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

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.

Environmental properties
None

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Yeast (dried)
Chicken flavour
Lactose Monohydrate
Microcrystalline Cellulose
Sodium Starch Glycolate (Type A)
Silica, Colloidal Anhydrous
Magnesium Stearate

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6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Any divided tablet portions remaining after 24 hours should be discarded.

6.4. Special precautions for storage

Keep the container in the outer carton in order to protect from light.
This veterinary medicinal product does not require any special temperature storage conditions
Divided tablets should be stored in the blister pack.

6.5 Nature and composition of immediate packaging

Aluminum/PVC strips with 10 tablets packed in cardboard boxes with 5, 10, 25, 50 or 100 strips.
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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

Vm 19994/4006

9. DATE OF FIRST AUTHORISATION

04 March 2010

10. DATE OF REVISION OF THE TEXT

January 2018

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PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

Approved 17 January 2018

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