

ANNEX I
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 hour survival rate when Oxmax 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). 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 Oxmax 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-administration, 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.

Acetylcysteine 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 acetylcysteine should administer the veterinary medicinal product with caution.

4.6 Adverse reactions (frequency and seriousness)

Diarrhoea, abnormal stool colouration, blood in faeces, vomiting, shivering, sneezing, injection site reddening and injection site swelling were very commonly reported.

Discolouration of mucous membranes (necropsy finding), discolouration of tissues (necropsy finding) and discoloured urine were commonly reported.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- 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).

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 Amounts 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.

Apart from concomitant use with Lactated Ringer's solution (see below), 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 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.

ATC vet 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 bw of the veterinary medicinal product or 10 ml/kg bw 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 Oxmax 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

New Alpha Innovation Biopharmaceutical Ireland Limited
The Black Church,
St. Mary's Place,
Dublin, D07 P4AX,
Ireland
+353 1 443 3800

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/23/299/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19/10/2023.

10. DATE OF REVISION OF THE TEXT

DD/MM/YYYY

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

- A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. STATEMENT OF THE MRLs**
- D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Klifovet GmbH
Geyerspergerstrasse 27
Schwanthalerhoehe-Laim
80689 Munich
GERMANY

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription

C. STATEMENT OF THE MRLs

Not applicable.

**D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING
AUTHORISATION**

SPECIFIC PHARMACOVIGILANCE REQUIREMENTS

The marketing authorisation holder shall record in the pharmacovigilance database all results and outcomes of the signal management process, including a conclusion on the benefit-risk balance, according to the following frequency: annually.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Aluminium Overwrap & Carton Box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oxmax 65 mg/ml solution for infusion for dogs
Hemoglobin betafumaril (bovine)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 65 mg hemoglobin betafumaril (bovine)

3. PHARMACEUTICAL FORM

Solution for infusion.

4. PACKAGE SIZE

100 ml (Aluminium overwrap)
2 x 100 ml (Carton box)

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

To be used as single administration.
Read the package leaflet before use.
Intravenous use only.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
Excessive administration rate (>10 ml/kg/h) may result in circulatory overload.

10. EXPIRY DATE

EXP {month/year}

Once opened use immediately.

11. SPECIAL STORAGE CONDITIONS

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

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

Disposal: read package leaflet.

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.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

New Alpha Innovation Biopharmaceutical Ireland Limited
The Black Church,
St. Mary’s Place,
Dublin, D07 P4AX,
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/23/299/001

17. MANUFACTURER’S BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Infusion Bag

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oxmax 65 mg/ml solution for infusion for dogs
hemoglobin betafumaril (bovine)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains 65 mg hemoglobin betafumaril (bovine)

3. PHARMACEUTICAL FORM

Solution for infusion

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

To be used as single administration.
Read the package leaflet before use.
Intravenous use only.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
Excessive administration rate (>10 ml/kg/h) may result in circulatory overload.

10. EXPIRY DATE

EXP {month/year}
Once opened use immediately.

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY**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”**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

New Alpha Innovation Biopharmaceutical Ireland Limited
The Black Church,
St. Mary’s Place,
Dublin, D07 P4AX,
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/23/299/001

17. MANUFACTURER’S BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Oxmax 65 mg/ml solution for infusion for dogs

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

Marketing authorisation holder:

New Alpha Innovation Biopharmaceutical Ireland Limited
The Black Church,
St. Mary's Place,
Dublin, D07 P4AX,
Ireland
+353 1 443 3800

Manufacturer responsible for batch release:

KLIFOVET GmbH
Geyerspergerstr. 27
D-80689 Munich,
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oxmax 65 mg/ml solution for infusion for dogs
hemoglobin betafumaril (bovine)

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

Each ml contains:
65 mg hemoglobin betafumaril (bovine)

Dark purple solution.

4. INDICATION(S)

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

5. 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.

6. ADVERSE REACTIONS

Diarrhoea, abnormal stool colouration, blood in faeces, vomiting, shivering, sneezing, injection site reddening and injection site swelling were very commonly reported.

Discolouration of mucous membranes (necropsy finding), discolouration of tissues (necropsy finding) and discoloured urine were commonly reported.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- 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)

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.

7. TARGET SPECIES

Dogs

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

For intravenous use only.

To be used as single administration.

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

Apart from concomitant use with Lactated Ringer's solution (see below), do not administer in combination with other fluids or medicinal products using the same infusion set.

This 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 12), 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.

9. ADVICE ON CORRECT ADMINISTRATION

This veterinary medicine product should be administered using aseptic technique via a standard intravenous infusion set and catheter.

Excessive administration rate (>10 ml/kg/h) may result in circulatory overload.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

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

Do not use this veterinary medicinal product after the expiry date which is stated on the label.

Shelf life after first opening the immediate packaging: use immediately.

12. SPECIAL WARNING(S)

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.

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). 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 Oxmax 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-administration, 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.

Acetylcysteine 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 acetylcysteine should administer the veterinary medicinal product with caution.

Pregnancy and lactation:

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

Interaction with other medicinal products and other forms of interaction:

None known.

Overdose (symptoms, emergency procedures, antidotes):

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 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 infusion of the veterinary medicinal product immediately until signs abate. Treatment of circulatory overload may be necessary.

Major incompatibilities:

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

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 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

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (<http://www.ema.europa.eu/>).

15. OTHER INFORMATION

A cardboard box contains 2 bags.