[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alzane 5 mg/ml solution for injection for dogs and cats
(In Finland and Sweden: Alzane vet. 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:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Methyl parahydroxybenzoate (E 218)	1.0 mg
Sodium chloride	
Water for injections	

Clear and colourless aqueous solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats.

3.2 Indications for use for each 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.

3.3 Contraindications

Do not use in cases of 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 3.7.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

After administration of the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product with skin, eyes and mucous membranes should be avoided. In case of accidental contact of the veterinary medicinal product with skin or eyes rinse abundantly with fresh water. Remove contaminated clothes that are in direct contact with the skin. Seek medical advice if irritation persists. Care should be taken to avoid accidental ingestion or self-injection. In case of accidental ingestion or self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Do not drive. The patient should not be left unattended.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cats:

Rare (1 to 10 animals / 10,000 animals treated):	Hyperactivity, impaired vocalisation, Tachycardia Hypersalivation, vomiting, involuntary defecation Muscle tremor Increased respiratory rate Urinary incontinence
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypotension[1] Sedation prolonged, recovery prolonged Hypothermia[2]

(1) During the first 10 minutes after the injection.
(2) 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.

Dogs:

Rare (1 to 10 animals / 10,000 animals treated):	Hyperactivity, impaired vocalisation Tachycardia Hypersalivation, vomiting, involuntary defecation Muscle tremor

	Increased respiratory rate Urinary incontinence
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypotension[1] Sedation prolonged, recovery prolonged

(1) During the first 10 minutes after the injection.

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 and lactation:

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

Fertility:
Do not use in breeding animals.

3.8 Interaction with other 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.

3.9 Administration routes and dosage

Intramuscular use.

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.

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

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 veterinary medicinal 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 those 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 veterinary medicinal 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 veterinary medicinal product to that of the previously administered medetomidine or dexmedetomidine should be given.

Due to the 50-fold concentration compared to those 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 veterinary medicinal product.

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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 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.

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

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QV03AB90

4.2 Pharmacodynamics

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 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 medetomidine and dexmedetomidine hydrochloride in dogs and cats to normal and may lead to a transient increase in heart rate.

4.3 Pharmacokinetics

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.

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: 2 years
Shelf-life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

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

5.4 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.

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

Laboratorios SYVA S.A.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

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

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).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box with 1 vial of 10 ml
Cardboard box with 5 vials of 10 ml
Cardboard box with 10 vials of 10 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alzane 5 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Atipamezole hydrochloride 5.0 mg
(equivalent to 4.27 mg atipamezole base)

3. PACKAGE SIZE

10 ml
5x10ml
10x10ml

4. TARGET SPECIES

Dogs and cats

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intramuscular use

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days
Once opened use by…

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Laboratorios SYVA S.A.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alzane

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Atipamezole hydrochloride 5.0 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 28 days
Once opened use by…

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Alzane 5 mg/ml solution for injection for dogs and cats
(In Finland and Sweden: Alzane vet. 5 mg/ml, solution for injection for dogs and cats)

2. 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

Clear and colourless aqueous solution.

3. Target species

Dogs and cats.

4. Indications for use

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 cases of 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 6, pregnancy and lactation.

6. Special warnings

Special precautions for safe use in the target species:
After administration of the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product with skin, eyes and mucous membranes should be avoided. In case of accidental contact of the veterinary medicinal product with skin or eyes rinse abundantly with fresh water. Remove contaminated clothes that are in direct contact with the skin. Seek medical advice if irritation persists.

Care should be taken to avoid accidental ingestion or self-injection. In case of accidental ingestion or self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Do not drive. The patient should not be left unattended.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation. The use is not recommended during pregnancy and lactation.

Fertility:
Do not use in breeding animals.

Interaction with other 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:
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.

Special restrictions for use and special conditions for use:

Major incompatibilities:
In the absence of compatibility studies this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Cats:

Rare (1 to 10 animals / 10,000 animals treated):	Hyperactivity, impaired vocalisation, Tachycardia (rapid heart rate) Hypersalivation, vomiting, involuntary defecation Muscle tremor Increased respiratory rate Urinary incontinence
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypotension (low blood pressure)[1] Sedation prolonged, recovery prolonged Hypothermia (low body temperature)[2]

(1) During the first 10 minutes after the injection.
(2) 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.

Dogs:

Rare	Hyperactivity, impaired vocalisation

(1 to 10 animals / 10,000 animals treated):	Tachycardia (rapid heart rate) Hypersalivation, vomiting, involuntary defecation Muscle tremor Increased respiratory rate Urinary incontinence
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypotension (low blood pressure)[1] Sedation prolonged, recovery prolonged

(1) During the first 10 minutes after the injection.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.
Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder <or the local representative of the marketing authorisation holder> using the contact details at the end of this leaflet, or via your national reporting system: <To be completed in accordance with national requirements after conclusion of the MRP>.

8. Dosage for each species, routes and method of administration

Intramuscular use.

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

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 veterinary medicinal 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 those 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 veterinary medicinal 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 veterinary medicinal product to that of the previously administered medetomidine or dexmedetomidine should be given.

Due to the 50-fold concentration compared to those 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 veterinary medicinal product.

9. Advice on correct administration

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10. Withdrawal periods

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 immediate packaging: 28 days

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Pack size:
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.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder:
Laboratorios SYVA S.A.,
Calle Marqués de la Ensenada, 16
28004 Madrid
Spain

Manufacturer responsible for batch release:
Laboratorios SYVA S.A.
Avenida del Párroco Pablo Díez, 49-57
San Andrés del Rabanedo
24010 León
Spain

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

<17. Other information>