1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alzane 5 mg/ml, solution for injection for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:	
Atipamezole hydrochloride	5.0 mg
(equivalent to 4.27 mg atipamezole base)	
Excipients	
Methyl parahydroxybenzoate (E 218)	1.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear and 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 a selective α2-antagonist and indicated for reversal of the sedative effects of medetomidine and dexmedetomidine in dogs and cats.

4.3 Contraindications

Do not use in animals with known hypersensitivity to the active substance or to any of the excipients.
Do not use in breeding animals or animals suffering from hepatic, renal or cardiac diseases.
See also section 4.7

4.4 Special warnings for each target species

None

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 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 using the product off label in animals other than the target species.
If sedatives other than medetomidine or dexmedetomidine are given, it must be kept in mind that the effects of those other agents may persist after the reversal of the effect of the α2-agonist.
Atipamezole does not reverse the effect of ketamine, which may cause seizures in dogs and elicit cramps in cats when used alone. Do not administer atipamezole within 30–40 minutes of prior

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, contact of the product with skin, eyes and mucous membranes should be avoided. In case of accidental contact of the product with skin or eyes rinse abundantly with fresh 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 oral intake or self-injection, seek medical advice immediately and show the package insert to the physician. Do not drive. The patient should not be left unattended.

4.6. Adverse reactions (frequency and seriousness)

A transient hypotensive effect has been observed during the first 10 minutes after the injection of atipamezole hydrochloride. In rare cases hyperactivity, tachycardia, salivation, atypical vocalisation, 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 a low dose to partially reverse the effects of medetomidine or dexmedetomidine, the possibility of hypothermia (even when aroused from sedation) should be kept in mind.

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 or lactation.

The safety of the product has not been established during pregnancy and lactation. Therefore the use is not recommended during pregnancy and lactation.

4.8. Interactions with other veterinary medicinal products and other forms of interaction

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

4.9 Amounts to be administered and administration route

. For single intramuscular use. The dose depends on the previously administered medetomidine or dexmedetomidine dose. Use of an appropriately graduated syringe is recommended to ensure accurate dosing when administering small volumes. Atipamezole is generally administered 15-60 minutes after medetomidine or dexmedetomidine injection.

Dogs: The dose of atipamezole hydrochloride (in µg per kg of bodyweight) is five times that of the previous dose of medetomidine hydrochloride or ten times that of the dose of dexmedetomidine hydrochloride. Due to the fivefold concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the tenfold concentration compared to that of preparations containing 0.5 mg dexmedetomidine hydrochloride, an equal volume of each preparation is required.

Due to the 50-fold concentration compared to that preparations containing 0.1 mg dexmedetomidine hydrochloride, a volume 5 times lower of the atipamezole preparation is required.

Dosage example dogs:

Medetomidine 1.0 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.04 ml/kg body weight (bw), corresponding with 40 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.04 ml/kg body weight (bw), corresponding with 20 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw
Dexmedetomidine 0.1 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.2 ml/kg body weight (bw), corresponding with 20 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw

Cats: The atipamezole hydrochloride dose (in µg per kg of bodyweight) is 2.5 times that of the previous dose of medetomidine hydrochloride or five times that of the dose of dexmedetomidine hydrochloride. Due to the fivefold concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the tenfold 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.

Due to the 50-fold concentration compared to that preparations containing 0.1 mg dexmedetomidine hydrochloride, a volume 10 times lower of the atipamezole preparation is required.

Dosage example cats:

Medetomidine 1.0 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.08 ml/kg body weight (bw), corresponding with 80 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.08 ml/kg body weight (bw), corresponding with 40 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw
Dexmedetomidine 0.1 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.4 ml/kg body weight (bw), corresponding with 40 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw

The recovery time for dogs and cats is shortened to approximately 5 minutes. The animals become 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 signs may be reversed by a medetomidine or dexmedetomidine hydrochloride dose which is lower than usually used clinically.

If atipamezole hydrochloride is inadvertently administered to an animal not previously treated with medetomidine or dexmedetomidine 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

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

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 such as impact on the cardiovascular system are mild, although a transient decrease in blood pressure may occur within the first 10 minutes following administration of atipamezole hydrochlodride. 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 medetomidine and dexmedetomidine 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 (Vd) is about 1–2.5 l/kg. The half-life (t½) of atipamezole hydrochloride is reported to be approximately 1 hour. Atipamezole hydrochloride is rapidly and completely metabolised. The metabolites are mainly excreted in urine with a small amount excreted in faeces.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E 218)
Sodium chloride
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.
See also section 4.8.

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:	28 days

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Clear glass type II vials of 10 ml, with type I bromobutyl stopper and aluminium cap.

Pack sizes:
Cardboard box with 1 vial of 10 ml
Cardboard box with 5 vials of 10 ml
Cardboard box with 10 vials of 10 ml

Not all pack sizes may be marketed.

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 material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Laboratorios SYVA S.A.U
Avda. Párroco Pablo Díez 49-57
24010 León
Spain

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

dd.mm.yyyy

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

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

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{cardboard box}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alzane 5 mg/ml solution for injection for dogs and cats
atipamezole hydrochloride

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Atipamezole hydrochloride 5 mg/ml

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

10 ml
5x10ml
10x10ml

5. TARGET SPECIES

Dogs and cats

6. INDICATION(S)

Read the package leaflet before use

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 - Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached use within 28 days

11. SPECIAL STORAGE CONDITIONS

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

Laboratorios SYVA S.A.U, Spain
Avda. Párroco Pablo Díez, 49-57
24010 León (Spain)

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alzane 5 mg/ml solution for injection for dogs and cats
atipamezole hydrochloride

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

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

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once broached use by _____

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

PACKAGE LEAFLET FOR:
Alzane 5 mg/ml solution for injection for 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 and manufacturer responsible for batch release:
Laboratorios SYVA S.A.U, Avda. Párroco Pablo Díez 49-57, 24010 León, Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alzane 5 mg/ml solution for injection for dogs and cats
atipamezole hydrochloride

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

The product is a clear and colourless sterile aqueous solution. Each ml of solution contains 5 mg of atipamezole hydrochloride as active substance and 1 mg of methyl parahydroxybenzoate (E218) as preservative.

4. INDICATIONS

Atipamezole hydrochloride is a selective α2-antagonist and indicated for reversal of the sedative effects of medetomidine and dexmedetomidine in dogs and cats.

5. CONTRAINDICATIONS

Do not use in animals with known hypersensitivity to the active substance or to any of the excipients.

Do not use in breeding animals or animals suffering from hepatic, renal or cardiac diseases.

See also section 12.

6. ADVERSE REACTIONS

A transient hypotensive effect has been observed during the first 10 minutes after the injection of atipamezole hydrochloride. In rare cases hyperactivity, tachycardia, salivation, atypical vocalisation, 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 a low dose to partially reverse the effects of medetomidine or dexmedetomidine, the possibility of hypothermia (even when aroused from sedation) should be kept in mind.

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 other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs and cats

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

For single intramuscular use. The dose depends on the previously administered medetomidine or dexmedetomidine dose. Use of an appropriately graduated syringe is recommended to ensure accurate dosing when administering small volumes. Atipamezole is generally administered 15-60 minutes after medetomidine or dexmedetomidine injection.
Dogs: The dose of atipamezole hydrochloride (in µg per kg of bodyweight) is five times that of the previous dose of medetomidine hydrochloride or ten times that of the dose of dexmedetomidine hydrochloride. Due to the fivefold concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the tenfold concentration compared to that of preparations containing 0.5 mg dexmedetomidine hydrochloride, an equal volume of each preparation is required.

Due to the 50-fold concentration compared to that preparations containing 0.1 mg dexmedetomidine hydrochloride, a volume 5 times lower of the atipamezole preparation is required.

Dosage example dogs:

Medetomidine 1.0 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.04 ml/kg body weight (bw), corresponding with 40 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.04 ml/kg body weight (bw), corresponding with 20 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw
Dexmedetomidine 0.1 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.2 ml/kg body weight (bw), corresponding with 20 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw

Cats: The atipamezole hydrochloride dose (in µg) is 2.5 times that of the previous dose of medetomidine hydrochloride or five times that of the dose of dexmedetomidine hydrochloride. Due to the fivefold concentration of the active ingredient (atipamezole hydrochloride) in this product compared to that of preparations containing 1 mg medetomidine hydrochloride per ml and the tenfold 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.

Due to the 50-fold concentration compared to that preparations containing 0.1 mg dexmedetomidine

hydrochloride, a volume 10 times lower of the atipamezole preparation is required.

Dosage example cats:

Medetomidine 1.0 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.08 ml/kg body weight (bw), corresponding with 80 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw
Dexmedetomidine 0.5 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.08 ml/kg body weight (bw), corresponding with 40 µg/kg bw	0.04 ml/kg body weight (bw),, corresponding with 200 µg/kg bw
Dexmedetomidine 0.1 mg/ml solution for injection dosage	**Atipamezole hydrochloride 5.0 mg/ml solution for injection dosage**
0.4 ml/kg body weight (bw), corresponding with 40 µg/kg bw	0.04 ml/kg body weight (bw), corresponding with 200 µg/kg bw

The recovery time for dogs and cats is shortened to approximately 5 minutes. The animals become mobile after approximately 10 minutes after administration of the product.

9. ADVICE ON CORRECT ADMINISTRATION

-

10. WITHDRAWAL PERIOD

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP: The expiry date refers to the last day of that month.
Shelf-life after first opening the container: 28 days

12. SPECIAL WARNINGS

Special precautions for use in animals**:** After administration of the product, the animals should be allowed to rest in a quiet place. During recovery 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 using the product off label in animals other than the target species. If sedatives other than medetomidine or dexmedetomidine are given, it must be kept in mind that the effects of those other agents may persist after the reversal of the effect of the α2-agonist. Atipamezole does not reverse the effect of ketamine, which may cause seizures in dogs and elicit cramps in cats when used alone. Do not administer atipamezole within 30–40 minutes of prior 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, contact of the product with skin, eyes and mucous membranes should be avoided. In case of accidental contact of the product with skin or eyes rinse abundantly with fresh 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 oral intake or self-injection, seek medical advice immediately and show the package insert to the physician. Do not drive. The patient should not be left unattended.

Pregnancy**:**

The safety of the product has not been established during pregnancy. Therefore the use is not recommended during pregnancy.

Lactation**:**
The safety of the product has not been established during lactation. Therefore the use is not recommended during lactation.

Interactions with other veterinary medicinal products and other forms of interaction**:** Simultaneous administration of atipamezole with other centrally acting medicinal products such as diazepam, acepromazine or opiates is not recommended.

Overdose (symptoms, emergency procedures, antidotes):
Overdose of atipamezole hydrochloride may result in transient tachycardia and over-alertness (hyperactivity, muscle tremor). If necessary, these signs may be reversed by a medetomidine hydrochloride dose which is lower than usually used clinically. If atipamezole hydrochloride is inadvertently administered to an animal not previously treated with medetomidine or dexmedetomidine 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.
See section 12.

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. Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack sizes:
Cardboard box with 1 vial of 10 ml
Cardboard box with 5 vials of 10 ml
Cardboard box with 10 vials of 10 ml

Not all pack sizes may be marketed.
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

When the container is broached (opened) for the first time, the date on which any product remaining in the container should be discarded and be worked out using the in-use shelf-life which is specified on this package leaflet. This discard date should be written in the space provided on the label.