1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Procactive 300 mg/ml suspension for injection for cattle, sheep and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Benzylpenicillin procaine monohydrate…….300 mg
(corresponding to 170.40 mg benzylpenicillin)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Sodium methyl parahydroxybenzoate (E219)	1.25 mg
Lecithin	
Sodium citrate	
Disodium edetate	
Povidone	
Carmellose sodium	
Citric acid monohydrate	
Water for injections	

White suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, sheep and pigs.

3.2 Indications for use for each target species

For the treatment of systemic infections in cattle, sheep and pigs caused by or associated with bacteria susceptible to benzylpenicillin.

3.3 Contraindications

Do not inject intravenously.
Do not use in cases of hypersensitivity to the active substance, penicillins, cephalosporins, procaine or to any of the excipients.
Do not use in cases of severe renal dysfunction with anuria and oliguria.
Do not use in the presence of β-lactamase producing pathogens.
Do not use in very small herbivores such as guinea pigs, gerbils and hamsters.

3.4 Special warnings

Complete cross-resistance has been shown between benzylpenicillin procaine and other penicillins.

After absorption, benzylpenicillin poorly penetrates biological membranes (e.g. blood-brain barrier) since it is ionised and poorly lipid soluble. Use of the veterinary medicinal product for treatment of meningitis or CNS infections due to e.g. *Streptococcus suis* or *Listeria monocytogenes* may not be

efficacious. Furthermore, benzylpenicillin penetrates mammalian cells poorly and hence this veterinary medicinal product may have little effect in treating intracellular pathogens e.g. *Listeria monocytogenes*.

Elevated MIC values or bi-modal distribution profiles suggesting acquired resistance have been reported for the following bacteria:
- *Glaesserella parasuis*, *Staphylococcus* spp. causing MMA/PPDS, *Streptococcus* spp. and *S. suis* in pigs;
- *Fusobacterium necrophorum* causing metritis and *Mannheimia haemolytica* (only in some member states), as well as *Bacteroides* spp., *Staphylococcus chromogenes*, *Actinobacillus lignieresii* and *Trueperella pyogenes* in cattle.

Use of the veterinary medicinal product may result in a lack of clinical efficacy when treating infections caused by these bacteria.

3.5 Special precautions for use

Special precautions for safe use in the target species

Administer by deep injection only.
The use of the veterinary medicinal 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 veterinary medicinal product is used.
Use of the veterinary medicinal 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.
The feeding of waste milk containing residues of antibiotics to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial-resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

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

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious. This veterinary medicinal product also contains a paraben preservative which may cause a contact hypersensitivity reaction in previously sensitised individuals.

1. People with known hypersensitivity to this veterinary medicinal product, or if you have been advised not to work with such preparations, should avoid contact with the veterinary medicinal product.
2. Handle this veterinary medicinal product with great care to avoid exposure, taking all recommended precautions.
3. If you develop symptoms following exposure, such as a skin rash, you should seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips and eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

People developing a reaction after contact with the veterinary medicinal product should avoid handling the veterinary medicinal product and other penicillin and cephalosporin containing products in the future.
Personal protective equipment consisting of gloves should be worn when handling and administering the veterinary medicinal product.

In case of accidental eye contact, rinse thoroughly with water.
In case of accidental skin contact wash exposed skin thoroughly 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.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle:

Rare (1 to 10 animals / 10 000 animals treated):	Anaphylactic-type reaction[1], Hypersensitivity reaction[2], Anaphylactic shock[2].

[1] May be caused by the content of povidone.
[2] May be caused by penicillins and cephalosporins following administration. May occasionally be serious.

Sheep:

Rare (1 to 10 animals / 10 000 animals treated):	Hypersensitivity reaction[1], Anaphylactic shock[1].

[1] May be caused by penicillins and cephalosporins following administration. May occasionally be serious.

Pigs:

Rare (1 to 10 animals / 10 000 animals treated):	Pyrexia[1], Listless[1], Systemic disorder[2]; Vomiting[1]; Shivering[1], Incoordination[1]; Vaginal discharge[3] Hypersensitivity reaction[4], Anaphylactic shock[4].

[1] In suckling and fattening pigs. May be caused by the release of procaine.
[2] Toxic effects have been observed in young piglets. Transient but can be potentially lethal, especially at higher doses.
[3] In pregnant sows and gilts. Could be associated with abortion.
[4] May be caused by penicillins and cephalosporins following administration. May occasionally be serious.

In case of side effects, the animal has to be treated symptomatically.

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.
There is no evidence that this veterinary medicinal product presents any particular hazard to the dam or foetus. However, in pregnant sows and gilts, a vulvar discharge which could be associated with abortion has been reported.

Pregnancy and lactation:
Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

The bactericidal efficacy of penicillin is counteracted by bacteriostatic medicinal products.
The effect of aminoglycosides can be enhanced by penicillins.
The excretion of benzylpenicillin is prolonged by acetylsalicylic acid.
Cholinesterase inhibitors delay the degradation of procaine.

3.9 Administration routes and dosage

Intramuscular use.

Shake well before use.
The recommended dosage rate is 10 mg/kg bodyweight procaine benzylpenicillin (corresponding to 5.66 mg benzylpenicillin/kg bodyweight) equivalent to 1 ml per 30 kg bodyweight daily. The treatment duration is 3 to 7 days.
Do not inject more than 2.5 ml per injection site in pigs.
Do not inject more than 12 ml per injection site in cattle.
Do not inject more than 2 ml per injection site in sheep.

If no clinical response is seen within 3 days, redetermine the diagnosis and change the treatment if necessary.

The appropriate treatment duration should be chosen based on the clinical needs and individual recovery of the treated animal. Consideration should be given to the accessibility of the target tissue and characteristics of the target pathogen.

To ensure a correct dosage, body weight should be determined as accurately as possible.
The use of suitability calibrated measuring equipment is recommended.
The cap may be safely punctured up to 50 times.

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

In the case of overdose, central nervous symptoms and/or convulsions may occur.

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.

Not applicable.

3.12 Withdrawal periods

Pigs:
Meat and offal: 6 days for treatment duration 3-5 days
8 days for treatment duration 6-7 days

Cattle:
Meat and offal: 6 days for treatment duration 3-5 days

8 days for treatment duration 6-7 days
Milk: 96 hours (4 days)

Sheep:
Meat and offal: 4 days for treatment duration 3-5 days
6 days for treatment duration 6-7 days
Milk: 156 hours (6.5 days)

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ01CE09

4.2 Pharmacodynamics

Procaine benzylpenicillin is a β-lactam antibiotic that is included in the group G natural penicillins, for exclusively parenteral administration and of reduced spectrum.

It has a fundamentally bactericidal action against most gram-positive bacteria and a limited number of gram-negative bacteria.

Mechanism of action: Benzylpenicillin, procaine is a depot penicillin which is not easily dissolved in water and which releases benzylpenicillin and procaine in the animal by means of dissociation. Penicillins have a bactericidal effect on proliferating pathogens by inhibiting cell wall synthesis. Benzylpenicillin is acid-labile and is inactivated by bacterial ß-lactamases.

Resistance to benzylpenicillin is recognised to occur in some isolates of pathogens for which this veterinary medicinal product is indicated. The most common resistance mechanism is the production of β-lactamase enzyme. Resistance may also result from alterations to penicillin binding proteins (PBP).
There is cross-resistance between penicillins and cephalosporins. Where a pathogen has acquired penicillin resistance by the transfer of mobile genetic elements, co-resistance to other antimicrobial classes may also be present.

Enterobacterales, *Bacteroides fragilis*, most *Campylobacter* spp., *Nocardia* spp. and *Pseudomonas* spp. as well as beta-lactamase–producing *Staphylococcus* spp. are resistant.

Clinical breakpoints for penicillins based on European Committee on Antimicrobial Susceptibility Testing, version 11.0, 2021:

Bacterial groups	**MIC breakpoint (µg/ml)**	
	Susceptible	**Resistant**
Listeria spp.	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

4.3 Pharmacokinetics

In pigs after a single intramuscular dose of 10 mg/kg body weight (bw), maximum plasma concentrations of 2.78 µg/mL were reached after 1 hour; the terminal elimination half-life (t½) was 2.96 hours.

In cattle after a single intramuscular dose of 10 mg/kg body weight (bw), maximum plasma concentrations of 0.65 µg/mL were reached after 2 hours; the terminal elimination half-life (t½) was 5.91 hours.

In sheep after a single intramuscular dose of 10 mg/kg body weight (bw), maximum plasma concentrations of 1.59 µg/mL were reached after 1.3 hours; the terminal elimination half-life (t½) was 3.63 hours.

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

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Polyethylene terephthalate (PET) colourless vial (100 ml) or bottle (250 ml) with type I bromobutyl rubber stoppers and flip-off caps.

Pack sizes:
Carton box with 1 vial of 100 ml
Carton box with 1 bottle of 250 ml
Carton box with 10 boxes containing 1 vial of 100 ml
Carton box with 30 boxes containing 1 vial 100 ml
Carton box with 12 boxes containing 1 bottle of 250 ml

Not all pack sizes may be marketed.

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

Laboratorios Syva, S.A.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

03/05/2019

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

10/10/2025

10. CLASSIFICATION OF THE 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*).