SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Xyla, 20 mg/ml solution for injection for cattle, horses, dogs and cats (EE)
Sedachem 20 mg/ml solution for injection for cattle, horses, dogs and cats (AT, BE, BG, HR, CY, CZ, DK, FR, DE, EL, HU, IS, IT, LV, MT, NL, NO, PL, PT, RO, SI, SK, ES)
Sedachem vet, 20 mg/ml solution for injection for cattle, horses, dogs and cats (SE)
Xyla vet 20 mg/ml solution for injection for cattle, horses, dogs and cats (FI)
Sedectin, 20 mg/ml solution for injection for cattle, horses, dogs and cats (IE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:

Active substances:
Xylazine 20.00 mg (equivalent to 23.32 mg of xylazine hydrochloride)

Excipients:
Methyl parahydroxybenzoate (E218) 1.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution without visible particles.

4. CLINICAL PARTICULARS

4.1. Target species

Cattle, horses, dogs, cats.

4.2. Indications for use, specifying the target species

Cattle
For sedation, muscle relaxation and analgesia in minor surgery.
In combination with other substances for anaesthesia.

Horses
For sedation and muscle relaxation.
In combination with other substances for analgesia and anaesthesia.

Dogs, cats
For sedation.
In combination with other substances for muscle relaxation, analgesia and anaesthesia.

4.3. Contraindications

Cattle, horses, dogs, cats
Do not use in known cases of hypersensitivity to the active substance or to any of the excipients.

Do not use in animals with gastrointestinal obstruction, as it is muscle relaxant and the properties of the 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.
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 4.7).

4.4. 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.

Dogs, 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 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 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 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.

4.5. Special precautions for use

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 4.3. 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

People with a known hypersensitivity to the active substance, parabens or any of the excipients should avoid contact with the product.
This 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.
Immediately after exposure, wash any exposed skin with large amounts of fresh water. If symptoms occur, seek medical advice.
Remove contaminated clothes that are in direct contact with skin.
In the case of accidental contact of the product with eyes, rinse with large amounts of fresh water. If symptoms occur, seek medical advice.
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 alpha2-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.

4.6. Adverse reactions (frequency and seriousness)

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:
- Reversible local tissue irritation.
- 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, dyspnoea, bradypnea, pulmonary edema, hypotension) and neurological signs (seizures, prostration, pupillary disorders, tremors) were observed.

Cattle:
- Reversible local tissue irritation.
- 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:
- Reversible local tissue irritation.

- 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

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

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.

4.8. 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 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.

4.9. Amounts to be administered and administration route

For intravenous, intramuscular or subcutaneous use.

Cattle: intravenous or intramuscular
Horse: intravenous
Dog: intravenous or intramuscular
Cat: intramuscular or subcutaneous

To ensure a correct dosage body weight should be determined as accurately as possible.

The intravenous injection should be given slowly, especially in horses.

Cattle (intravenous or intramuscular use)
Intravenous administration:
The onset of action is accelerated by intravenous administration, whereas the duration of the action is usually shortened. As in all substances with a central nervous effect, it is recommended to inject the product slowly intravenously.

Cattle (i.v.)

Dose level	Xylazine mg/kg bw	Product ml per 100 kg bw	Product ml per 500 kg bw
I	0.016 – 0.024	0.08 – 0.12	0.4 – 0.6
II	0.034 – 0.05	0.18 – 0.25	0.85 – 1.25
III	0.066 – 0.10	0.33 – 0.5	1.65 – 2.5

Cattle (i.m.)

Dose level	Xylazine mg/kg bw	Product ml per 100 kg bw	Product ml per 500 kg bw
I	0.05	0.25	1.25
II	0.1	0.5	2.5
III	0.2	1.0	5.0
IV	0.3	1.5	7.5

If necessary, the effect of the product can be deepened or prolonged by a second administration.

To amplify the effect, an additional dose may be administered 20 minutes after the first injection, to prolong the effect up to 30 – 40 minutes after the first application. The total dose administered should not exceed dose level IV.

Dosage I: Sedation with slight reduction of muscle tone. The cattle are still able to stand.
Dosage II: Sedation with pronounced reduction of the 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 the muscle tone, partial analgesia. The cattle lie down.

Horse (intravenous use)
0.6 – 1.0 mg/kg bw corresponding to 3 - 5 ml of the product per 100 kg bw **intravenously**.

Depending on the dosage, light to deep sedation with individually variable analgesia and profound decrease in muscle tone is obtained. Generally, the horse does not become recumbent.

Dog (intravenous or intramuscular use)
For sedation:
1 mg xylazine/kg bodyweight intravenously (corresponding to 0.5 ml of the product per 10 kg bodyweight).
1 to 3 mg xylazine/kg bw intramuscularly (corresponding to 0.5 to 1.5 ml of the product per 10 kg bodyweight).

Very often the application of the product causes vomiting in dogs. This effect, if unwanted, can be mitigated by fasting.

Cat (intramuscular or subcutaneous use)
For sedation:
2 mg xylazine/kg bodyweight intramuscularly (corresponding to 0.1 ml of the product per kg bodyweight).
2 to 4 mg xylazine/kg bw subcutaneously (corresponding to 0.1 to 0.2 ml of the product per kg bodyweight).

Very often the application of the product causes vomiting in cats. This effect, if unwanted, can be mitigated by fasting.

The bromobutyl stopper can be punctured up to 15 times.

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

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.

4.11. Withdrawal period(s)

Cattle, horse:
Meat and offal: one day.

Cattle, horse:
Milk: zero hours.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: nervous system; psycholeptics; hypnotics and sedatives
ATCvet code: QN05CM92.

5.1. Pharmacodynamic properties

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 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 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- an 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.

5.2. Pharmacokinetic particulars

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). 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.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Methyl parahydroxybenzoate (E218)
Sodium chloride
Sodium carbonate (for pH adjustment)
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: 3 years.
Shelf life after first opening the container: 28 days.

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
After opening the immediate packing, store below 25 °C.

6.5. Nature and composition of the immediate packaging

50 ml clear, type II glass bottle, closed with a bromobutyl rubber stopper and secured with an aluminium cap.
Package size: 50 ml or 5x50 ml in a cardboard box.

6.6. Special precautions for the disposal of unused veterinary medicinal products 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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Vanapere tee 14, Püünsi
Viimsi rural municipality
Harju county 74013
Estonia
Tel.: +372 6 005 005
E-mail: info@interchemie.ee

8. MARKETING AUTHORISATION NUMBER(S)

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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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

10. DATE OF REVISION OF THE TEXT

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

PROHIBITION OF SALE, SUPPLY AND/OR USE

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