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ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Butasal-100, 100 mg/ml + 0.05 mg/ml solution for injection for horses, cattle and dogs (EE)
Butasal-100 100 mg/ml + 0.05 mg/ml solution for injection for horses, cattle and dogs (BE, HR, CY, CZ, FR, EL, NL, PT, SK)
Butasal vet 100 mg/ml + 0.05 mg/ml solution for injection for horses, cattle and dogs (DK, FI, IS, SE)
Butasal 100 mg/ml + 0.05 mg/ml solution for injection for horses, cattle and dogs (HU, RO, AT, PL, IE, SI, UK)
Catochem 100 mg/ml + 0.05 mg/ml solution for injection for horses, cattle and dogs (IT, ES, NO)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Butafosfan	100.0 mg
Cyanocobalamin (vitamin B12)	0.05 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	10.5 mg
Sodium citrate	
Citric acid (for pH adjustment)	
Water for injections	

Clear red solution without visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Horses, cattle and dogs.

3.2 Indications for use for each target species

All target species:
- Supportive treatment and prevention of hypophosphatemia and/or cyanocobalamin (vitamin B12) deficiency.

Cattle:
- Supportive treatment to restore rumination following surgical treatment of displaced abomasum associated with secondary ketosis.
- Complementary treatment of parturient paresis in addition to Ca/Mg therapy.

- Prevention of ketosis development, if administered before calving.

Horses:
- Adjunctive therapy in horses suffering from muscular exhaustion.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Intravenous administration should be done very slowly since cases of circulatory shock may be associated with too rapid injection.

In dogs suffering from chronic renal insufficiency the veterinary medicinal product should only be used according to the benefit-risk assessment by the responsible veterinarian.

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

Benzyl alcohol may cause hypersensitivity (allergic reactions). People with known hypersensitivity to benzyl alcohol or any of the excipients should avoid contact with the veterinary medicinal product.

This veterinary medicinal product may cause skin and eye irritation. Avoid contact with skin and eyes. In case of accidental exposure, rinse the affected area thoroughly with water.

Self-injection should be avoided. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle, horses, dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Injection site pain[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Circulatory shock[2]

[1]Has been reported following subcutaneous administration in dogs.
[2]In cases where rapid intravenous infusion has occurred.

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 the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Can be used during pregnancy and lactation in cows.

The safety of the veterinary medicinal product has not been established during pregnancy and lactation in mares and bitches. Laboratory studies in rats have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Cattle, horses: intravenous (i.v.) use
Dogs: intravenous (i.v.), intramuscular (i.m.) and subcutaneous (s.c.) use

It is recommended that the solution is warmed to body temperature before administration.
The dose depends on the animal's body weight (bw) and condition.

Species	Dose butafosfan (mg/kg bw)	Dose cyanocobalamin (mg/kg bw)	Dose volume of the veterinary medicinal product	Route of administration
Cattle Horses	5–10	0.0025–0.005	5–10 ml/100 kg	i.v.
Dogs	10–15	0.005–0.0075	0.1–0.15 ml/kg	i.v., i.m., s.c.

For the supportive treatment of secondary ketosis in cows, the recommended dose should be administered on three consecutive days.
For the prevention of ketosis in cows, the recommended dose should be administered on three consecutive days within the period of 10 days before expected calving.
For other indications, treatment should be repeated as necessary.

For multiple bottle entry, an aspirating needle or multi-dose syringe is recommended to avoid excessive broaching of the stopper. The stopper may be safely punctured up to 15 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No adverse effect was reported after intravenous administrations up to 5 times the recommended dose in cattle.
Except transient slight swelling at the injection site, no other adverse effect was reported after subcutaneous administrations up to 5 times the recommended dose in dogs.
No overdose data are available for dogs after intravenous and intramuscular administrations.
No overdose data are available for horses.

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

Cattle, horses:
Meat and offal: Zero days
Milk: Zero hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QA12CX99

4.2 Pharmacodynamics

Butafosfan is a synthetically produced organic phosphorus compound. It is used as an exogenous source of phosphorus, which is important for energy metabolism. It is essential for gluconeogenesis since most intermediates of that process need to be phosphorylated.

Cyanocobalamin is a unique cobalt-containing vitamin which is a semi-synthetic form of vitamin B12. It functions as a co-factor for two of the enzymes important in fatty acid synthesis and in the biosynthesis of glucose from propionate.
Cyanocobalamin belongs to the family of water-soluble B-vitamins which are synthesized by the microbial flora in the digestive tract of domestic animals (forestomachs and large intestine).
When administered parenterally, cyanocobalamin is directly available as a source of vitamin B12.

4.3 Pharmacokinetics

Butafosfan is rapidly absorbed from the injection site when administered subcutaneously or intramuscularly. The maximum plasma concentration is reached approximately 30 minutes after administration. Butafosfan is distributed to the liver, kidney, muscle and skin/fat and is excreted rapidly, mainly in urine (74 % in the first 12 hours), while less than 1 % is excreted in faeces.
In studies in cattle after a single intravenous administration of a single dose of 5 mg/kg body weight elimination is relatively rapid with a terminal half-life of 3.2 hours. In cows it was established that milk excretion was low.
In studies in horses, after intravenous administration of butafosfan at a dose of 10 mg/kg of body weight, the value C_{max} was reached within 1 minute, while the biological half-life is approximately 78 minutes.
In studies in dogs after a single subcutaneous administration of a single dose of 20 mg/kg body weight, absorption and butafosfan elimination is relatively rapid. T_{max} in dogs is 0.75 h, while the terminal half-life is approximately 9 hours.

Cyanocobalamin is rapidly and extensively absorbed into the blood after subcutaneous or intramuscular administration to animals. In serum, it is bound to specific transport proteins called transcobalamins. It is distributed extensively into all tissues and tends to accumulate in the liver. The principal routes of excretion of absorbed vitamin B12 are via urine, bile, and faeces. Urinary excretion of unmetabolised vitamin B12 by kidney glomerular filtration is minimal and biliary excretion via faeces is the major excretory route. Much of the cobalamin excreted in bile is reabsorbed; at least 65 to 75 % is reabsorbed in the ileum by means of the “intrinsic factor” active transport mechanism.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Do not store above 25 °C.
Keep the vial in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Amber glass vial, closed with a bromobutyl rubber stopper and secured with an aluminium cap or flip-off cap with polypropylene cover.

Package size:
Cardboard boxes of 1 vial of 50 mL or 100 mL
Cardboard box of 6 carton boxes of 1 vial of 50 mL or 100 mL

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 or household waste.

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

Interchemie Werken De Adelaar Eesti AS

7. MARKETING AUTHORISATION NUMBER(S)

Number allocated by the Member State. To be completed in accordance with national requirements and after conclusion of the MRP.

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: *To be completed in accordance with national requirements and after conclusion of the MRP.*

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

To be completed in accordance with national requirements after conclusion of the procedure.

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).