ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE

{NATURE/TYPE} CARTON AND LABEL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Euthoxin 500 mg/ml solution for injection

pentobarbital sodium

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains pentobarbital 455.7 mg
(equivalent to 500 mg pentobarbital sodium)

3. PHARMACEUTICAL FORM

Solution for Injection

4. PACKAGE SIZE

100ml

5. TARGET SPECIES

Dogs, cats, minks, polecats, hares, rabbits, guinea pigs, hamsters, rats, mice, chickens, pigeons, ornamental birds, small snakes, tortoises, lizards, frogs, horses, cattle, pigs.

6. INDICATION(S)

Euthanasia

7. METHOD AND ROUTE(S) OF ADMINISTRATION

lintravenous use
Intracardiac use
Intrapulmonary use
Intraperitoneal use
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal Period:
Do not use in animals intended for human or animal consumption.

Adequate measures should be taken to ensure that carcasses of animals treated with this product and the by-products of these animals do not enter the food chain and are not used for human or animal consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
For full user warnings, see package leaflet

10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the immediate packaging: 28 days
Once broached use by……

11. SPECIAL STORAGE CONDITIONS

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read package leaflet.

Text will be printed only on the carton.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

Text will be printed only on the carton.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Chanelle Pharmaceuticals Manufacturing Ltd.
Loughrea
Co Galway
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

Vm 08749/4055

17. MANUFACTURER'S BATCH NUMBER

Batch number

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Euthoxin 500 mg/ml solution for injection

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder
Chanelle Pharmaceuticals Manufacturing Ltd.
Loughrea
Co Galway
Ireland

Manufacturer responsible for batch release:
Labiana Life Sciences,
c/ Venus, 26. Can Parellada Industrial,
08228 Terrassa ,
Barcelona, Spain

Chanelle Pharmaceuticals Manufacturing Ltd
Loughrea
Co. Galway
Ireland

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Euthoxin 500 mg/ml solution for injection

pentobarbital sodium

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Solution for injection.
Clear, pink solution

Each ml contains pentobarbital 455.7 mg
(equivalent to 500 mg pentobarbital sodium)

Excipients:
Erythrosine red (E127) 0.05 mg

4. INDICATION(S)

Euthanasia.

5. CONTRAINDICATIONS

Do not use for anaesthetic purposes.

Do not use for intracoelomic injection in chelonia as the time to death may be unnecessarily prolonged compared with intravenous administration.

6. ADVERSE REACTIONS

Minor muscle twitching may occur after injection. In cattle, gasping may occur if Pentobarbital-Sodium is administered below the recommended dose.
Use of the product may result in transient agitation and symptoms of shortness of breath.
Death may be delayed if the injection is administered perivascularly or into organs/tissues with low capacity for absorption.
Barbiturates can cause irritation when administered subcutaneously or perivascularly.

Frequencies of adverse reactions:
Vocalisation, minor muscle twitching after injection are commonly observed.
One or few gasps after cardiac arrest are uncommonly reported.
Excitation, leg movements, defecation and urine loss, gasping (in cattle), mostly due to under-dosing were noted in very rare cases
Convulsions, contraction of the diaphragm and vomiting are reported in very rare cases.

The frequency of adverse reactions is defined using the following convention:
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports)

Administration by the intrapulmonary route is highly likely to cause coughing, gasping and respiratory distress.

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 inform your veterinary surgeon.

Alternatively you can report via your national reporting system.

7. TARGET SPECIES

Dogs, cats, minks, polecats, hares, rabbits, guinea pigs, hamsters, rats, mice, chickens, pigeons, ornamental birds, small snakes, tortoises, lizards, frogs, horses, cattle, pigs.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Depending on species and circumstances this product may be administered via several routes.
The applicable dose depends on animal species and route of administration.
Therefore, the instructions described in the dosage scheme should be carefully followed:

Intravenous route
The intravenous route of administration should be the route of choice and adequate sedation should be administered if deemed necessary by the attending veterinarian. For horses and cattle premedication is mandatory.

Intracardiac route
Where intravenous administration is difficult, and only following deep sedation or anaesthesia, the product may be administered via the intracardiac route in all target species except avian species.

Intraperitoneal route
Alternatively, for small animals only, administration via the intraperitoneal route could be used, but only following appropriate sedation.

Intrapulmonary route
Intrapulmonary administration must only be used as a **last resort** and only if the animal is heavily sedated, unconscious or anaesthetised and shows no response to noxious stimuli. This route of administration may only be used in chickens, pigeons, ornamental birds, snakes, tortoises, lizards and frogs.

Recommendations for dilution of product
Pigs (in case of administration in ear vein) and small animals (dogs, cats, mink, polecats, hares, rabbits, guinea pigs, hamsters, rats, mice, chickens, pigeons, ornamental birds): For ease of administration the product should be diluted with isotonic (0.9%) sodium chloride solution in a mixing ration of 1:1 prior to administration with needles thinner than 20G.

Dosage table:

Target species	Route	Dose expressed as ml of the product	Dose expressed as mg pentobarbital sodium
Horses The product should be injected as quickly as possible. Premedication before administration is mandatory.	Intravenous (rapid injection)	1.0 ml per 5 kg	100 mg per kg
Cattle The product should be injected as quickly as possible. In cattle, in particular at	Intravenous (rapid injection)	1 - 2 ml per 10 kg	50mg to 100 mg per kg

lower dosages, it is possible to observe gasping in isolated cases. Premedication before administration is mandatory.			
<u>Pigs</u> The product should be injected as quickly as possible. The route of administration depends on the age and weight of the individual and can be intravenous (vena cava cranialis or ear vein) or intracardiac. The injection duration can - depending on the age and body weight of the pig –vary from 1 second (piglets) and 38 seconds (in boars> 100 kg body weight).	Intravenous (vena cava cranialis) by rapid injection Intravenous (ear vein) by rapid injection after dilution with isotonic (0.9%) NaCl solution at a ratio of 1:1 Intracardiac (in unconscious or deeply sedated/anaesthetised patients)	0.16 ml per kg up to 30 kg 0.08 ml per kg over 30 kg 0.16 ml per kg up to 30 kg 0.08 ml per kg over 30 kg 0.16 ml per kg up to 30 kg 0.08 ml per kg over 30 kg	80 mg per kg up to 30kg 40 mg per kg over 30kg 80 mg per kg up to 30kg 40 mg per kg over 30kg 80 mg per kg up to 30kg 40 mg per kg over 30kg
<u>Dogs & Cats</u>	Intravenous; slow continuous injection until unconscious then rapid injection of remaining quantity Intracardiac & intraperitoneal: in unconscious or deeply sedated/anaesthetised patients.	1.0 ml per 4 kg Dog 1.0 ml per 3 kg Cat 1.0 ml per 3 kg Dog 1.0 ml per 2 kg Cat	125 mg per kg Dog 166 mg per kg Cat 166 mg per kg Dog 250 mg per kg Cat

Mink, polecats	Intravenous Intracardiac (in unconscious or deeply sedated/anaesthetised patients)	1.0 ml per animal	500 mg per animal
Hares, rabbits, guinea pigs, hamsters, rats, mice	Intravenous Intracardiac (in unconscious or deeply sedated/anaesthetised patients) Intraperitoneal (in unconscious or deeply sedated/anaesthetised patients)	1.0 ml per 1.5 kg 1.0 ml per 1kg	333 mg per kg 500 mg per kg
Chickens, pigeons, ornamental birds The method of choice in birds is intravenous injection. If venepuncture cannot be performed (due to e.g. haematoma, collapse of cardiovascular system) intrapulmonary injection could be an option. In birds, intrapulmonary injection is performed by inserting the cannula in a dorso-ventral direction on the left or right side of the backbone into the lung (3rd or 4th intercostal segment between backbone and scapula).	Intravenous & Intrapulmonary (in unconscious or deeply sedated/anaesthetised patients)	1.0 ml per 1 kg	500 mg per kg

Small snakes, tortoises, lizards, frogs	Depending on the size, inject into the body cavity near the heart; death is expected after about 5 to 10 minutes in unconscious or deeply sedated/anaesthetised patients	0.4 – 0.8 ml per animal	200 to 400 mg per animal

9. ADVICE ON CORRECT ADMINISTRATION

This veterinary medicinal product does not contain any antimicrobial preservative.
The stopper should not be punctured more than 50 times.

10. WITHDRAWAL PERIOD

Do not use in animals intended for human or animal consumption.
Adequate measures should be taken to ensure that carcasses of animals treated with this product and the by-products of these animals do not enter the food chain and are not used for human or animal consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions
Do not use this veterinary medicinal product after the expiry date which is stated on the bottle and carton. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 28 days

12. SPECIAL WARNING(S)

Special warnings for each target species
To reduce the risk of CNS excitement, it is recommended to perform euthanasia in a quiet area.

In pigs, it was shown that there is a direct correlation between restraint and level of excitation and agitation. Therefore, injection in swine should be done with the least amount of restraint necessary.
In individual cases – especially in restrained animals – agitation/excitation could occur during administration resulting in accidental paravenous administration of the product. Due to the difficulty of safe intravenous injections in swine adequate sedation of the animal before IV administration of pentobarbital is recommended. Application via marginal ear vein should at least initially be performed without fixation. The animals should be restrained between the legs of an assisting person. If fixation is necessary, a snout rope should be used.

In horses and cattle, premedication with an appropriate sedative must be used to produce profound sedation before euthanasia, and an alternative method of euthanasia should be available should it become necessary.

When euthanasia of **poikilotherms** is undertaken, the animal must be maintained at its preferred optimum temperature, otherwise efficacy may be unreliable. Species appropriate measures (e.g. pithing) should be taken to ensure that euthanasia is complete and that spontaneous recovery does not occur.

Venomous snakes are best euthanised by injecting pentobarbital solution into the body cavity near the heart, with judicious use of prior sedation in order to minimise danger to humans.

Intravenous injection of pentobarbital has the ability to cause CNS excitement in several species of animal and adequate sedation should be administered if deemed necessary by the veterinary surgeon. Measures must be taken to avoid perivascular administration (e.g. by using an intravenous catheter).

The **intraperitoneal** route of administration may cause a prolonged onset of action with an increased risk of CNS excitement. Intraperitoneal administration must only be used following appropriate sedation. Measures must be taken to avoid administration into the spleen or organs/tissue with low capacity for absorption. This route of administration is only suitable for small mammals.

Intracardiac injection must only be used if the animal is heavily sedated, unconscious or anaesthetised.

The **intrapulmonary** route of administration may cause a prolonged onset of action with an increased risk of adverse effects noted in section “Adverse reaction” and must be reserved for cases where other routes of administration are not possible. Intrapulmonary administration may only be used in chickens, pigeons, ornamental birds, snakes, tortoises, lizards and frogs. Animals must be heavily sedated, unconscious or anaesthetised before this route of administration is employed. Do not use intrapulmonary administration in any other target animal species.

Check regularly, up to about 10 minutes post-administration, in case signs of life return (respiration, heartbeat, corneal reflex). In clinical trials it has been established that signs of life may return. If this occurs, it is advised to repeat the administration using between 0.5 and 1 times the recommended dose.

Special precautions for use in animals

This veterinary medicinal product does not contain any antimicrobial preservative.

When an aggressive animal is to undergo euthanasia, premedication with a more easily administered (oral, subcutaneous or intramuscular) sedative is recommended.

In the event of accidental administration to an animal not presented for euthanasia, measures such as artificial respiration, administration of oxygen and the use of analeptics are appropriate.

Pigs and small animals: See also section “Dosage for each species, route(s) and method of administration” for recommendations regarding dilution of product.

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

Pentobarbital is a potent drug which is toxic in humans – particular care must be taken to avoid accidental ingestion and self-injection. Only carry this veterinary medicinal product in an unarmed syringe to avoid accidental injection.
Systemic uptake (including absorption via skin or eye) of pentobarbital causes sedation, sleep induction, and CNS and respiratory depression.
The concentration of pentobarbital in the product is such that the accidental injection or ingestion of quantities as small as 1 ml in human adults can have serious CNS effects. A dose of pentobarbital sodium of 1 g (equivalent to 2 ml of product) has been reported to be fatal in humans.

Avoid direct contact with the skin and eyes, including hand-to-eye contact.
Wear suitable protective gloves when handling this product – pentobarbital can be absorbed via skin and mucosa.
Moreover, this product may be irritating to the eye and can cause irritation to the skin as well as hypersensitivity reactions (due to the presence of pentobarbital and benzyl alcohol). People with known hypersensitivity to pentobarbital or to any other ingredient should avoid contact with the veterinary medicinal product.

This product should only be used in the presence of another person that can assist in case of accidental exposure. Instruct that person if not a medical professional about the risks of the product.
After administration of this product, collapse will occur within 10 seconds. In case the animal is standing at time of administration, care should be taken by the person administering the veterinary medicinal product and any other persons present to keep a safe distance from the animal to avoid injury.

In the event of accidental exposure the following action should be taken:

Skin – Wash immediately with water and then thoroughly with soap and water. Seek medical advice immediately and show the package leaflet or the label to the physician.

Eyes – Rinse immediately with plenty of cold water. Seek medical advice immediately and show the package leaflet or the label to the physician.

Ingestion –Wash out mouth. Seek medical advice immediately and show the package leaflet or the label to the physician. Keep warm and rest.

Accidental self-injection – Obtain URGENT medical attention (take the package leaflet with you), advising medical services of barbiturate poisoning. Do not leave the patient unattended.

DO NOT DRIVE as sedation may occur.

This product is flammable. Keep away from sources of ignition. Do not smoke.

To the physician: Urgent care should be taken to maintain airways and cardiac function. In case of severe intoxication, additional measures should be taken to enhance the elimination of the barbiturate. Give symptomatic and supportive treatment.
Information for the health professional in case of exposure:
The concentration of pentobarbital in the product is such that the accidental injection or ingestion of quantities as small as 1 ml in human adults can have serious CNS effects. A dose of pentobarbital sodium of 1g (equivalent to 2 ml of product) has been reported to be fatal in humans. Treatment should be supportive with appropriate intensive therapy and maintenance of respiration.

Carcasses of animal's euthanised with this product should be disposed of in accordance with national legislation. Carcasses of animal's euthanised with this product should not be fed to other animals due to the risk of secondary intoxication.

Use during pregnancy, lactation or lay

If euthanasia is necessary, the product can be used in pregnant or lactating animals. The increased body weight of pregnant animals should be taken into account in the dose calculation. Whenever possible, the product should be injected intravenously. The foetus must not be removed from the maternal body (e.g. for examination purposes) earlier than 25 minutes after confirmation of the death of the mother. In this case, the foetusis to be examined for signs of life and, if necessary, euthanised separately.

Interaction with other medicinal products and other forms of interaction
Although premedication with sedatives may delay the desired effect of the product due to decreased circulatory function this may not be clinically noticeable since CNS depressant drugs (opioids, α2 adrenoreceptor agonists, phenothiazines, etc.) can also increase the effect of pentobarbital.

Incompatibilities
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products except sterile, isotonic sodium chloride (0.9%) solution.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

December 2020

15. OTHER INFORMATION

Pack sizes – 100ml

Approved 07 May 2021