Part I B Summary of product characteristics, label and package insert

Summary of Product Characteristics

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Narcostop 5 mg/ml solution for injection for cats and dogs
(NL, AT, BE, CZ, EL, FR, HU, IS, LU, PL, SK)

Sedastop 5 mg/ml solution for injection for cats and dogs
(SE, NO, DK, ES, IE, PT, IT, UK, FI)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution for injection contains:

Active substance:
Atipamezole hydrochloride 5.0 mg
(Equivalent to 4.27 mg of atipamezole)

Excipients:
Methyl parahydroxybenzoate (E 218) 1.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A clear colourless, sterile aqueous solution.

4. CLINICAL PARTICULARS

4.1 Target species
Dogs and cats

4.2 Indications for use, specifying the target species
Atipamezole hydrochloride is indicated for reversal of the sedative effects and cardiovascular effects after use of alpha-2- agonists like medetomidine and dexmedetomidine in dogs and cats.

4.3 Contraindications
Do not use in:
- Breeding animals
- Animals suffering from liver-, renal or cardiac diseases

See also section 4.7

4.4 Special warnings for each target species

Make sure the animal has regained a normal swallowing reflex before any food or drink is offered.

4.5 Special precautions for use

Special precautions for use in animals

After administration of the product, the animals should be allowed to rest in a quiet place. During recovery time animals should not be left unattended.

Due to different dosing recommendations caution should be taken if using the product off-label in animals other than the target species.

If other sedatives than medetomidine are given it must be kept in mind that the effects of those other agents may persist after reversal of (dex)medetomidine.

Atipamezole does not reverse the effect of ketamine, which may cause seizures in dogs and elicit cramps in cats when used alone. Do not use atipamezole earlier than 30-40 minutes after concomitant administration of ketamine.

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

Due to the potent pharmacological activity of atipamezole, skin-, eye- and mucous membrane-contact with this product should be avoided. In case of accidental spillage wash the affected area immediately with clean running water. Seek medical attention if irritation persists. Remove contaminated clothes that are in direct contact with the skin.

Care should be taken to avoid accidental ingestion or self-injection. In case of accidental ingestion or self-injection occurs, seek medical advice immediately and show the package leaflet to the physician."

4.6 Adverse reactions (frequency and seriousness)

A transient hypotensive effect has been observed during the first 10 minutes post-injection of atipamezole hydrochloride. In rare cases hyperactivity, tachycardia, salivation, atypical vocalization, muscle tremor, vomiting, increased respiratory rate, uncontrolled urination and uncontrolled defecation may occur.

In very rare cases recurrence of sedation may occur or the recovery time may not be shortened after administration of atipamezole.

In cats, when using low doses to partially reverse the effects of medetomidine or dexmedetomidine, the possibility of hypothermia (even when aroused from sedation) should be guarded against.

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)."

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.
The product should not be administered to pregnant and lactating bitches and queens

4.8 Interaction with other medicinal products and other forms of interaction

A simultaneous administration of atipamezole with other centrally acting medicinal products such as diazepam, acepromazine or opiates is not recommended.

4.9 Amount to be administered and administration route

For single intramuscular use.

Atipamezole hydrochloride is administered 15-60 min after medetomidine or dexmedetomidine hydrochloride administration.

Dogs: the intramuscular atipamezole hydrochloride dose [in µg] is five times that of the previous medetomidine hydrochloride dose or ten times that of the dexmedetomidine hydrochloride dose. Due to the 5-fold higher concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the 10-fold higher concentration compared to that of preparations containing 0.5 mg dexmedetomidine hydrochloride, an equal volume of each preparation is required.

Dosage example Dogs:

Medetomidine 1 mg/ml solution for injection dosage	Narcostop 5 mg/ml solution for injection for dogs dosage
0.04 ml/kg body weight (bw), i.e. 40 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml solution for injection dosage	Narcostop 5 mg/ml solution for injection for dogs dosage
0.04 ml/kg body weight (bw), i.e. 20 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw

Cats: the intramuscular atipamezole hydrochloride dose [in µg] is two-and-a-half times that of the previous medetomidine hydrochloride dose or five times that of the dexmedetomidine hydrochloride dose. Due to the 5-fold higher concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the 10-fold higher concentration compared to that of preparations containing 0.5 mg dexmedetomidine hydrochloride, half the volume of the product to that of the previously administered medetomidine or dexmedetomidine should be given.

Dosage example Cats:

Medetomidine 1 mg/ml solution for injection dosage	Narcostop 5 mg/ml solution for injection for cats dosage
0.08 ml/kg body weight (bw), i.e. 80 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml	Narcostop 5 mg/ml solution for

solution for injection dosage	injection for cats dosage
0.08 ml/kg body weight (bw), i.e. 40 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw

The recovery time is shortened to approximately 5 minutes. The animal becomes mobile after approximately 10 minutes after administration of the product.

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

Overdose of atipamezole hydrochloride may result in transient tachycardia and over-alertness (hyperactivity, muscle tremor). If necessary, these symptoms may be reversed by a (dex)medetomidine hydrochloride dose which is lower than the usually used clinical dose.

If atipamezole hydrochloride is inadvertently administered to an animal not previously treated with (dex)medetomidine hydrochloride, hyperactivity and muscle tremor may occur. These effects may persist for about 15 minutes. Over-alertness in the cat is best handled by minimizing external stimuli.

4.11 Withdrawal periods

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

ATCvet code: QV03AB90
Pharmacotherapeutic group: α2-receptor antagonist (Antidote)

5.1 Pharmacodynamic properties

Atipamezole is a potent and selective α2-receptor blocking agent (α2-antagonist), which promotes the release of the neurotransmitter noradrenaline in the central as well as in the peripheral nervous systems. This leads to activation of the central nervous system due to sympathetic activation. Other pharmacodynamic effects as for example influence of the cardiovascular system are only mild – but a transient decrease of blood pressure may be seen with the first 10 minutes after injection of atipamezole hydrochloride.

As a α2-antagonist, atipamezole is capable of eliminating (or inhibiting) the effects of the α2-receptor agonist, medetomidine or dexmedetomidine. Thus atipamezole reverses the sedative effects of (dex)medetomidine hydrochloride in dogs and cats to normal and may lead to a transient increase in heart rate.

5.2 Pharmacokinetic particulars

Atipamezole hydrochloride is rapidly absorbed after intramuscular injection. The maximal concentration in the central nervous system is reached in 10-15 minutes. Volume of distribution (V_d) is about 1 – 2.5 l/kg. The half-life of atipamezole hydrochloride is reported to be approximately 1 hour. Atipamezole hydrochloride is rapidly and completely metabolized. The metabolites are mainly excreted in urine and in a small amount in faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E 218)
Sodium chloride
Hydrochloric acid (for pH-adjustment)
Sodium hydroxide (for pH-adjustment)
Water for injections

6.2 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 immediate packaging: 28 days.

6.4 Special precautions for storage

Keep the vial in the outer carton in order to protect from light.
Do not freeze.

6.5 Nature and composition of immediate packaging

Clear glass (type I) vial with bromobutylrubber stopper (type I) containing 10 ml solution for injection.
Cardboard box with 1 vial containing 10 ml.
Cardboard box with 5 vials containing 10 ml.
Cardboard box with 10 vials containing 10 ml.

Not all pack sizes may be marketed.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION

10. DATA OF REVISION OF THE TEXT

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Narcostop 5 mg/ml solution for injection
Atipamezole hydrochloride

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml solution for injection contains:

Active substance:
Atipamezole hydrochloride 5.0 mg
(Equivalent to 4.27 mg of atipamezole)

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

10 ml,
5 x 10 ml
10 x 10 ml

5. TARGET SPECIES

For dogs and cats.

6. INDICATIONS

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use. Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

Accidental injection is dangerous.

10. EXPIRY DATE

EXP:
Shelf life after first opening the container: 28 days.
Once broached, use by…….

11. SPECIAL STORAGE CONDITIONS

Do not freeze
Keep the vial in the outer carton in order to protect from light.

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

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

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot:

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Narcostop 5 mg/ml solution for injection
Atipamezole hydrochloride

2. QUANTITY OF THE ACTIVE SUBSTANCE

Atipamezole hydrochloride 5 mg/ml

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

10 ml

4. ROUTE(S) OF ADMINISTRATION

IM

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Batch:

7. EXPIRY DATE

EXP:

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

PACKAGE LEAFLET

Narcostop 5 mg/ml solution for injection for cats and 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:

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

Manufacturer responsible for batch release:

Produlab Pharma B.V.
Forellenweg 16
4941 SJ Raamsdonksveer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Narcostop 5 mg/ml - solution for injection for cats and dogs
Active substance: Atipamezole hydrochloride

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

Narcostop is an aqueous solution for injection containing:

Active substance:
Atipamezole hydrochloride 5.0 mg/ml
(Equivalent to 4.27 mg of atipamezole)

Excipients:
Methyl parahydroxybenzoate (E 218) 1.0 mg/ml

4. INDICATION(S)

Dogs and Cats:
Atipamezole hydrochloride is indicated for reversal of the sedative effects and cardiovascular effects after use of alpha-2- agonists like medetomidine and dexmedetomidine in dogs and cats.

5. CONTRAINDICATIONS

Do not use in:
- Breeding animals
- Animals suffering from liver-, renal or cardiac diseases

6. ADVERSE REACTIONS

A transient hypotensive effect has been observed during the first 10 minutes post-injection of atipamezole hydrochloride. In rare cases hyperactivity, tachycardia, salivation, atypical vocalization, muscle tremor, vomiting, increased respiratory rate, uncontrolled urination and uncontrolled defecation may occur.
In very rare cases recurrence of sedation may occur or the recovery time may not be shortened after administration of atipamezole.

In cats, when using low doses to partially reverse the effects of medetomidine or dexmedetomidine, the possibility of hypothermia (even when aroused from sedation) should be guarded against.

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).

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

7. TARGET SPECIES

Dogs and Cats

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

For single intramuscular use.

Atipamezole hydrochloride is administered 15-60 min after medetomidine or dexmedetomidine hydrochloride administration.

Dogs: the intramuscular atipamezole hydrochloride dose [in µg] is five times that of the previous medetomidine hydrochloride dose or ten times that of the dexmedetomidine hydrochloride dose. Due to the 5-fold higher concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the 10-fold higher concentration compared to that of preparations containing 0.5 mg dexmedetomidine hydrochloride, an equal volume of each preparation is required.

Dosage example Dogs:

Medetomidine 1 mg/ml solution for injection dosage	Narcostop 5 mg/ml solution for injection for dogs dosage
0.04 ml/kg body weight (bw), i.e. 40 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml solution for injection dosage	Narcostop 5 mg/ml solution for injection for dogs dosage
0.04 ml/kg body weight (bw), i.e. 20 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw

Cats: the intramuscular atipamezole hydrochloride dose [in µg] is two-and-a-half times that of the previous medetomidine hydrochloride dose or five times that of the dexmedetomidine hydrochloride dose. Due to the 5-fold higher concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the 10-fold higher concentration compared to that of preparations containing 0.5 mg dexmedetomidine hydrochloride, half the volume of the product to that of the previously administered medetomidine or dexmedetomidine should be given.

Dosage example Cats:

Medetomidine 1 mg/ml solution for injection dosage	Narcostop 5 mg/ml solution for injection for cats dosage
0.08 ml/kg body weight (bw), i.e. 80 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml solution for injection dosage	Narcostop 5 mg/ml solution for injection for cats dosage
0.08 ml/kg body weight (bw), i.e. 40 µg/kg bw	0.04 ml/kg bw, i.e. 200 µg/kg bw

The recovery time is shortened to approximately 5 minutes. The animal becomes mobile after approximately 10 minutes after administration of the product.

9. ADVICE ON CORRECT ADMINISTRATION

None

10. WITHDRAWAL PERIOD

Not applicable

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Keep the vial in the outer carton in order to protect from light. Do not freeze
Do not use this veterinary medicinal product after the expiry date which is stated on the label and on the carton after EXP
Shelf-life after first opening the immediate packaging: 28 days.

When the container is broached (opened) 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 carton should be discarded should be worked out. This discard date should be written in the space provided.

12. SPECIAL WARNING(S)

Special precautions for use in animals

After administration of the product, the animals should be allowed to rest in a quiet place. During recovery time animals should not be left unattended.

Make sure the animal has regained a normal swallowing reflex before any food or drink is offered.

Due to different dosing recommendations caution should be taken if using the product off-label in animals other than the target species.

If other sedatives than medetomidine are given it must be kept in mind that the effects of those other agents may persist after reversal of (dex)medetomidine.

Atipamezole does not reverse the effect of ketamine, which may cause seizures in dogs and elicit cramps in cats when used alone. Do not use atipamezole earlier than 30-40 minutes after concomitant administration of ketamine.

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

Due to the potent pharmacological activity of atipamezole, skin-, eye- and mucous membrane- contact with this product should be avoided. In case of accidental spillage wash the affected area immediately with clean running water. Seek medical attention if irritation persists. Remove contaminated clothes that are in direct contact with the skin.

Care should be taken to avoid accidental ingestion or self-injection In case of accidental ingestion or self-injection occurs, seek medical advice immediately and show the package leaflet to the physician."

Use during pregnancy, lactation or lay

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

The product should not be administered to pregnant and lactating bitches and queens

Interaction with other medicinal products and other forms of interaction

A simultaneous administration of atipamezole with other centrally acting medicinal products such as diazepam, acepromazine or opiates is not recommended.

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

Overdose of atipamezole hydrochloride may result in transient tachycardia and over-alertness (hyperactivity, muscle tremor). If necessary, these symptoms may be reversed by a (dex)medetomidine hydrochloride dose which is lower than the usually used clinical dose.

If atipamezole hydrochloride is inadvertently administered to an animal not previously treated with (dex)medetomidine hydrochloride, hyperactivity and muscle tremor may occur. These effects may persist for about 15 minutes. Over-alertness in the cat is best handled by minimizing external stimuli.

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 requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

<MM/YYYY>

15. OTHER INFORMATION

1 x 1 glass vial with 10 ml.
5 x 1 glass vials with 10 ml.
10 x 1 glass vial with 10 ml.
Not all pack sizes may be marketed.

To be supplied only on veterinary prescription.