SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Epilease 250 mg Capsules for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient	mg per capsule
Potassium Bromide	250
Excipients	
Capsule Body	
Gelatine	35.72
Titanium dioxide	0.73
FD&C red 3 (E127)	0.08
Quinoline yellow (E104)	0.07
Capsule Cap	
Gelatine	24.13
Titanium dioxide	0.24
FD&C blue 2 (E132)	0.03

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Capsule, hard
Orange and blue coloured hard gelatine capsule

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

This product is indicated for use as an anti-epileptic therapy adjunct to phenobarbital in refractory cases of epilepsy in dogs.

4.3 Contraindications

Do not use in cases of known hypersensitivity to bromide, or to any of the excipients.

4.4 Special warnings for each target species

The concentration of bromide in serum, the clinical response and the therapeutic effect of administration of the product vary between individuals (see section 4.9)

A high chloride intake can increase the elimination of bromide (see section 4.8). Therefore, whilst it is not necessary for dogs receiving this product to be on a low salt diet, an increase in the dog's salt intake may require an adjustment in bromide dose. The salt content of a dog's diet during the treatment period should not be altered drastically, and should be maintained at a stable level. It is advisable not to change the dog's diet during therapy.

4.5 Special precautions for use

i) Special precautions for use in animals

Do not abruptly discontinue therapy as this may precipitate seizures.

This product should be used with caution in dogs with renal insufficiency (see section 4.6 and 4.10).

A reduction in chloride intake could cause bromide intoxication (see section 4.8 and 4.10).

Dogs weighing less than 16.67 kg cannot be accurately dosed with the recommended initial dose rate of 15 mg/kg twice daily as the minimum dose achievable is 500 mg per day as two 250 mg capsules, see section 4.9.

Close monitoring for adverse reactions is advisable at higher serum bromide concentrations.

ii) Special precautions for the person administering the veterinary medicinal product to animals

- Do not break capsules.
- Do not use this product if you have known sensitivity to bromide.
- Discontinue handling this product if you develop any signs of skin irritation, including itchiness, rash, peeling or flaking of skin or redness. Seek medical attention if irritation persists, showing the physician the carton or package leaflet.
- If this product is ingested, seek medical attention immediately and show the physician the carton or package leaflet.
- Wash hands thoroughly immediately after handling and/or administering the product.
- Advice to doctor: Bromide intoxication can be treated by administration of sodium chloride or a suitable chloruretic agent.

iii) Other precautions

None.

4.6 Adverse reactions (frequency and seriousness)

The most common adverse reactions are somnolence, ataxia (hind end weakness and loss of coordination), polyuria, polydipsia, nausea which may be accompanied by vomiting, pancreatitis and erythematous dermatitis (bromide rash).

Less common adverse reactions are behavioural changes such as irritability or restlessness.

Side effects may appear in dogs on higher doses of therapy, and symptoms usually disappear after the dose is decreased. If the dog appears too sedated, assess the serum concentrations of both bromide and phenobarbital to determine whether the dose of either should be reduced.
If potassium bromide dose is reduced, serum bromide concentrations should be monitored in order to ensure that they fall within the therapeutic range.

4.7 Use during pregnancy, lactation or lay

Bromide transfer to the offspring occurs when administered in high amounts to dam rats in early pregnancy, with detrimental effects on the offspring. In the absence of studies to demonstrate the safety of bromide in pregnant and lactating bitches when used at the recommended doses, the product should not be used in these animals.

4.8 Interaction with other medicinal products and other forms of interaction

Bromide and chloride compete for reabsorption by the kidneys. Increasing dietary chloride (salt) intake will decrease reabsorption of bromide by the kidneys, causing decreased serum bromide concentrations, which could lead to seizures. Conversely, changing to a diet low in chloride will cause bromide levels to increase, which could cause bromide intoxication (see section 4.5 i and 4.10).

Loop diuretics (e.g. furosemide) can increase bromide excretion and can lower the level of bromide in the blood.

Administration of fluids or drug formulations containing chloride can lower serum bromide concentrations.

Bromide is synergistic with other GABA-ergic drugs such as phenobarbital.

4.9 Amount(s) to be administered and administration route

For oral use. Administer with food.
The dose should be titrated to the individual dog as the required dosage and serum bromide concentration will vary between individual animals

Administer with food at an initial dose of 15 mg/kg bodyweight twice daily (equivalent to a total daily dose of 30 mg/kg). Twice daily administration is advised in order to reduce the risk of gastrointestinal disturbances. Due to the 24 day half-life of bromide, it can take several weeks or months to achieve steady-state serum concentrations.

At the beginning of treatment, serum bromide levels should be checked regularly, e.g. at 4, 8 and 12 weeks after the first dose. The expected therapeutic serum bromide concentration (when used in conjunction with phenobarbital) is 800 to 2000 µg/ml. Adjustments to the dose should be made with regard to the frequency of seizures, the half-life of bromide and the serum bromide concentration.

Long term monitoring of serum bromide (and associated phenobarbital) concentrations should be performed as clinically justified by the individual case.

Use in dogs with a bodyweight of less than 16.67 kg should be subject to a risk/benefit assessment, see section 4.5.

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

Bromide toxicity is uncommon. It can occur in dogs with renal insufficiency or those that are on a very high dose of bromide (see sections 4.5 i and 4.9). However, an overdose of this product can produce brominism, characterised by ataxia, somnolence, nausea and pancreatitis (i.e. symptoms similar to those listed under section 4.6).

If overdose is suspected, the dosage of the product should be reduced immediately, with close monitoring of bromide serum concentrations in order to establish an appropriate therapeutic level.

In cases of overdose, if necessary and appropriate, 0.9% sodium chloride may be used intravenously to reduce serum bromide concentrations.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:

Psycholeptics: other hypnotics and sedatives: bromides.

ATC Vet Code:

QN05CM11.

5.1 Pharmacodynamic properties

Potassium bromide is a halide anticonvulsant. Bromide replaces chloride in all t competes with chloride transport across nerve cell membranes

and inhibits sodium transport and so causes membrane hyperpolarisation. This hyperpolarisation raises the seizure threshold and prevents the spread of epileptic discharges. Bromide has effects on active transport across ganglial cell membranes and affects passive movements of ions by competition with chloride for anion channels in post-synaptic membranes that are activated by inhibitory neurotransmitters. This potentiates the effect of GABA which results in a synergistic activity of bromide with other drugs that have GABA-ergic activity, such as phenobarbital.

5.2 Pharmacokinetic particulars

The pharmacokinetics of potassium bromide has been studied in dogs. The half-life is approximately 24 days, but can vary with dietary chloride content. Due to this extremely long half-life, it can take several weeks / months to achieve steady state serum concentrations. Potassium bromide is well absorbed orally with peak absorption in about 1.5 hours. Once ingested, the potassium bromide salt dissociates, and the bromide ion is rapidly absorbed by the gastrointestinal tract.

After absorption, the bromide ion rapidly distributes, as does chloride, throughout the extra-cellular space and into cells. Chloride is distributed passively across most cell membranes according to the trans-membrane potential, and it is likely that bromide distributes in the same manner. As the bromide level is increased in the body, the concentration of chloride is decreased in direct proportion to the increase in bromide.

Bromide is not metabolised by the body, it enters and leaves the body only as the monovalent anion. Bromide is eliminated from the body by the kidneys. Bromide is not cleared by the liver, so may be used in dogs with hepatic compromise.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Brown rice flour
Magnesium stearate
Capsule Body
Gelatine
Titanium dioxide
FD&C Red 3 (E127)
Quinoline Yellow (E104)

Capsule Cap
Gelatine
Titanium dioxide
FD&C Blue 2 (E132)

6.2 Incompatibilities

None known.

6.3 Shelf life

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

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and composition of immediate packaging

Triplex PVC with foil.
Blister packs containing 30 capsules on each blister strip.
Two blister strips to a carton, giving a pack size of 60 capsules.

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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

VetPlus Ltd
Docklands
Dock Road
Lytham
Lancashire
FY8 5AQ

8. MARKETING AUTHORISATION NUMBER

Vm 18182/4002

9. DATE OF FIRST AUTHORISATION

27 May 2016

10. DATE OF REVISION OF THE TEXT

June 2016

29 June 2016