**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**Carton box**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nerfasin vet. 20 mg/ml, solution for injection for cattle, horses, dogs and cats
xylazine

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Per ml: Xylazine 20 mg (equivalent to 23.31 mg xylazine hydrochloride)

## 3. PHARMACEUTICAL FORM

Solution for injection.

## 4. PACKAGE SIZE

10 ml
25 ml
50 ml

## 5. TARGET SPECIES

Cattle, horses, dogs and cats.

## 6. INDICATION(S)

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

Cattle: intravenous, intramuscular.
Horses: intravenous.
Dogs: intramuscular.
Cats: intramuscular, subcutaneous.

Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD

Withdrawal period:

Cattle, horses:

| | |
|---|---|
| Meat and offal: | 1 day |
| Milk: | zero hours |

## 9. SPECIAL WARNING(S), IF NECESSARY

Accidental injection is dangerous.
Accidental intake and contact with skin, eyes and mucous membranes is dangerous.

## 10. EXPIRY DATE

EXP: <month/year>
Shelf life after first opening the vial: 28 days.
Once broached, use by…..

## 11. SPECIAL STORAGE CONDITIONS

Do not refrigerate or freeze.

## 12. SPECIFIC 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.
Administration only by a veterinary surgeon.

## 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

Le Vet B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

## 16. MARKETING AUTHORISATION NUMBER(S)

Vm 19994/4017

## 17. MANUFACTURER'S BATCH NUMBER

Batch: <number>

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**Vial**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nerfasin vet. 20 mg/ml, injection for cattle, horses, dogs and cats
xylazine

## 2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Per ml: Xylazine 20 mg (equivalent to 23.31 mg xylazine hydrochloride)

## 3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

10 ml
25 ml
50 ml

## 4. ROUTE(S) OF ADMINISTRATION

Cattle: IV, IM.
Horses: IV.
Dogs: IM.
Cats: IM, SC.

## 5. WITHDRAWAL PERIOD

Withdrawal period:

Cattle, horses:
Meat and offal: 1 day
Milk: zero hours

## 6. BATCH NUMBER

Batch: <number>

## 7. EXPIRY DATE

EXP: <month/year>
Once broached, use by…

## 8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

# PACKAGE LEAFLET

Nerfasin vet. 20 mg/ml, solution for injection for cattle, horses, dogs and cats

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

Marketing authorisation holder
Le Vet B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands

Manufacturer for the batch release:
Produlab Pharma B.V.
Forellenweg 16
4941 SJ Raamsdonksveer
The Netherlands

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nerfasin vet. 20 mg/ml, solution for injection for cattle, horses, dogs and cats
Xylazine (as hydrochloride)

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

per ml:

**Active substance:**
Xylazine (as hydrochloride): 20.0 mg
(equivalent to 23.31 mg xylazine hydrochloride)

**Excipients:**
Methyl parahydroxybenzoate (E218)1.0 mg

Clear, colourless solution.

## 4. INDICATION(S)

Sedation.
Premedication in combination with an anaesthetic.

## 5. CONTRAINDICATIONS

- Do not use in case of hypersensitivity to the active substance or to any of the excipients.
- Do not use in animals with gastrointestinal obstruction as the muscle relaxant properties of the drug appear to accentuate the effects of the obstruction and because of possible vomiting.
- Do not use in animals with severe renal or hepatic impairment, respiratory dysfunction, cardiac abnormalities, hypotension and/or shock.
- Do not use in diabetic animals.
- Do not use in animals with a history of seizures.
- Do not use in calves younger than 1 week of age, foals younger than 2 weeks or in puppies and kittens younger than 6 weeks.
- Do not use during the last stage of pregnancy (danger of premature birth), except at parturition (see section 12).

## 6. ADVERSE REACTIONS

In general, side effects, typical for an α2-adrenergic agonist, like bradycardia, reversible arrhythmia and hypotension can occur. Thermoregulation can be influenced and consequently body temperature can decrease or increase dependant on the ambient temperature. Depression of respiration and / or respiratory arrest can occur, especially in cats.

Cats and dogs

- Cats and dogs frequently vomit during the onset of the xylazine-induced sedation, especially when the animals have just been fed.
- Animals may show profound salivation following an injection with xylazine.
- Other adverse effects for dogs and cats include: muscle tremors, bradycardia with AV-block, hypotension, reduced respiratory rate, movement in response to strong auditory stimuli, hyperglycaemia and increased urination in cats.
- In cats xylazine causes uterine contractions and it may induce premature parturition.
- In dogs, adverse effects are generally more pronounced after subcutaneous administration compared to intramuscular and the effect (efficacy) can be less predictable.
- In susceptible dog breeds with a large chest (Great Dane, Irish Setter) rare cases of bloating have been reported.
- In anaesthetized animals, mainly during and after the recovery period, in very rare cases, cardio-respiratory disturbances (cardiac arrest, dyspnea, bradypnea, pulmonary edema, hypotension) and neurological signs (seizures, prostration, pupillary disorders, tremors) were observed.

Cattle

- In cattle xylazine may induce premature parturition, and it also reduces implantation of the ovum.
- Cattle, which have received high doses of xylazine sometimes suffer from loose faeces for 24 hours afterwards.
- Other adverse reactions include snoring, profound salivation, ruminal atony,

atony of the tongue, regurgitation, bloating, nasal stridor, hypothermia, bradycardia, increased urination and reversible prolapse of the penis.
- In cattle, adverse effects are generally more pronounced after intramuscular administration compared to intravenous

Horses
- Horses often sweat as the effects of the sedation are wearing off.
- Severe bradycardia and reduced respiratory rate have been reported especially in horses.
- Following administration to horses, a transient rise followed by a fall in blood pressure usually occurs.
- More frequent urination has been reported
- Muscle tremors and movement in response to sharp auditory or physical stimuli are possible. Although rare, violent reactions have been reported in horses following the administration of xylazine.
- Ataxia and reversible prolapse of the penis may occur.
- In very rare cases xylazine may induce mild colic as the gut motility is depressed temporarily. As a preventive measure the horse should receive no feed after sedation until the effect has faded completely.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals )
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

## 7. TARGET SPECIES

Cattle, horses, dogs and cats.

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

Cattle: intravenous, intramuscular.
Horses: intravenous.
Dogs: intramuscular.
Cats: intramuscular, subcutaneous.
To ensure a correct dosage body weight should be determined as accurately as possible.

Cattle:

*Dosage:*

| **Dosage for cattle** | | | |
|---|---|---|---|
| Dosage level* | xylazine (mg/kg) | Nerfasin vet. 20 mg/ml (ml/100 kg) | Nerfasin vet. 20 mg/ml (ml/500 kg) |
| **A. Intramuscular** | | | |
| I | 0.05 | 0.25 | 1.25 |
| II | 0.1 | 0.5 | 2.5 |
| III | 0.2 | 1 | 5 |
| IV | 0.3 | 1.5 | 7.5 |
| **B. Intravenous** | | | |
| I | 0.016-0.024 | 0.08-0.12 | 0.4-0.6 |
| II | 0.034-0.05 | 0.17-0.25 | 0.85-1.25 |
| III | 0.066-0.10 | 0.33-0.5 | 1.65-2.5 |

*Dose 1: Sedation, with a slight decrease of muscle tone. The ability to stand is maintained.
Dose 2: Sedation, marked decrease of muscle tone and some analgesia. The animal usually remains standing, but may lie down.
Dose 3: Deep sedation, further decrease of muscle tone and a degree of analgesia. The animal lies down.
Dose 4: Very deep sedation, a profound decrease in muscle tone and a degree of analgesia. The animal lies down.

Horses
*Dosage:* single dose of 0.6-1 mg xylazine per kg body weight.
(3-5 ml product per 100 kg body weight).

Dogs
*Dosage:* single dose of 0.5-3 mg xylazine per kg body weight.
(0.025-0.15 ml product per 1 kg body weight).

Cats
*Dosage:* single intramuscular or subcutaneous dose of 0.5-1 mg xylazine per kg body weight.
(0.025-0.05 ml product per 1 kg body weight).

## 9. ADVICE ON CORRECT ADMINISTRATION

The intravenous injection should be given slowly, especially in horses.
The stopper should not be punctured more than 20 times.
The number of punctures should be recorded on the outer packaging

## 10. WITHDRAWAL PERIOD

Cattle:
Meat and offal: 1 day
Milk: zero hours

Horses:
Meat and offal: 1 day
Milk: zero hours

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not refrigerate or freeze.
Do not use after the expiry date stated on the vial and the carton after EXP.
Shelf-life after first opening the immediate packaging: 28 days.
When the container is broached for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be determined. This discard date should be written in the space provided.

## 12. SPECIAL WARNING(S)

Special warnings for each target species

Horses:
- Xylazine inhibits the normal intestinal motility. Therefore, it should only be used in horses with colic, that are not responsive to analgesics. The use of xylazine should be avoided in horses with caecal malfunction.
- After treatment of horses with xylazine, the animals are reluctant to walk, so whenever possible the drug should be administered in the place where the treatment/investigation is going to take place.
- Caution should be taken in the administration of the product to horses susceptible to laminitis.
- Horses with airway disease or malfunction may develop life-threatening dyspnoea.
- The dose should be kept as low as possible.
- The association with other pre-anaesthetic agents or anaesthetic agents should be the subject of a benefit/risk assessment. This assessment should consider the composition of the products, their dose and the nature of the surgery. Recommended dosages are likely to vary according to the choice of the anaesthetic association.

Cats and dogs:
- Xylazine inhibits the normal intestinal motility. This may make xylazine sedation undesirable for upper gastro-intestinal radiographs, because it promotes filling of the stomach with gas and makes interpretation less certain.
- Brachycephalic dogs with air way disease or malfunction may develop life-threatening dyspnoea.
- The association with other pre-anaesthetic agents or anaesthetic agents should be the subject of a benefit/risk assessment. This assessment should consider the composition of the products, their dose and the nature of the surgery. Recommended dosages are likely to vary according to the choice of the anaesthetic association.

Cattle:

- Ruminants are highly susceptible to the effects of xylazine. Normally cattle remain standing at the lower doses, but some animals may lie down. At the highest recommended doses most animals will lie down and some animals may lapse in lateral recumbency.
- Reticulo-ruminal motor functions are depressed after injection of xylazine. This may results in bloat. It is advisable to withhold feed and water for several hours before administration of xylazine.
- In cattle the ability to eructate, cough and swallow is retained but reduced during the period of sedation, therefore cattle must be closely watched during the recovery period: the animals should be maintained in sternal recumbency.
- In cattle life threatening effects may occur after intramuscular doses above 0.5 mg/kg body weight (respiratory and circulatory failure). Therefore very precise dosing is required.
- The association with other pre-anaesthetic agents or anaesthetic agents should be the subject of a benefit/risk assessment. This assessment should consider the composition of the products, their dose and the nature of the surgery. Recommended dosages are likely to vary according to the choice of the anaesthetic association.

Special precautions for use in animals

Keep the animals calm, because they may respond to external stimuli.
Avoid intra-arterial administration.
Tympany may occasionally occur in recumbent cattle and can be avoided by maintaining the animal in sternal recumbency.
To avoid aspiration of saliva or food, lower the animal's head and neck. Fast the animals before use of the product.

- Older and exhausted animals are more sensitive to xylazine, whilst nervous or highly excitable animals may require a relatively high dose.
- In case of dehydration, xylazine should be used cautiously.
- Emesis is generally seen within 3-5 minutes after xylazine administration in cats and dogs. It is advisable to fast dogs and cats for 12 hours prior to surgery; they may have free access to drinking water.
- Pre-medication with atropine in cats and dogs may reduce salivation and bradycardia effects
- Do not exceed the recommended dosage.
- Following administration animals should be allowed to rest quietly until the full effect has been reached.
- It is advised to cool animals when the ambient temperature is above 25°C and to keep animals warm at low temperatures.
- For painful procedures, xylazine should always be used in combination with local or general anaesthesia.
- Xylazine produces a certain degree of ataxia; therefore, xylazine must be used cautiously in procedures involving the distal extremities and in standing castrations in the horse.
- Treated animals should be monitored until the effect has faded totally (e.g. cardiac and respiratory function, also in the post-operative phase) and should be segregated to avoid bullying.

- For use in young animals, see the age restriction mentioned in section 5. If the product is intended to be used in young animals below these age-limits, a benefit/risk assessment should be made by the veterinarian.

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

- Care should be taken to avoid accidental self-injection. In case of accidental oral intake or self-injection, seek medical advice immediately and show the package leaflet to the physician but DO NOT DRIVE as sedation and changes in blood pressure may occur.
- Avoid skin, eye or mucosal contact.
- Wash the exposed skin immediately after exposure with large amounts of water.
- Remove contaminated clothes that are in direct contact with skin.
- In the case of accidental contact of the product with eyes, rinse abundantly with fresh water. If symptoms occur, seek the advice of a physician.
- If pregnant women handle the product, special caution should be observed not to self-inject as uterine contractions and decreased foetal blood pressure may occur after accidental systemic exposure.

Advice to doctors:
Xylazine is an α2-adrenoreceptor agonist, symptoms after absorption may involve clinical effects including dose-dependent sedation, respiratory depression, bradycardia, hypotension, a dry mouth and hyperglycaemia. Ventricular arrhythmias have also been reported. Respiratory and haemodynamic symptoms should be treated symptomatically.

Pregnancy
Although laboratory studies in rats have not shown any evidence of teratogenic or foetotoxic effects the use of the product during the first two trimesters of pregnancy should only be made according to the benefit/risk assessment by the responsible veterinarian.
Do not use in the later stages of pregnancy (particularly in cattle and cats) except at parturition, because xylazine causes uterine contractions and it may induce premature labour.
Do not use in cattle receiving ovum transplants as the increased uterine tone may reduce the chance of implantation of the ovum.

Interaction with other medicinal products and other forms of interaction
Other CNS depressant agents (barbiturates, narcotics, anaesthetics, tranquillizers, etc.) may cause additive CNS depression if used with xylazine. Dosages of these agents may need to be reduced. Xylazine should therefore be used cautiously in combination with neuroleptics or tranquillizers.
Xylazine should not be used in combination with sympathomimetic drugs such as epinephrine as ventricular arrhythmia may follow.
The concurrent intravenous use of potentiated sulphonamides with alpha-2 agonists has been reported to cause cardiac arrhythmias which may be fatal. Whilst no such effects have been reported with this product, it is recommended that intravenous administration of Trimethoprim/Sulphonamide containing products should not be undertaken when horses have been sedated with xylazine.

Overdose (symptoms, emergency procedures, antidotes)
In the event of an accidental overdose, cardiac arrhythmias, hypotension, and profound CNS and respiratory depression may occur. Seizures have also been reported after an overdose. Xylazine can be antagonized by α2-adrenergic antagonists.

To treat the respiratory depressant effects of xylazine, mechanically respiratory support with or without respiratory stimulants (e.g. doxapram) can be recommended.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirement.

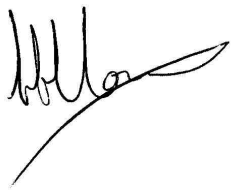
## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

August 2017

## 15. OTHER INFORMATION

Vials containing 10 ml, 25 ml or 50 ml.
Not all pack sizes may be marketed.

Administration only by a veterinary surgeon.



Approved 30 August 2017