Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Pronestesic 40 mg/ml / 0.036 mg/ml solution for injection for horses, cattle, pigs and sheep

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:
Active substances:

Procaine hydrochloride	40 mg (equivalent to 34.65 mg procaine)
Epinephrine tartrate	0.036 mg (equivalent to 0.02 mg epinephrine)

Excipients:

Sodium metabisulfite (E223)	1 mg
Sodium methyl parahydroxybenzoate (E219)	1.15 mg
Disodium edetate	0.1 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
Clear colourless solution, free of visible particles.

4 CLINICAL PARTICULARS

4.1 Target Species

Horses, cattle, pigs and sheep.

4.2 Indications for use, specifying the target species

Local anaesthesia with a long-lasting anaesthetic effect.

Horses, cattle, pigs and sheep: infiltration anaesthesia and perineural anaesthesia (see section 4.5.).

4.3 Contraindications

Do not use in animals in a state of shock.
Do not use in animals with cardiovascular problems.
Do not use in animals treated with sulphonamides.
Do not use in animals treated with phenothiazine (see section 4.8).
Do not use with cyclopropane- or halothane-based anaesthetics (see section 4.8).
Do not use to anaesthetise regions with terminal circulation (ears, tail, penis, etc.), owing to the risk of tissue necrosis following complete circulatory arrest, due to the presence of epinephrine (substance with a vasoconstrictor action).
Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not administer by the intravenous or the intra-articular route.
Do not use in case of hypersensitivity to local anaesthetics belonging to the esters subgroup or in case of possible allergic cross reactions to p-aminobenzoic acid and sulphonamides.

4.4 Special warnings for each target species

None

4.5 Special precautions for use

Special precautions for use in animals

To avoid inadvertent intravenous administration, draw back the plunger of the syringe to check for the absence of blood before injecting.
Due to local tissue damage wounds or abscesses may be difficult to anaesthetise using local anaesthetics.
Perform local anaesthesia at ambient temperature. At higher temperatures, the risk of toxic reactions is higher owing to the greater absorption of procaine.
As with other local anaesthetics containing procaine, the product should be used with caution in animals with epilepsy or with changes in respiratory or renal function.

When injected near to wound edges, the product may lead to necrosis along the edges.
The product should be used with caution in lower limb blocks due to the risk of digital ischaemia.
Use with caution in horses due to risk of coat colour at the site of injection turning permanently white.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Avoid direct contact of the skin with the veterinary medicinal product. In case of spillage onto skin or eyes, rinse immediately with plenty of water. If irritation occurs, seek medical advice immediately and show the package leaflet or label to the physician.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or label to the physician.
People with known hypersensitivity to procaine or epinephrine should avoid contact with the veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

The procaine may cause hypotension.
In a few cases, particularly in horses, phenomena of excitability to the CNS may be observed (agitation, tremors, convulsions) following the administration of procaine.
Allergic reactions to procaine are quite common; only in rare cases anaphylactic reactions have been observed.
A hypersensitivity to local anaesthetics belonging to the esters subgroup is known.
In exceptional cases, tachycardia may occur (epinephrine). In case of inadvertent intravascular injection toxic reactions frequently appear. These manifest in an excitation of the central nervous system (restlessness, tremors, convulsions), followed by depression; death is the result of respiratory paralysis. In case of CNS, excitation short acting barbiturates should be administered, as well as products for acidification of urine, so as to support renal excretion. In case of allergic reactions, antihistamines or corticoids can be given. Allergic shock is treated with epinephrine.

4.7 Use during pregnancy, lactation or lay

Procaine crosses the placental barrier and is excreted in milk. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Procaine inhibits the action of the sulphonamides owing to biotransformation to p-aminobenzoic acid, a sulphonamide antagonist.
Procaine prolongs the action of myorelaxants.
Procaine potentiates the action of antiarrhythmics e.g. procainamide.
Epinephrine potentiates the action of analgesic anaesthetics on the heart.
Do not use with cyclopropane- or halothane-based anaesthetics, as they increase cardiac sensitivity to epinephrine (a sympathomimetic) and may cause arrhythmia.
Due to these interactions, the veterinarian may adjust the dosage and should carefully monitor the effects on the animal.

4.9 Amounts to be administered and administration route

- For subcutaneous and perineural use.
- For onset and duration of effect, please see section 5.1

1. Local anaesthesia or by infiltration: inject into the subcutis or around the area involved

Horses, cattle, pigs and sheep: 2.5 - 10 ml of the product/animal (corresponding to 100 - 400 mg of Procaine hydrochloride + 0.09 - 0.36 mg of Epinephrine tartrate)

2. Perineural anaesthesia: inject close to the branch of the nerve

Horses, cattle, pigs and sheep: 5 - 10 ml of the product/animal (corresponding to 200 - 400 mg of Procaine hydrochloride + 0.18 - 0.36 mg of Epinephrine tartrate).

For lower limb blocks in horses, the dose should be divided between two or more injection sites depending on the dose. See also section 4.5.

The vial may be broached up to 20 times.

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

Symptoms related to overdose correlate with symptoms occurring after inadvertent intravascular injection as described in section 4.6

4.11 Withdrawal Period(s)

Horses, cattle and sheep:
Meat and offal: zero days
Milk: zero hours

Pigs:
Meat and offal: zero days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: anaesthetics, local, procaine, combinations
ATCvet code: QN01BA52

5.1 Pharmacodynamic properties

Procaine
Procaine is a synthetic local anaesthetic belonging to the esters group.
It is an ester of p-aminobenzoic acid, which is considered the lipophilic part of this molecule. Procaine has a stabilising effect on the membrane, that is, it reduces the permeability of the membrane of nerve cells, preventing the diffusion of sodium and potassium ions. In this way, there is no action potential and the conduction of excitability is inhibited. This inhibition leads to a local anaesthesia, which is reversible. Nerve fibres show different sensitivity to local anaesthetics, which is determined by the thickness of the myelin sheath: fibres, which are not surrounded by the myelin sheath, are the most sensitive and fibres with a thin layer of myelin are anaesthetised more rapidly than those surrounded by a thicker myelin sheath.

Procaine has a latency period from 5 to 10 minutes after subcutaneous administration. Procaine has a short duration of action (maximum 30 - 60 minutes); with the addition of epinephrine to the solution, the duration of action is prolonged up to 45 - 90 minutes. The speed at which the anaesthesia is obtained depends on the animal species and age.
In addition to its local anaesthetic properties, procaine also has a vasodilator and antihypertensive action.

Epinephrine
Epinephrine is a catecholamine with sympathomimetic properties. It causes a local vasoconstriction which, slowing down absorption of procaine hydrochloride, prolongs the anaesthetic effect of procaine. The slow reabsorption of procaine decreases the risk of systemic toxic effects. Epinephrine also has a stimulant action on the myocardium.

5.2 Pharmacokinetic properties

Procaine
After parenteral administration, procaine is rapidly reabsorbed in the blood, particularly owing to its vasodilatory properties. The absorption also depends on the degree of vascularisation of the injection site. The duration of action is relatively short, owing to rapid hydrolysis by serum cholinesterase. The addition of epinephrine, which has a vasoconstrictor action, slows down absorption, prolonging the local anaesthetic effect.
Binding to proteins is negligible (2 %).
Procaine does not easily penetrate the tissues, owing to its poor liposolubility. However, it penetrates the central nervous system and the foetal plasma.
Procaine is rapidly and almost entirely hydrolysed to p-aminobenzoic acid and diethylaminoethanol by non-specific pseudocholinesterases, principally present in the plasma but also in the microsomes of the liver and other tissues. P-aminobenzoic acid, which inhibits the action of sulphonamides, is conjugated in its turn, for example with glucuronic acid, and excreted renally. Diethylaminoethanol, which is an active metabolite, decomposes in the liver. The metabolism of procaine differs from one animal species to the other.
The plasma half-life of procaine is short (60 - 90 minutes). It is rapidly and totally excreted renally in the form of metabolites. Renal clearance depends on the pH of the urine: in the case of an acid pH, renal excretion is higher; if the pH is alkaline, elimination is slower.

Epinephrine
After parenteral administration, epinephrine is well absorbed, but slowly, owing to the vasoconstriction induced by the substance itself. It can only be found in small quantities in the blood, because it has already been reabsorbed by the tissues.
Epinephrine and its metabolites distribute rapidly to the different organs.
Epinephrine is transformed into inactive metabolites in the tissues and in the liver by monoamine oxidase (MAO) enzymes and catechol-O-methyltransferase (COMT).
The systemic activity of epinephrine is short, owing to the rapidity of its excretion, which takes place largely by the renal route in the form of inactive metabolites.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulfite (E223)
Sodium methyl parahydroxybenzoate (E219)
Disodium edetate
Sodium chloride
Hydrochloric acid, dilute (pH adjuster)
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.
The solution is incompatible with alkaline products, tannic acid or metal ions.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the vial: 28 days.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Keep the vial in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Type II amber glass vials, closed with a chlorobutyl siliconised rubber stopper type I and a flip-off aluminium collar, in a cardboard box.

Pack sizes:
1 x 50 ml
1 x 100 ml
1 x 250 ml

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

FATRO S.p.A.
Via Emilia 285 - 40064
Ozzano Emilia
Bologna
Italy

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10836/004/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15th April 2016

10 DATE OF REVISION OF THE TEXT

July 2016