1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Xylexx 20 mg/ml solution for injection for cattle, horses, dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

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

Excipients:

Qualitative composition of excipients	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzethonium chloride	0.11 mg
Sodium hydroxide (for pH adjustment)	
Hydrochloric acid, dilute (for pH adjustment)	
Water for injections	

Clear, colourless to almost colourless solution, practically free from visible particles .

3. CLINICAL INFORMATION

3.1 Target species

Cattle, horses, dogs and cats.

3.2 Indications for use for each target species

Sedation.
Premedication in combination with an anaesthetic.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with gastrointestinal obstruction, as it is a muscle relaxant and the properties of the veterinary medicinal product appear to enhance the effects of an obstruction, and because of the risk of vomiting.
Do not use in cases of pulmonary disease (breathing deficiency) or cardiac disorders (especially in case of ventricular arrhythmia).
Do not use in cases of impaired liver or renal function.
Do not use in cases of predetermined history of seizures.
Do not use in cases of hypotension and shock.
Do not use in animals with diabetes mellitus.
Do not administer simultaneously with sympathomimetic amines (e.g. epinephrine).
Do not use in calves less than 1 week of age, foals less than 2 weeks of age or puppies and kittens under 6 weeks of age.
Do not use during the last stage of pregnancy (danger of premature birth), except at parturition (see section 3.7).

3.4 Special warnings

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 into lateral recumbency.
- Reticulo-ruminal motor functions are depressed after injection of xylazine. This may result in bloat. It is advisable to withhold feed and water in adult cattle for several hours before administration of xylazine. Fasting in calves might be indicated but should only be done at the discretion of a benefit/risk assessment made by the responsible veterinarian.
- 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 combination 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 veterinary medicinal products, their dose and the nature of the surgery. Recommended dosages are likely to vary according to the choice of the anaesthetic combination.

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 veterinary medicinal 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 combination 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 veterinary medicinal products, their dose and the nature of the surgery. Recommended dosages are likely to vary according to the choice of the anaesthetic combination.

Dogs and cats:

- Xylazine inhibits 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 airway disease or malfunction may develop life-threatening dyspnoea.
- The combination 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 veterinary medicinal products, their dose and the nature of the surgery. Recommended dosages are likely to vary according to the choice of the anaesthetic combination.

3.5 Special precautions for use

Special precautions for safe use in the target species:

- 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 veterinary medicinal 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 3.3. If the veterinary medicinal 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:
This veterinary medicinal product is a sedative. Care should be taken to avoid accidental self-injection. In the case of accidental oral intake or self-injection, seek medical advice immediately and show the package leaflet to the doctor, but DO NOT DRIVE, as sedation and changes in blood pressure may occur.
Avoid skin, eye or mucosal contact. In the case of accidental contact of the veterinary medicinal product with the skin or eyes, rinse with large amounts of fresh water. Remove contaminated clothes that are in direct contact with the skin. If symptoms occur, seek medical advice.
If pregnant women handle the veterinary medicinal 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 the physician:
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.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data:	Injection site irritation[1]; Hypothermia[2], hyperthermia[2]; Rumen atony, bloated, regurgitation, loose stool[3], hypersalivation, tongue disorder[4]; Respiratory depression, respiratory arrest, snoring, stridor[5]; Hypotension, bradycardia[6], arrhythmia[1]; Polyuria; Premature parturition; uterine disorder[7], penile prolapse[1].

[1] reversible.
[2] thermoregulation can be influenced and consequently body temperature can decrease or increase dependant on the ambient temperature.
[3] for 24 hours after high doses of xylazine.
[4] atony.
[5] nasal stridor.
[6] can be severe.
[7] reduced implantation of the ovum.
In cattle, adverse effects are generally more pronounced after intramuscular administration compared to intravenous.

Horses:

Rare (1 to 10 animals / 10,000 animals treated):	Abnormal behaviour[1];
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Colic [2,4], digestive tract hypomotility[3,4];
Undetermined frequency (cannot be estimated from the available data:	Injection site irritation[5]; Ataxia, muscle tremor[6], involuntary movement[6]; Penile prolapse[5]; Hypothermia[7], hyperthermia[7]; Hypotension[8], hypertension[8], bradycardia[9], arrhythmia[5]; Increased sweating[10]; Frequent urination; Respiratory depression, respiratory arrest, decreased respiratory rate.

[1] violent reactions.
[2] mild.
[3] temporarily.
[4] to prevent this, horses should not consume any feed after sedation until the effect has completely subsided.
[5] reversible.
[6] in response to sharp auditory or physical stimuli.
[7] thermoregulation can be influenced and consequently body temperature can decrease or increase dependant on the ambient temperature.
[8] following administration, a transient rise followed by a fall in blood pressure usually occurs.
[9] can be severe.
[10] as the effects of the sedation are wearing off.

Dogs, cats:

Rare (1 to 10 animals / 10,000 animals treated):	Bloated[1];
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Cardio-respiratory disorders[2] (cardiac arrest[2], dyspnoea[2], bradypnea[2], pulmonary oedema[2]); Neurological disorders[2] (seizure, prostration[2], pupil disorder[2], tremor [2]);
Undetermined frequency (cannot be estimated from the available data:	Injection site irritation[3]; Bradycardia[4,5], hypotension, arrhythmia[3];

	Hypothermia[6], hyperthermia[6]; Involuntary movement[7], muscle tremor; Hyperglycaemia; Hypersalivation, vomiting[8]; Polyuria; Premature parturition[9], uterine contraction[9]; Respiratory arrest[9].

[1] in susceptible dog breeds with a large chest (Great Dane, Irish Setter).
[2] in anaesthetized animals, mainly during and after the recovery period.
[3] reversable.
[4] with AV-block.
[5] can be severe.
[6] thermoregulation can be influenced and consequently body temperature can decrease or increase dependant on the ambient temperature.
[7] in response to sharp auditory stimuli.
[8] during the onset of sedation, especially when the animals have just been fed.
[9] in cats.
In dogs, adverse effects are generally more pronounced after subcutaneous administration compared to intramuscular and the effect (efficacy) can be less predictable.

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:
Although laboratory studies in rats have not shown any evidence of teratogenic or foetotoxic effects the use of the veterinary medicinal product during the first two thirds 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 or in cattle at the time of implantation of the ovum as the increased uterine tone may reduce the chance of implantation of the ovum.

Lactation:
The veterinary medicinal product can be used in lactating animals.

3.8 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 α-2 agonists has been reported to cause cardiac arrhythmias which may be fatal. Whilst no such effects have been reported with this veterinary medicinal product, it is recommended that intravenous administration of trimethoprim / sulphonamide containing veterinary medicinal products should not be undertaken when horses have been sedated with xylazine.

3.9 Administration routes and dosage

Cattle: intravenous or intramuscular use.
Horses: intravenous use.
Dogs: intramuscular use.
Cats: intramuscular or subcutaneous use.

To ensure a correct dosage body weight should be determined as accurately as possible.
The intravenous injection should be given slowly, especially in horses.
This veterinary medicinal product is for administration only by a veterinarian or under their supervision.

Cattle (i.v., i.m.)

Dosage cattle			
Dose level	xylazine (mg/kg)	xylazine 20 mg/ml (ml/100 kg)	xylazine 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

Dosage I: Sedation with slight reduction of muscle tone. The cattle are still able to stand.
Dosage II: Sedation with pronounced reduction of muscle tone and slight analgesia. The cattle mostly remain able to stand but may also lie down.
Dosage III: Deep sedation, further reduction in muscle tone, partial analgesia. The cattle lie down.
Dosage IV: Very deep sedation with a pronounced reduction in muscle tone, partial analgesia. The cattle lie down.

Horses (i.v.)
Dosage: single injection of 0.6-1 mg xylazine per kg body weight. (3-5 ml veterinary medicinal product per 100 kg bodyweight).

Dogs (i.m.)
Dosage: single injection of 0.5-3 mg xylazine per kg body weight. (0.25-1.5 ml veterinary medicinal product per 10 kg bodyweight).

Cats (i.m., s.c.)
Dosage: single injection of 0.5-1 mg xylazine per kg body weight. (0.025-0.05 ml veterinary medicinal product per kg bodyweight).

The stopper can be broached up to 30 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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, mechanical respiratory support with or without respiratory stimulants (e.g. doxapram) can be recommended.

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.

For administration by a veterinarian or under their direct supervision.

3.12 Withdrawal periods

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

Horses:
Meat and offal: 1 day.
Not authorised for use in mares producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN05CM92

4.2 Pharmacodynamics

Xylazine belongs to the α2-adrenoceptor agonists.

- Xylazine is a α2-adrenoceptor agonist, that acts by stimulation of central and peripheral α2-adrenoceptors. Through its central stimulation of α2-adrenoceptors, xylazine has potent antinociceptive activity. In addition to α2-adrenergic activity, xylazine has α1-adrenergic effects.
- Xylazine also produces skeletal muscle relaxation by inhibition of intraneuronal transmission of impulses at the central level of the central nervous system. The analgesic and skeletal muscle relaxation properties of xylazine show considerable interspecies variations. Sufficient analgesia generally will be attained in combination with other veterinary medicinal products only.
- In many species, administration of xylazine produces a short-lived arterial pressor effect followed by a longer period of hypotension and bradycardia. These contrasting actions upon the arterial pressure apparently are related to the α2- and α1-adrenergic actions of xylazine.
- Xylazine has several endocrine effects. Insulin (mediated by α2-receptors in pancreatic β-cells which inhibit insulin release), ADH (decreased production of ADH, causing polyuria) and FSH (decreased) are reported to be influenced by xylazine.

4.3 Pharmacokinetics

Absorption (and action) is rapid following intramuscular injection. Levels of drug peak rapidly (usually within 15 minutes) and then decline exponentially. Xylazine is a highly lipid soluble organic base and diffuses extensively and rapidly (Vd 1.9-2.7 L/kg body weight). Within minutes after an intravenous injection, it can be found in a high concentration in the kidneys, the liver, the CNS, the hypophyses, and the diaphragm. So, there is a very rapid transfer from the blood vessels to the tissues. Intramuscular bioavailability is incomplete and variable ranging from 52-90% in the dog to 40-48% in the horse. Xylazine is metabolised extensively and eliminated rapidly (± 70% via the urine, while the enteric elimination is ±30%). The rapid elimination of xylazine is probably attributable to the extensive metabolism rather than to the renal excretion of unchanged xylazine.

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: 3 years.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Do not refrigerate or freeze.

5.4 Nature and composition of immediate packaging

Clear type II glass vials containing 30 ml veterinary medicinal product, closed with a bromobutyl rubber stopper and aluminium cap in a cardboard or polystyrene box.

Pack sizes:
Cardboard box with 1 vial of 30 ml
Cardboard box with 5 vials of 30 ml
Polystyrene box with 24 vials of 30 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

Alfasan Nederland B.V.

7. MARKETING AUTHORISATION NUMBER(S)

VPA10980/020/001

8. DATE OF FIRST AUTHORISATION

07/10/2022

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

18/10/2024

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).