1. NAME OF THE MEDICINAL PRODUCT

Pentobarbital Medimarket Veterinary.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Pentobarbital sodium 500 mg per ml (equivalent to 455.7 mg pentobarbital).
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Intravenous, Intracardiac, Intraperitoneal Solution for injection.
Clear, pink solution free from visible particles.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs, cats, rodents, rabbits, cattle, sheep, goats, horses and mink.

4.2 Therapeutic indications

Euthanasia in dogs, cats, rodents, rabbits, cattle, sheep, goats, horses and mink.

4.3 Contraindications

Do not use for anesthesia.

4.4 Special warnings for each target species

- Intravenous injection of pentobarbital has the ability to cause induction excitement in several species of animal and adequate sedation should be applied if deemed necessary by the veterinary surgeon. Measures should be taken to avoid perivascular administration (e.g., by using intravenous catheter).
- The intraperitoneal route of administration may cause a prolonged onset of action with an increased risk of induction excitement. Intraperitoneal administration must only be used following appropriate sedation. Measures should 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 animals.
- Intracardiac injection must only be used if the animal is heavily sedated, unconscious, or anesthetized.
- To reduce the risk of induction excitement, euthanasia should be performed in a quiet area.

4.5 Special precautions for use

Special precautions for use in animals

- The intravenous route of administration should be the route of choice and adequate sedation should be applied if deemed necessary by the veterinary surgeon. For horses and cattle premedication is mandatory. Where intravenous administration is impossible, and only following deep sedation, the product may be administered via the intracardiac route in all named species. Alternatively, for small animals only, administration via the intraperitoneal route could be used, following appropriate sedation.
- 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.
- 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.

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

Pentobarbital is a potent hypnotic and a sedative, and thus potentially toxic in man. It can be absorbed systemically through the skin and if swallowed. Particular care should be taken to avoid accidental ingestion and self-injection.

Systemic uptake (including absorption via skin or eye) of pentobarbital causes sedation, sleep, CNS and respiratory depression. 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).
Embryotoxic effects cannot be excluded.

Avoid direct contact with the skin and eyes, including hand-to-eye contact.

Avoid accidental self-injection or accidental injection of other persons when administering the product.

People with known hypersensitivity to pentobarbital should avoid contact with the veterinary medicinal product.

Handle the product with utmost care, especially pregnant and breastfeeding women. Wear protective gloves. This medicine should only be administered by veterinarians and should only be used in the presence of another professional that can assist in case of accidental exposure.
Instruct the professional, if not a medical professional, about the risks of the product.

Accidental spillage on the skin or in the eyes, must be washed with plenty of water. If there has been serious skin or eye contact or in the case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. In case of accidental ingestion, wash out mouth and obtain medical attention immediately. But DO NOT drive as sedation may occur.

Information for the health professional in case of exposure:
Emergency measures should be directed toward maintenance of respiration and cardiac function. In severe intoxication measures to enhance elimination of absorbed barbiturate may be necessary.

The concentration of pentobarbital in the product is such that the accidental injection or ingestion of quantities as small as 0.4 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. Treatment should be supportive with appropriate intensive therapy and maintaining the respiration.

Other precautions

Ingestion of euthanised animals by other animals may lead to intoxication, anesthesia and even death. Barbiturates are also highly persistent in carcasses and also stable to cooking temperature. Due to the risk of secondary intoxication, animals euthanised with the veterinary medicinal product should not be fed to other animals but should be disposed of in accordance with national legislation and in a manner that other animals cannot have access to the carcasses.

4.6 Adverse reactions (frequency and seriousness)

Minor muscle twitching may occur after injection.

Death may be delayed if the injection is administered perivascularly or into organs/tissues with low capacity for absorption.
Barbiturates can be irritating when administered perivascularly.

Pentobarbital sodium has the ability to cause induction excitement.
Premedication/sedation significantly reduces the risk of experiencing induction excitement.

Very occasionally one or a few gasping respirations occur after cardiac arrest. At this stage the animal is already clinically dead.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation using an online form:
https://sideeffects.health.gov.il.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy, lactation or lay. Use accordingly to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

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

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.

4.9 Amount to be administered and administration route

A dose of 140 mg/kg, equivalent to 0.28 ml/kg, is considered sufficient for all indicated routes of administration.
The intravenous route of administration should be the route of choice and adequate sedation should be applied if deemed necessary by the veterinary surgeon. For horses and cattle premedication is mandatory.
When intravenous administration is difficult and only following deep sedation or anaesthesia, the product may be administered via the intracardiac route.

Alternatively, for small animals only, administration via the intraperitoneal route could be used, but only following appropriate sedation.
The intravenous injection in companion animals should be carried out with a continuous injection rate until unconsciousness occurs.
In horses and cattle, pentobarbital should be injected rapidly.
The stopper should not be punctured more than 50 times.

Recommendations for dilution of product

Small animals (dogs, cats, rodents, rabbits and mink):

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.

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

Not applicable.

4.11 Withdrawal period(s)

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.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: **Products for euthanasia, barbiturates, pentobarbital**.

ATCvet code: **QN51AA01**.

5.1 Pharmacodynamic properties

Pentobarbital sodium is an oxybarbiturate derivative of Barbituric acid. Barbiturates depress the entire central nervous system but, quantitatively, various areas are affected differently, making the product a potent hypnotic and sedative. The immediate effect is the unconsciousness of deep anaesthesia followed by, at high dose rates, rapid depression of the respiratory center. Breathing stops and cessation of heart action quickly follows, leading to rapid death.

5.2 Pharmacokinetic properties

When injected into the bloodstream, a barbiturate ionises, the degree depending on the dissociation constant of the agent and the pH of the blood.

Barbiturates bind with plasma proteins, forming an equilibrium of bound and unbound drug in circulating blood. Cell penetration can only occur with the undissociated form.

After cell penetration, dissociation again occurs and binding of the drug to intracellular organelles takes place.

Tissue changes due to cellular penetration and intracellular binding have not been described. In general, the effects on tissues can be categorized as direct and indirect. In general, these effects are subtle and little is known concerning them.

Following intracardiac use unconsciousness is almost immediate and cardiac arrest follows within 10 seconds.

Following intravenous use unconsciousness follows in 5-10 seconds after completion of administration.

Death follows 5-30 seconds later. Intraperitoneally, euthanasia is achieved in 3-10 minutes (due to depression of the respiratory center, the animal may be clinically dead prior cardiac arrest).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene Glycol
Erythrosine red E127
Water for Injection

6.2 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.

6.3 Shelf-life

The expiry date of the product is indicated on the packaging materials.

Shelf life after opening: 28 days, store at not more than 25°C.

The stopper should not be punctured more than 50 times.

Use immediately after dilution.

6.4 Special precautions for storage

Store at not more than 25°C.

6.5 Nature and contents of container

100 ml Type I amber multi-dose glass vials closed with a bromobutyl rubber stopper and sealed with an aluminium overseal containing 100 ml solution.

The product is presented in a carton.

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 AUTHORIZATION HOLDER

A.L. Medi-Market Ltd., 18 Hakadar St., Netanya, 42138 (POB 13261).

8. MANUFACTURER

Chanelle Pharmaceuticals Manufacturing Ltd., Dublin Road, Loughrea, County Galway, Ireland.

9. MARKETING AUTHORIZATION NUMBER

162-72-35327-00

פורמט עלון זה נקבע ע"י משרד הבריאות ותוכנו נבדק ואושר ע"י משרד הבריאות בתאריך אוקטובר 2019, ועודכן בהתאם להוראות משרד הבריאות בתאריך נובמבר 2019.