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

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Reverse 5 mg/ml solution for injection for dogs and cats (ES, PT)
Atidorm 5 mg /ml solution for injection for dogs and cats (IT)

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 solution

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats.

3.2 Indications for use for each target species

To reverse the sedative effects produced by medetomidine or dexmedetomidine in dogs and cats in order to recover the animal.
To reverse the possible overdose of medetomidine.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals suffering from hepatic or renal or cardiac diseases or poor health status.
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:

Atipamezole does not reverse the effect of ketamine, which can cause seizures in dogs and cause cramps in cats when used alone. Do not administer atipamezole within 30-40 minutes of prior administration of ketamine.

After administration of the veterinary medicinal product, the animals should be allowed to rest in a quiet place. During the recovery phase, 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 other sedatives different than (dex)medetomidine are administered, it must be taken into account that the effects of these other agents are likely to persist after the reversal of the effects of (dex)medetomidine.

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 spillage onto skin, wash the affected area immediately with clean running water. Seek medical attention if irritation persists. Remove contaminated clothes that are in direct contact with skin.
Care should be taken to avoid accidental ingestion or self-injection. In case of accidental self-injection or ingestion, 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

Dogs and cats:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Tachycardia, low blood pressure[a]; Increased respiratory rate, dyspnoea; Faecal incontinence, vomiting, diarrhoea, hypersalivation; Urinary incontinence; Hyperactivity, impaired vocalisation; Muscle tremor, sedation prolonged, recovery prolonged.

[a] slight transient decrease of arterial pressure during the first ten minutes post-injection.

Cats:

Undetermined frequency (cannot be estimated from the available data)	Hypothermia[a].

[a] 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.

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 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.

3.8 Interaction with other medicinal products and other forms of interaction

Concurrent use of atipamezole with other drugs affecting the Central nervous system (such as diazepam, acepromazine or opiates) is not recommended.

3.9 Administration routes and dosage

For single intramuscular use.

The dose depends on the previously administered medetomidine or dexmedetomidine dose.

Dogs: The dose of atipamezole hydrochloride (in µg/kg of body weight) is five times that of the previous dose of medetomidine hydrochloride or ten times that of the dose of dexmedetomidine hydrochloride. Due to the 5-fold higher concentration of the active ingredient (atipamezole hydrochloride) in this veterinary medicinal product compared to that of preparations containing 1 mg/ml medetomidine hydrochloride, and the 10-fold concentration compared to that preparations containing 0.5 mg/ml dexmedetomidine hydrochloride, an equal volume of each preparation is required. Due to the 50-fold concentration compared to that preparations containing 0.1 mg/ml dexmedetomidine hydrochloride, a volume 5 times lower of the atipamezole preparation is required.

Dosage example in 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 dose of atipamezole hydrochloride (in µg/kg of body weight) is 2.5 times that of the previous dose of medetomidine hydrochloride or 5 times that of the dose of dexmedetomidine hydrochloride. Due to the 5-fold concentration of the active ingredient (atipamezole hydrochloride) in this veterinary medicinal product compared to that of preparations containing 1 mg/ml medetomidine hydrochloride and the 10-fold concentration compared to that of preparations containing 0.5 mg/ml 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 that preparations containing 0.1 mg/ml dexmedetomidine hydrochloride, a volume 10 times lower of the atipamezole preparation is required.

Dosage example in 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

In dogs and cats, atipamezole hydrochloride is administered 15-60 min after medetomidine or dexmedetomidine hydrochloride injection. The recovery time for dogs and cats is shortened to approximately 5 minutes. The animal becomes mobile 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 tremors). 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 tremors 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

To be completed nationally.

ES: <For administration only by a veterinarian>

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QV03AB90

4.2 Pharmacodynamics

Atipamezole is a selective and potent agent which blocks the α-2 receptors (α-2 antagonist) which induces the release of neurotransmitter, noradrenalin, in central and peripheral nervous system which results in an activation of the central nervous system through sympathetic activation. Other pharmacodynamics effects that may be observed, such as influence on the cardiovascular system, for example, are light.

As α-2 antagonist, atipamezole is capable of eliminating (or inhibiting) the effects of the α-2 receptor agonists such as medetomidine or dexmedetomidine.

4.3 Pharmacokinetics

Atipamezole hydrochloride is quickly absorbed after intramuscular injection. The maximal concentration in the central nervous system is reached in 10-15 minutes. It is also quickly and completely metabolised. Metabolites are excreted mainly in urine and faeces in small amounts.

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

Type I colourless glass vial of 10 ml fitted with a bromobutyl rubber stopper and sealed with an aluminium cap with plastic flip-off in a cardboard box.

Package size:
Cardboard box with 1 vial of 10 ml

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

FATRO S.p.A.

7. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: DD/MM/YYYY.

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

MM/YYYY

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:
1 x 10 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Reverse 5 mg/ml solution for injection for dogs and cats (ES, PT)
Atidorm 5 mg/ml solution for injection for dogs and cats (IT)

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

4. TARGET SPECIES

Dogs and cats.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

For intramuscular use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp{mm/yyyy}
Once broached use within 28 days.
Once broached 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

FATRO S.p.A.

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally.

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

10 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Reverse (ES, PT)
Atidorm (IT)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

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

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp {mm/yyyy}
Once broached use within 28 days.
Once broached use by ….

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Reverse 5 mg/ml solution for injection for dogs and cats (ES, PT)
Atidorm 5 mg/ml solution for injection for dogs and cats (IT)

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 solution.

3. Target species

Dogs and cats.

4. Indications for use

To reverse the sedative effects produced by medetomidine or dexmedetomidine in dogs and cats in order to recover the animal.
To reverse the possible overdose of medetomidine.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals suffering from hepatic or renal or cardiac diseases or poor health status.
See also pregnancy and lactation subsection at point 6.

6. Special warnings

Special precautions for safe use in the target species:
Atipamezole does not reverse the effect of ketamine, which can cause seizures in dogs and cause cramps in cats when used alone. Do not administer atipamezole within 30-40 minutes of prior administration of ketamine.
After administration of the veterinary medicinal product, the animals should be allowed to rest in a quiet place. During the recovery phase, 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 other sedatives different than (dex)medetomidine are administered, it must be taken into account that the effects of these other agents are likely to persist after the reversal of the effects of (dex)medetomidine.

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 spillage onto skin, wash

the affected area immediately with clean running water. Seek medical attention if irritation persists. Remove contaminated clothes that are in direct contact with skin.
Care should be taken to avoid accidental ingestion or self-injection. In case of accidental self-injection or ingestion, 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 product has not been established during pregnancy and lactation. Therefore the use is not recommended during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:
Concurrent use of atipamezole with other drugs affecting the Central nervous system (such as diazepam, acepromazine or opiates) is not recommended.

Overdose:
Overdose of atipamezole hydrochloride may result in transient tachycardia and over-alertness (hyperactivity, muscle tremors). If necessary, these signs may be reversed by a medetomidine or dexmedetomidine 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 tremors 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:
Not applicable.

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

7. Adverse events

Dogs and cats:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Tachycardia, low blood pressure[a]; Increased respiratory rate, dyspnoea; Faecal incontinence, vomiting, diarrhoea, hypersalivation; Urinary incontinence; Hyperactivity, impaired vocalisation; Muscle tremor, sedation prolonged, recovery prolonged.

[a] slight transient decrease of arterial pressure during the first ten minutes post-injection.

Cats:

Undetermined frequency (cannot be estimated from the available data)	Hypothermia[a].

[a] 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.

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: {national system details}.

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

For single intramuscular use.
The dose depends on the previously administered medetomidine or dexmedetomidine dose.

Dogs: The dose of atipamezole hydrochloride (in µg/kg of body weight) is five times that of the previous dose of medetomidine hydrochloride or ten times that of the dose of dexmedetomidine hydrochloride. Due to the 5-fold higher concentration of the active ingredient (atipamezole hydrochloride) in this veterinary medicinal product compared to that of preparations containing 1 mg/ml medetomidine hydrochloride, and the 10-fold concentration compared to that preparations containing 0.5 mg/ml dexmedetomidine hydrochloride, an equal volume of each preparation is required. Due to the 50-fold concentration compared to that preparations containing 0.1 mg/ml dexmedetomidine hydrochloride, a volume 5 times lower of the atipamezole preparation is required.

Dosage example in 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 dose of atipamezole hydrochloride (in µg/kg of body weight) is 2.5 times that of the previous dose of medetomidine hydrochloride or 5 times that of the dose of dexmedetomidine hydrochloride. Due to the 5-fold concentration of the active ingredient (atipamezole hydrochloride) in this veterinary medicinal product compared to that of preparations containing 1 mg/ml medetomidine hydrochloride and the 10-fold concentration compared to that of preparations containing 0.5 mg/ml 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 that preparations containing 0.1 mg/ml dexmedetomidine hydrochloride, a volume 10 times lower of the atipamezole preparation is required.

Dosage example in 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 animal becomes mobile approximately 10 minutes after administration of the veterinary medicinal product.

9. Advice on correct administration

In dogs and cats, atipamezole hydrochloride is administered 15-60 min after medetomidine or dexmedetomidine hydrochloride injection.

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 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 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

Cardboard box with 1 vial of 10 ml.

15. Date on which the package leaflet was last revised

MM/YYYY

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:

FATRO S.p.A.
Via Emilia, 285
40064, Ozzano dell'Emilia (BO)
Italy

Manufacturer responsible for batch release:

LABIANA LIFE SCIENCES, S.A.
C/ Venus, 26, Pol. Ind. Can Parellada,
Terrasa, 08228 Barcelona
Spain

Local representative and contact details to report suspected adverse reactions:

To be completed nationally.

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