1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl 60mg Flavoured Tablets for Dogs (AT, BE, BG, CY, CZ, DK, DE, IE, IT, NL, PT, SI, SK, ES & UK(NI))
Epityl vet 60mg Tablets for Dogs (SE and FI)
Epityl 60mg Tablets for Dogs (FR and PL)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Phenobarbital 60 mg

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate
Microcrystalline cellulose
Magnesium stearate
Maize starch
Talc
Grilled meat flavour

White, circular tablet with cross breakline on one side.
The tablets can be divided into two or four equal parts.

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 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 6 kg body weight.
Do not use in case of hypersensitivity to the active substance or to any other barbiturates or to any of the excipients.

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.
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:
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, 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 stabilised epileptic patients, it is not recommended to switch between phenobarbital formulations. However, if this cannot 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 or transition from other types of anti-epileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures.

The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the 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 product.
- 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.
- 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 product in its original packaging to avoid accidental ingestion.
- It is advisable to wear disposable gloves during administration of the product to reduce skin contact.
- 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.
- 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.
- Wash hands thoroughly after use.

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

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Ataxia and sedation[1] Paradoxical hyperexcitability[2] Polyuria, polydipsia and polyphagia [3] Hepatotoxicity[4] Pancytopenia and/or neutropenia[5] Low free thyroxine (FT4) or low thyroxine (T4)[6]

[1]: During start of therapy these effects can occur but are usually transitory and disappear in most, but not all, patients with continued medication. Sedation and ataxia often become significant concerns as serum levels reach the higher ends of the therapeutic range.
[2]: Some animals can demonstrate a paradoxical hyperexcitability, particularly after first starting therapy. As this hyperexcitability is not linked to overdosage, no reduction of dosage is needed.
[3]: These effects can occur at average or higher therapeutic active serum concentrations; these effects can be diminished by limiting intake of food.
[4]: High plasma concentrations may be associated with hepatotoxicity.
[5]: 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.
[6]: 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.

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 also the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
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 minimise these effects on the foetus.
The safety of the 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 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.
Use during pregnancy and lactation only according to the benefit/risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

A therapeutic dose of phenobarbital for antiepileptic therapy can significantly induce plasma proteins, (such as α1acid glycoprotein, AGP), which bind drugs. Phenobarbital may reduce the activity of some drugs by increasing the rate of metabolism through induction of drug-metabolising enzymes in liver microsomes. Therefore, special attention must be paid to the pharmacokinetics and doses of drugs

simultaneously administered. The plasmatic concentration of a range of drugs (for example cyclosporine, thyroid hormones and theophylline) is decreased in the case of concurrent administration of phenobarbital. Concurrent use with other drugs having a central depressive action (like narcotic analgesics, morphinic derivatives, phenothiazines, antihistamines, clomipramine and chloramphenicol) can increase the effect of phenobarbital.
Cimetidine and ketoconazole are inhibitors of hepatic enzymes: concurrent use with phenobarbital can induce an increase of serum concentration of phenobarbital. Phenobarbital may decrease the absorption of griseofulvin. Concurrent use with potassium bromide increases the risk of pancreatitis. Use of phenobarbital tablets in conjunction with primidone is not recommended as primidone is predominantly metabolised to phenobarbital.
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

For oral use. The required dosage will differ to some extent between individuals and with the nature and severity of the disorder.

Tablets must be given at the same time each day and should be co-ordinated with feeding times in a consistent manner to optimise treatment success.
Dogs should be dosed orally, starting with a dose of 2-5 mg per kg bodyweight per day. The dose should be divided and administered twice daily.

Steady-state serum concentrations are not reached until 1-2 weeks after treatment is initiated. The full effect of the medication does not appear for two weeks and doses should not be increased during this time.

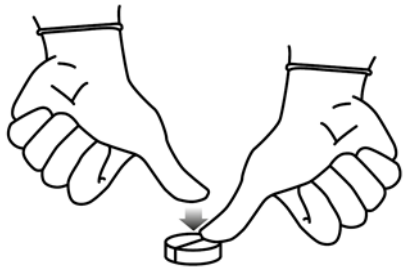
If seizures are not being controlled, the dosage may be increased by 20% at a time, with associated monitoring of serum phenobarbital levels. The phenobarbital serum concentration may be checked after steady-state has been achieved, and if it is less than 15 µg/ml the dose may be adjusted accordingly. If seizures recur the dose may be raised up to a maximum serum concentration of 45 µg/ml. High plasma concentrations may be associated with hepatotoxicity. 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.
Plasma concentrations should be interpreted in conjunction with the observed response to therapy and a full clinical assessment including monitoring for evidence of toxic effects in each animal.

Clinical data suggests that considerable variation in plasma concentrations of phenobarbital may be observed in some animals. This variation may result in an animal with a trough plasma concentration of phenobarbital below the typical minimum therapeutic level (15 µg/ml) and a peak plasma concentration approaching the maximum level (45 µg/ml). If the seizure control is inadequate in such animals, care should be taken when increasing the dose as toxic levels may be reached or exceeded. Peak and trough plasma concentrations of phenobarbital may need to be measured in such animals. (Peak plasma concentrations are reached within approximately 3 hours after administration).

If the seizures are not being satisfactorily controlled and if the maximum plasma concentration of phenobarbital is about 40 µg/ml, then the diagnosis should be reconsidered and/or a second antiepileptic product (such as bromides) should be added to the treatment protocol.

Tablets can be divided into equal halves or quarters to ensure accurate dosing.
To break a cross scored tablet into quarters, place the tablet on an even surface with the scored side up and apply pressure on the middle with your thumb.

To break a tablet into two halves, place the tablet on an even surface with the scored side up, hold one half of the tablet and press down on the other half.



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 product from the stomach, for example by lavage. Activated charcoal may be given. Offer respiratory and cardiovascular support as necessary.

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

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: 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 3 hours. Bioavailability is between 86%-96%. About 45% of the plasma concentration is protein bound. Metabolism is by aromatic hydroxylation of the phenyl group in the para position, and about one third of the drug is excreted unchanged in the urine. Elimination half-lives vary considerably between individuals and range from about 40-90 hours. Steady-state serum concentrations are not reached until 1-2 weeks after treatment is initiated.

After oral administration of the product to 16 beagle dogs twice daily, at 12 hours intervals, for 14 days, at a dose rate of 0.5 tablet per dog, which equated to 4-5 mg/kg bodyweight, maximum plasma concentrations reached within 3 hours varied from 32.30 to 47.64 µg/ml and minimum plasma concentrations varied from 12.94 to 21.05 µg/ml.

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
Shelf life of divided tablets:	2 days

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Keep the blisters in the outer carton.
Shelf life of divided tablets: 2 days.
Store divided tablets in the original package.

5.4 Nature and composition of immediate packaging

Blister strips (PVC/Aluminium) containing 10 tablets in cartons of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 500 and 1000 tablets.
White HDPE containers with a polypropylene child resistant cap containing 100 or 500 tablets.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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

Chanelle Pharmaceuticals Manufacturing Ltd

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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

24/06/2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database. (https://medicines.health.europa.eu/veterinary).

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{Carton}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl 60mg Flavoured Tablets (AT, BE, BG, CY, CZ, DK, DE, IE, IT, NL, PT, SI, SK, ES & UK(NI))
Epityl vet 60mg Tablets (SE and FI)
Epityl 60mg Tablets (FR and PL)

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Phenobarbital 60 mg

3. PACKAGE SIZE

For blisters:
10 tablets
20 tablets
30 tablets
40 tablets
50 tablets
60 tablets
70 tablets
80 tablets
90 tablets
100 tablets
500 tablets
1000 tablets

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Shelf life of divided tablets: 2 days
Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Divided tablets should be stored in the original pack. Keep the blister in the outer carton.

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 REACH AND SIGHT OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{Label}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl 60mg Flavoured Tablets (AT, BE, BG, CY, CZ, DK, DE, IE, IT, NL, PT, SI, SK, ES & UK(NI))
Epityl vet 60mg Tablets (SE and FI)
Epityl 60mg Tablets (FR and PL)

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:
Phenobarbital 60mg

3. TARGET SPECIES

Dogs

4. ROUTES OF ADMINISTRATION

Oral use

5. WITHDRAWAL PERIODS

6. EXPIRY DATE

Shelf life of divided tablets: 2 days

Exp {mm/yyyy}

7. SPECIAL STORAGE PRECAUTIONS

Divided tablets should be stored in the original pack.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

{Blisters}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Phenobarbital 60 mg/tablet

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Epityl 60mg Tablets for Dogs

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epityl 60mg Flavoured Tablets for Dogs (AT, BE, BG, CY, CZ, DK, DE, IE, IT, NL, PT, SI, SK, ES & UK(NI))
Epityl vet 60mg Tablets for Dogs (SE and FI)
Epityl 60mg Tablets for Dogs (FR and PL)

2. Composition

Each tablet contains:
Active substance:
Phenobarbital 60 mg

White, circular tablet with cross breakline on one side.
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 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 6 kg body weight.
Do not use in case of hypersensitivity to the active substance or to any other barbiturates or to any of the excipients.

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. 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:
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, 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 between phenobarbital formulations. However, if this cannot 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 or transition from other types of anti-epileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures.

The tablets are flavoured. In order to avoid any accidental ingestion, store tablets out of reach of the 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 product.
- 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.
- 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 product in its original packaging to avoid accidental ingestion.
- It is advisable to wear disposable gloves during administration of the product to reduce skin contact.
- 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.
- 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.
- Wash hands thoroughly after use.

Pregnancy and lactation:
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 minimise these effects on the foetus.
The safety of the 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 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.
Use during pregnancy and lactation only according to the benefit/risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Phenobarbital will potentially reduce therapeutic levels of a wide range of drugs due to its inducing effect on hepatic enzymes.

A therapeutic dose of phenobarbital for antiepileptic therapy can significantly induce plasma proteins, (such as α1acid glycoprotein, AGP), which bind drugs. Phenobarbital may reduce the activity of some drugs by increasing the rate of metabolism through induction of drug-metabolising enzymes in liver microsomes. Therefore, special attention must be paid to the pharmacokinetics and doses of drugs simultaneously administered. The plasmatic concentration of a range of drugs is decreased in the case of concurrent administration of phenobarbital.
Cimetidine and ketoconazole are inhibitors of hepatic enzymes: concurrent use with phenobarbital can induce an increase of serum concentration of phenobarbital. Phenobarbital may decrease the absorption of griseofulvin.
Concurrent use with potassium bromide increases the risk of pancreatitis.
Concurrent use with other drugs having a central depressive action can increase the effect of phenobarbital.
Use of phenobarbital tablets in conjunction with primidone is not recommended as primidone is predominantly metabolised to phenobarbital.

Overdose:
Toxicity may develop at doses over 20 mg/kg/day or when serum phenobarbital levels rise above 45 microgram/ml.

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 product from the stomach, for example by lavage. Activated charcoal may be given. Offer respiratory and cardiovascular support as necessary.

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

Major Incompatibilities
Not applicable.

7. Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Ataxia (incoordination) and sedation[1] Paradoxical hyperexcitability (unusually excitable)[2] Polyuria (increased urination), polydipsia (increased thirst) and polyphagia (increased appetite)[3] Hepatotoxicity[4] Pancytopenia and/or neutropenia[5] Low free thyroxine (FT4) or low thyroxine (T4)[6]

[1]: During start of therapy these effects can occur but are usually transitory and disappear in most, but not all, patients with continued medication. Sedation and ataxia often become significant concerns as serum levels reach the higher ends of the therapeutic range.
[2]: Some animals can demonstrate a paradoxical hyperexcitability, particularly after first starting therapy. As this hyperexcitability is not linked to overdosage, no reduction of dosage is needed.
[3]: These effects can occur at average or higher therapeutic active serum concentrations; these effects can be diminished by limiting intake of food.

[4]: High plasma concentrations may be associated with hepatotoxicity.
[5]: 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.
[6]: 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.

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.

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

For oral use.
The required dosage will differ to some extent between individuals and with the nature and severity of the disorder.

Tablets must be given at the same time each day and should be co-ordinated with feeding times in a consistent manner to optimise treatment success.

Dogs should be dosed orally, starting with a dose of 2-5 mg per kg bodyweight per day. The dose should be divided and administered twice daily.

Steady-state serum concentrations are not reached until 1-2 weeks after treatment is initiated. The full effect of the medication does not appear for two weeks and doses should not be increased during this time.

If seizures are not being controlled, the dosage may be increased by 20% at a time, with associated monitoring of serum phenobarbital levels. The phenobarbital serum concentration may be checked after steady-state has been achieved, and if it is less than 15 µg/ml the dose may be adjusted accordingly. If seizures recur the dose may be raised up to a maximum serum concentration of 45 µg/ml. High plasma concentrations may be associated with hepatotoxicity. 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.

Plasma concentrations should be interpreted in conjunction with the observed response to therapy and a full clinical assessment including monitoring for evidence of toxic effects in each animal.

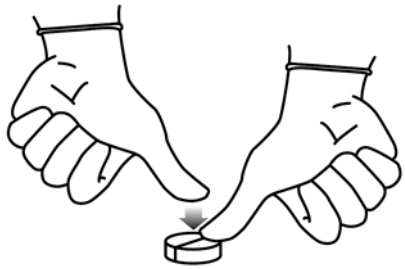
Clinical data suggests that considerable variation in plasma concentrations of phenobarbital may be observed in some animals. This variation may result in an animal with a trough plasma concentration of phenobarbital below the typical minimum therapeutic level and a peak plasma concentration approaching the maximum level. If the seizure control is inadequate in such animals, care should be taken when increasing the dose as toxic levels may be reached or exceeded. Peak and trough plasma concentrations of phenobarbital may need to be measured in such animals. (Peak plasma concentrations are reached within approximately 3 hours after administration).

If the seizures are not being satisfactorily controlled and if the maximum plasma concentration of phenobarbital is about 40 µg/ml, then the diagnosis should be reconsidered and/or a second antiepileptic product (such as bromides) should be added to the treatment protocol.

Tablets can be divided into equal halves or quarters to ensure accurate dosing.

To break a cross scored tablet into quarters, place the tablet on an even surface with the scored side up and apply pressure on the middle with your thumb.

To break a tablet into two halves, place the tablet on an even surface with the scored side up, hold one half of the tablet and press down on the other half.



9. Advice on correct administration

Steady-state serum concentrations are not reached until 1–2 weeks after treatment is initiated. The full effect of the medication does not appear for two weeks and doses should not be increased during this time.
If seizures are not being controlled the dosage may be increased by 20% at a time with associated monitoring of serum phenobarbital levels. The phenobarbital serum concentration may be checked after steady-state has been achieved and if it is less than 15 microgram/ml the dose may be adjusted accordingly. If seizures recur the dose may be raised up to a maximum concentration of 45 microgram/ml.
High plasma concentrations may be associated with hepatotoxicity. Blood samples should be taken at the same time to allow plasma phenobarbital concentrations to be determined preferably during trough levels shortly before the next dose of phenobarbital is due.
Withdrawal or transition from other types of anti-epileptic therapy 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.
This veterinary medicinal product does not require any special storage conditions.
Shelf-life of divided tablets: 2 days. Divided tablets should be stored in the original pack. Any divided tablet portions remaining after 2 days should be discarded. Keep the blister in the outer carton.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater.

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

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.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Blister strips (PVC/Aluminium) containing 10 tablets in cartons of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 500 and 1000 tablets.
White HDPE containers with a polypropylene child resistant cap containing 100 or 500 tablets.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

24/06/2024

Detailed information on this veterinary medicinal product is available in the Union Product Database. (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing Authorisation holder and Manufacturer responsible for batch release and contact details to report suspected adverse reactions:
Chanelle Pharmaceuticals Manufacturing Ltd
Loughrea
Co. Galway
Ireland
Telephone: +353 (0)91 841788
vetpharmacoviggroup@chanellegroup.ie

Local representatives and contact details to report suspected adverse reactions:

17. Other information