SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oxmax 65 mg/ml solution for infusion for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
65 mg hemoglobin betafumaril (bovine)
Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.
Dark purple solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Indicated as an adjunct therapy in the management of canine haemorrhagic shock. A beneficial effect of treatment was demonstrated for 24 hours survival rate when the veterinary medicinal product was administered concomitantly with low dose resuscitative fluids (Lactated Ringer's solution).

4.3 Contraindications

Do not use in dogs with identified kidney disease.

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

Do not use in animals at risk of volume overload (e.g. animals with oliguria/anuria or advanced cardiac disease) as this may cause adverse effects associated with circulatory overload.

Do not use in dogs previously treated with this veterinary medicinal product or other bovine haemoglobin-based oxygen carriers, to avoid a potential sensitivity-type reaction following repeated exposure.

4.4 Special warnings for each target species

There is no efficacy data available for dogs that have been rehydrated prior to administration of the product or in cases of normovolaemic anaemia.

4.5 Special precautions for use

Special precautions for use in animals
To be used as single administration.

Avoid food and water for the duration of administration.

The indication for use was established following the concomitant administration of the product and crystalloid resuscitative fluids (LRS). In the absence of a critical clinical situation, the product should not be administered to dogs that have already received fluid therapy to restore circulatory volume.

Due to the plasma expanding properties of the veterinary medicinal product, the possibility of circulatory overload and pulmonary oedema should be considered and monitored, especially when administering adjunctive intravenous fluids, particularly colloidal solutions.

Signs of circulatory overload should be carefully monitored. Rapid blood volume expansion may be controlled by slowing the rate of administration. If circulatory overload occurs, cease the infusion immediately, and consider administering diuretics.

Renal function should be monitored during and after use of the veterinary medicinal product. If clinical signs of renal impairment such as depression, reduced food intake, vomiting, polyuria or oliguria are noted, renal function should be assessed. Results of serum chemistry parameters to evaluate renal function should be interpreted with care, as the presence of the veterinary medicinal product at the recommended treatment dose may interfere with the results for BUN, CREA (Creatinine), BUN/CREA ratio and Urea. These are likely to be unreliable markers of renal function up to 12 hours (Urea) and up to 4 days (BUN, BUN/CREA ratio and CREA) after administration. Appropriate treatment should be instigated if impaired renal function is evident. Renal function can be assessed using tools such as abdominal ultrasound and urinalysis (specifically urine sediment examination and urine specific gravity measurement).

In the event of anaphylaxis, clinical signs that include a skin rash, swelling of the face or extremities, difficulty in breathing and/or vomiting will occur. If anaphylaxis does occur, treat symptoms immediately as considered appropriate, for example with adrenaline followed by corticosteroids.

Clinical pathology
In dogs with pre-existing haemolysis, routine analysis will not be able to distinguish the veterinary medicinal product from native haemoglobin in the plasma.

Chemistry and haematology
The presence of the veterinary medicinal product in serum may interfere with colourimetric readings and result in erroneous increases, or decreases, in the results of serum chemistry and haematology tests depending on the dose administered, the time after infusion, the type of analyser and the reagents used.

Measurement of lactate in canine blood may be affected by the presence of the veterinary medicinal product. It is advised to interpret the measured lactate concentration with caution, and to use other parameters in combination with lactate levels for clinical evaluation of the patient.

Coagulation
Prothrombin time (PT) and activated partial thromboplastin time (aPTT) can be accurately determined in the presence of the veterinary medicinal product using methods that are either mechanical, magnetic, or light scattering. Colourimetric methods may not be reliable for coagulation assays in the presence of the veterinary medicinal product.

Urinalysis:
Sediment examination and specific gravity measurements are accurate in the presence of the veterinary medicinal product. Dipstick measurements (e.g. pH, glucose, ketones, and protein) and gravity measurement using a refractometer, are likely to be inaccurate if there is visible discolouration of the urine.

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

If adverse reactions develop following accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

This product contains bovine-derived haemoglobin. There is a risk that immune mediated reactions (hypersensitivity reactions) may occur in sensitised persons if repeated accidental self-injection occurs. In case of hypersensitivity reactions, seek medical advice immediately and show the package leaflet or the label to the physician. Do not handle or administer the product if a previous hypersensitivity reaction has occurred.

N-acetyl-L-cysteine is an excipient in this veterinary medicinal product and has been associated with hypersensitivity reactions in humans following intravenous infusion. People with known hypersensitivity to N-acetyl-L-cysteine should take care to avoid accidental self-injection with this veterinary medicinal product.

Special precautions for the protection of the environment
Not applicable.

Other precautions
Not applicable.

4.6 Adverse reactions (frequency and seriousness)

Very common (>1 animal / 10 animals treated):	Diarrhoea, Abnormal stool colouration, Blood in faeces NOS, Vomiting, Shivering, Sneezing, Injection site reddening, Injection site swelling
Common (1 to 10 animals / 100 animals treated):	Discoloured urine, Discoloration of tissue (necropsy finding), Discolouration of mucous membranes (necropsy finding)

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 the national competent authority via the national reporting system. See also section 16 of the package leaflet for contact details.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy or lactation.

Use only accordingly to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amount(s) to be administered and administration route

For intravenous use only.

To be used as single administration.

Administer using aseptic technique via a standard intravenous infusion set and catheter.

Do not administer in combination with other fluids or medicinal products using the same infusion set.

The veterinary medicinal product should be brought to room temperature prior to administration. Do not microwave.

The recommended dose is 10 ml/kg bodyweight administered intravenously at a rate of up to 10 ml/kg/hour, to be administered concomitantly with low dose crystalloid fluids (Lactated Ringer's solution, at a dose of 20 ml/kg/hour). The suggested dose is based on the conditions of a laboratory study in which a dose of 10 ml/kg/hour was tested in experimental settings (controlled haemorrhage) and with concomitant administration of crystalloid fluids (Lactated Ringer's solution, at a dose of 20 ml/kg/hour).

Typing or cross-matching of the recipient's blood is not required before using this veterinary medicinal product.

Due to possible interference with assay results (see section 4.5), it is advisable to obtain clinical samples (blood, urine) for all necessary clinical tests before administration of this veterinary medicinal product.

The veterinary medicinal product should not be used if there is any colour change or any visible particulate in the dark purple solution or if the package is found damaged.

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

In a good laboratory practice (GLP) target animal safety study, two intravenous infusions of the veterinary medicinal product at dose levels of up to 90 ml/kg bodyweight were generally well-tolerated by male and female Beagle dogs.

Treatment-related renal histopathology change was seen in this study at all dose levels (30, 60 and 90 ml/kg bw); however the findings were reversible and are attributed to the effects of increased levels of free haemoglobin.

The presence of renal pathology, though reversible, suggests that 90 ml/kg bw may be close to the maximum tolerable dose.

Overdose or an excessive rate of administration (that is, more than 10 ml/kg/h) could result in immediate cardiopulmonary effects. If this occurs, discontinue the infusion of the veterinary medicinal product immediately until signs abate. Treatment of circulatory overload may be necessary.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Blood substitutes and perfusion solutions, blood substitutes and plasma protein fractions.

ATCvet code: QB05AA91

5.1 Pharmacodynamic properties

The veterinary medicinal product is a haemoglobin-based oxygen carrier, containing a solution of bovine-derived haemoglobin (Hb) with physical and chemical properties similar to that of native Hb contained within red blood cells. Since the active substance “hemoglobin betafumaril (bovine)” is not constrained intracellularly but is free in plasma, it can readily distribute oxygen throughout the circulation.

Efficacy was tested in laboratory settings with animals in induced haemorrhagic shock. After hypovolaemic shock and an oxygen imbalance dogs were treated with either 10 ml/kg the veterinary medicinal product or 10 ml/kg whole blood concomitantly with crystalloids (LRS 20 ml/kg at 20 ml/kg/h). The results indicated a survival rate of 80% (24 out of 30 dogs) for treatment with the veterinary medicinal product compared to 78% (29 out of 37 dogs) for whole blood (with both groups also receiving concomitant crystalloids).

5.2 Pharmacokinetic particulars

At the recommended dose of 10 ml/kg bodyweight, the veterinary medicinal product has a plasma half-life of approximately 17 hours and is eliminated from the plasma in 5 days. Haemoglobin dissociates in plasma and is progressively incorporated into the protein pool of the animal. Haem degrades according to common pathways to bilirubin and bile pigments.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetylcysteine
Sodium chloride
Sodium acetate trihydrate
Potassium chloride
Calcium chloride dihydrate
Sodium hydroxide
Acetic acid, glacial
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf life

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

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.

6.5 Nature and composition of immediate packaging

Multi-layered ethylene-vinyl acetate/ethylene-vinyl alcohol infusion bags containing 100 ml of infusion solution, each overwrapped with aluminium foil pouch with a twist off port.

A cardboard box contains 2 bags.

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

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8. MARKETING AUTHORISATION NUMBER

Vm 51132/5000

9. DATE OF FIRST AUTHORISATION

28 November 2023

10. DATE OF REVISION OF THE TEXT

November 2023

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Approved 28 November 2023