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

Each ml contains:

Active substances:
Procaine hydrochloride 40 mg
(equivalent to 34.65 mg of procaine)
Epinephrine tartrate 0.036 mg
(equivalent to 0.02 mg of epinephrine)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Sodium metabisulfite (E223)	1 mg
Sodium methyl parahydroxybenzoate (E219)	1.15 mg
Disodium edetate	0.1 mg
Sodium chloride	
Hydrochloric acid, dilute (for pH adjustment)	
Water for injections	

Clear colourless solution, free of visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Horses, cattle, pigs and sheep.

3.2 Indications for use for each target species

- Local anaesthesia with a long-lasting anaesthetic effect.
- Infiltration anaesthesia and perineural anaesthesia (see section 3.5).

3.3 Contraindications

Do not use in:
- animals in state of shock;
- animals with cardiovascular problems;
- animals treated with sulphonamides;
- animals treated with phenothiazine (see section 3.8);
- cases of hypersensitivity to the active substance or to any of the excipients;
- cases of hypersensitivity to local anaesthetics belonging to the esters subgroup or in case of possible allergic cross reactions to p-aminobenzoic acid and sulphonamides.

Do not use:
- with cyclopropane- or halothane-based volatile anaesthetics (see section 3.8);
- 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);
- intravenously or intra-articularly.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
To avoid inadvertent intravascular administration, correct placement of the injection needle should be verified thoroughly by aspiration 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 veterinary medicinal 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 veterinary medicinal product may lead to necrosis along the edges.
The veterinary medicinal 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

People with known hypersensitivity to procaine, epinephrine or other local anaesthetics of the ester group as well as derivatives of p-aminobenzoic acid and sulphonamides should avoid contact with the veterinary medicinal product.

The veterinary medicinal product may be irritant to the skin, eyes and oral mucosa. Avoid direct contact with the veterinary medicinal product. In case of spillage onto skin, eyes or oral mucosa, rinse immediately with plenty of water. If irritation occurs, seek medical advice immediately and show the package leaflet or the label to the physician.

Accidental self-injection may result in cardiorespiratory and/or CNS effects. Care should be taken to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Do not drive.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Horses, cattle, pigs and sheep

Common (1 to 10 animals / 100 animals treated):	Allergic reaction[a].
Rare (1 to 10 animals / 10,000 animals treated):	Anaphylactic-type reaction[b].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypotension; Agitation[c], Tremor[c], Convulsion[c]; Tachycardia[d]
Undetermined frequency (cannot be estimated from the available data):	Hypersensitivity reaction[e] Restlessness[f], Tremor[f], Convulsion[f], Depression[f], Death[f,g]

[a]It should be treated with antihistamines or corticoids.
[b]It should be treated with epinephrine.
[c]Particularly in horses, phenomena of excitability to the CNS are observed following the administration of procaine.
[d]Epinephrine-caused.
[e]To local anaesthetics belonging to the esters subgroup.
[f]Excitation of the central nervous system can occur in case of inadvertent intravascular injection.
Short acting barbiturates should be administered as well as products for acidification of urine, so as to support renal excretion.
[g]Due to respiratory paralysis.

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

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

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

3.8 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 volatile 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.
Do not administer with other sympathomimetic agents as increased toxicity may result.
Hypertension may result if adrenaline is used with oxytocic agents.
An increased risk of arrhythmias may occur if adrenaline is used concomitantly with digitalis glycoside (as digoxin).
Certain antihistaminics (as chlorpheniramine) may potentiate the effects of adrenaline.

3.9 Administration routes and dosage

Subcutaneous and perineural use.

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

2.5-10 ml of the veterinary medicinal product/animal (corresponding to 100-400 mg of procaine hydrochloride + 0.09-0.36 mg of epinephrine bitartrate).

Perineural anaesthesia: inject close to the branch of the nerve

5-10 ml of the veterinary medicinal product/animal (corresponding to 200-400 mg of procaine hydrochloride + 0.18-0.36 mg of epinephrine bitartrate).

For lower limb blocks in horses, the dose should be divided between two or more injection sites depending on the dose. See also section 3.5.

The stopper may be broached up to 20 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Symptoms related to overdose correlate with symptoms occurring after inadvertent intravascular injection as described in section 3.6.

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

Horses, cattle and sheep:
Meat and offal: Zero days
Milk: Zero hours
Pigs:
Meat and offal: Zero days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN01BA52

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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.

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

Do not store above 25 °C.
Keep the vial in the outer carton in order to protect from light.

5.4 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.

Package sizes:

Cardboard box with 1 vial of 50 ml
Cardboard box with 1 vial of 100 ml
Cardboard box with 1 vial of 250 ml
Cardboard box with 10 vials of 100 ml

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Vm 11557/4002

8. DATE OF FIRST AUTHORISATION

20 April 2016

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

November 2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCT

Veterinary medicinal product subject to prescription.

Find more product information by searching for the 'Product Information Database' on www.gov.uk.

Gavin Hall
Approved: 17 March 2025