SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

PRIMOPEN 300 mg/ml suspension for injection for cattle, pigs and horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Benzylpenicillin (procaine) monohydrate (corresponding to 170 mg benzylpenicillin)	300 mg

Excipients:

Sodium formaldeyde sulfoxylate	2.50 mg
Sodium methyl parahydroxybenzoate (E219)	1.15 mg
Disodium edetate	0.55 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
White to almost white, homogeneous suspension.

4. CLINICAL PARTICULARS

4.1. Target species

Cattle, pigs and horses.

4.2. Indications for use, specifying the target species

For the treatment of infections caused by penicillin-sensitive bacteria.

4.3. Contraindications

Do not use in known cases of hypersensitivity to the active substance, cephalosporins, procaine or to any of the excipients.
Do not use in rabbits, guinea pigs, hamsters or gerbils.
Do not use intravenously.

4.4. Special warnings for each target species

The product will not be effective against beta lactamase producing organisms.

4.5. Special precautions for use

Special precautions for use in animals

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
Official, national and regional antimicrobial policies should be taken into account when the product is used.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to benzylpenicillin and may decrease the effectiveness of treatment with other penicillins and cephalosporins due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Penicillins and cephalosporins may cause hypersensivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillin may lead to cross reactions to cephalosporins and vice versa. Allergic reactions to these substances are occasionally serious.
Do not handle this product if you know that you are sensitised or if you have been advised not to work with such preparations.
Handle this product with great care to avoid exposure, taking all recommended precautions.
If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes, or difficulty breathing are more serious symptoms and require urgent medical attention.
In case of accidental contact with eyes, rinse immediately with copious amounts of water.
Accidental spillage on the skin should be washed immediately with soap and water.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6. Adverse reactions (frequency and seriousness)

Allergies to penicillin have been observed but these are very rare.
Potentially fatal reactions associated with the administration of procaine penicillin in horses have been observed in very rare cases. Less serious symptoms of procaine toxicity include locomotor and behavioural changes.
In pregnant sows and gilts a vulval discharge which could be associated with abortion has been reported.
In sucking and fattening pigs, administration of products containing procaine penicillin may cause transient pyrexia, vomiting shivering, listlessness and incoordination.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reactions)
- 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

Laboratory studies in animals have not provided evidence of teratogenic, fetotoxic or maternal toxic effects.
The safety of this product has not been established during pregnancy and lactation.
Use only in accordance with the benefit / risk assessment of the responsible veterinarian during pregnancy and lactation.
See also section 4.6.

4.8. Interaction with other medicinal products and other forms of interaction

Benzylpenicillin is bactericidal. Avoid concurrent use of bactericidal and bacteriostatic antibiotics.
There is cross-resistance between penicillins and other beta-lactam antibiotics.

4.9. Amounts to be administered and administration route

For intramuscular use.
Administer by deep intramuscular injection once daily for up to 5 days.
The recommended daily dose is 12 mg of benzylpenicillin procaine/kg body weight equivalent to 1 ml/25 kg body weight/day.
The maximum volume to be administered per injection site is 15.5 ml in cattle and 3.2 ml in pigs.
To ensure a correct dosage, body weight should be determined as accurately as possible to avoid underdosing.

Clean the area of the injection site and swab with spirit.
Do not use the same injection site more than once during a course of treatment.

Shake well before use.
The bottle may be broached up to 20 times.

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

Penicillin is a compound with a very high therapeutic index.
However, overdosing in young animals and horses should be avoided in order to prevent procaine poisoning.

4.11. Withdrawal period

Meat and offal: Cattle 6 days.
Pigs 4 days.
Horses 6 months.

Milk: Cattle 4 days (96 hours).
Not authorised for use in horses producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterial for systemic use, beta-lactamase sensitive penicillins;
ATC-vet code: QJ01CE09

5.1. Pharmacodynamic properties

Penicillin is a beta-lactam antibiotic which has bactericidal activity against mainly Gram-positive bacteria and some Gram-negative aerobes such as:

- Gram-positive bacteria: *Trueperella pyogenes, Erysipelothrix rhusiopathiae, Listeria spp., Staphylococcus spp.* (non-penicillinase producing) and *Streptococcus spp*. susceptible to penicillin.
- Gram-negative bacteria: *Pasteurella multocida* and *Mannheimia haemolytica* susceptible to penicillin.

Benzylpenicillin exerts its effect on multiplying bacteria blocking the biosynthesis of the bacterial wall. The resistance of bacteria is due to beta-lactamase (penicillinase) inactivation, alteration or inaccessibility of the drug target.
Clinical breakpoints for penicillins based on European Committee of Antimicrobial Susceptibility Testing, version 9.0, 2019 and VetPath4 (2019):

Bacterial groups	**MIC breakpoint (µg/ml)**	
	Susceptible	**Resistant**
Listeria monocytogenes.	S≤1	R>1
Pasteurella multocida	S≤0.5	R>0.5
Staphylococcus spp.	S≤0.125	R>0.125
Streptococcus spp.	S≤0.25	R>0.25
Mannheimia haemolytica	S≤0.5	R>0.5

In the case of *Trueperella pyogenes, Erysipelothrix rhusiopathiae* no breakpoints have been determined.

The following Minimum Inhibitory Concentrations (MIC) have been determined by VetPath4 programme (2019) for penicillin in target bacteria isolated from diseased animals throughout Europe:

Organisms	**MIC_{50} (µg/ml)**	**MIC_{90}(µg/ml)**
Mannheimia haemolytica	0.12	0.5
Pasteurella multocida	0.12	0.25
Staphylococcus aureus	0.06	4
Streptococcus suis	0.03	0.5
Trueperella pyogenes	0.008	0.015

5.2. Pharmacokinetic particulars

The following pharmacokinetic data were recorded in the target species following the single administration of the recommended dose:

Species	**C_{max} (µg/ml)**	**T_{max} (hours)**
Cattle	1.14	2.03
Pigs	2.07	1.25
Horses	0.93	4.20

Penicillin is widely distributed in the extracellular fluids after absorption, and eliminated almost entirely by the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium citrate
Povidone K30
Disodium edetate
Sodium methyl-parahydroxybenzoate (E219)
Sodium formaldeyde sulfoxylate
Hydrochloric acid dilute (for pH adjustment)
Lecithin
Water for injections

6.2. Major incompatibilities

In 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: 3 years
Shelf-life after first opening the immediate packaging: 28 days

6.4. Special precautions for storage

Store in a refrigerator (2°C - 8°C)
Do not freeze.
Keep the bottle in the outer carton in order to protect from light.

6.5. Nature and composition of immediate packaging

Type II colourless glass bottles and colourless polyethylene terephthalate (PET) bottles, closed with chlorobutyl rubber stopper (Type I) and flip-off aluminium collar with tamper-evident polypropylene seal, in a cardboard boxes.

Pack-sizes:
1 x 100 ml glass or PET bottle
1 x 250 ml glass or PET bottle
10 x 100 ml PET bottles
30 x 100 ml PET bottles
6 x 250 ml PET bottles

Not all pack sizes may be marketed.

6.6. Special precautions for the disposal of unused veterinary medicinal product 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
Ozzano Emilia - Bologna
Italy

8. MARKETING AUTHORISATION NUMBER

Vm 11557/4005

9. DATE OF FIRST AUTHORISATION

10 September 2020

10. DATE OF REVISION OF THE TEXT

September 2020

Approved 16 September 2020