ANNEX I

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 ..... 4.27 mg
(equivalent to atipamezole hydrochloride 5.0 mg)

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 solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and Cats.

4.2 Indications for use, specifying the 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.

4.3 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 4.7

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

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 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 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 for 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 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 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.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, the following clinical signs may be observed:
- Cardiovascular: tachycardia, slight transient decrease of arterial pressure during the first ten minutes post-injection
- Respiratory: increased respiratory rate, dyspnea
- Digestive: uncontrolled defecation, vomiting, diarrhea
- Urinary: uncontrolled urination
- Behaviour: hyperactivity, abnormal vocalization
- Neurological: hypersalivation, muscle tremors. Recurrent sedation may occur or the recovery time may not be shortened after the 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 treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)

- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

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

4.8 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.

4.9 Amounts to be administered and administration route

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 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 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 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 product.

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

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.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: α 2-receptor antagonist (antidote)
ATC Vet Code: QV03AB90

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E 218)
Sodium chloride
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 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

Type I colourless glass vial fitted with a bromobutyl rubber stopper and sealed with an aluminium cap with plastic flip-off.

Package size:
Cardboard box with 1 vial of 10 ml

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

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

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

To be completed nationally.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: *To be completed nationally.*
Date of last renewal: *To be completed nationally.*

10. DATE OF REVISION OF THE TEXT

To be completed nationally.

PROHIBITION OF SALE, SUPPLY AND/OR USE

(For Spain only, include:
For animal treatment only – to be supplied only on veterinary prescription.
Administration only by a veterinary surgeon.)