

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Procactive 300 mg/ml Suspension for injection for cattle and pigs.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

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

Excipients:

Sodium methyl parahydroxybenzoate (E219) 1.25 mg
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection.

White suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle and pigs (weighing more than 25 kg).

4.2 Indications for use, specifying the target species

For the treatment of systemic infections in cattle and pigs (weighing more than 25 kg) caused by bacteria sensitive to penicillin.

4.3 Contraindications

Do not inject intravenously.

Do not use in known cases of hypersensitivity to penicillins, cephalosporins, procaine or to any of the excipients.

Do not use in case 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.

4.4 Special warnings for each target species

None

4.5 Special precautions for use

Special precautions for use in animals

The product is not to be used in pigs weighing less than 25 kg bodyweight.

Administer by deep injection only.

The 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

Penicillin and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillin may lead to cross sensitivity to cephalosporins and vice versa. Allergic reaction to these substances may occasionally be serious.

1. Do not handle this product if you know you are sensitised or if you have been advised not to work with such preparations.
2. Handle this 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 doctor this warning. Swelling of the face, lips and eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

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.

4.6 Adverse reactions (frequency and seriousness)

In suckling and fattening pigs, pyrexia, vomiting, shivering, listlessness and incoordination have been reported rarely, which may be caused by the release of procaine.

In pregnant sows and gilts, a vulvar discharge which could be associated with abortion has been reported rarely.

In cattle, anaphylactic reactions have been reported rarely, which may be caused by the content of povidone.

Penicillins and cephalosporins may cause hypersensitivity (allergy) following administration of the product. Allergic reactions to these substances may occasionally be serious.

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

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 produced any evidence of teratogenic, foetotoxic or maternotoxic effects.

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. However, in pregnant sows and gilts, a vulvar discharge which could be associated with abortion has been reported.

Use during pregnancy and lactation only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interactions

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.

4.9 Amounts to be administered and administration route

For 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 for 3-5 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.

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

To ensure a correct dosage, body weight should be determined as accurately as possible to avoid underdosing.

The cap may be safely punctured up to 50 times.

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

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

4.11 Withdrawal period(s)Pigs:

Meat and offal: 6 days

Cattle:

Meat and offal: 6 days

Milk: 96 hours (4 days)

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactamase-sensitive penicillins

ATC vet code: QJ01CE09

5.1 Pharmacodynamic properties

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, including the following microorganisms in its spectrum of action:

Gram-positive bacteria: *Trueperella pyogenes*, *Erysipelothrix rhusiopathiae*, *Listeria spp.*, *Staphylococcus spp.* (non-penicillinase producing) and *Streptococcus spp.*

Gram-negative bacteria: *Pasteurella multocida* and *Mannheimia haemolytica*.

Mechanism of action: It exerts its effect on multiplying bacteria blocking the biosynthesis of the bacterial wall. It is fixed by covalent binding after opening of the β -lactam nucleus on certain enzymatic proteins PBP (transpeptidase).

Resistance: some microorganisms become resistant by R plasmid-mediated production of β -lactamases, which break the β -lactam ring of the penicillins, making them inactive.

Clinical breakpoints for penicillins based on European Committee on Antimicrobial Susceptibility Testing, version 8.1, 2018:

Bacterial groups	MIC breakpoint ($\mu\text{g/ml}$)	
	Susceptible	Resistant
<i>Listeria spp.</i>	$S \leq 1$	$R > 1$
<i>Pasteurella multocida</i>	$S \leq 0.5$	$R > 0.5$
<i>Staphylococcus spp.</i>	$S \leq 0.125$	$R > 0.125$
<i>Streptococcus spp.</i>	$S \leq 0.25$	$R > 0.25$

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

The following Minimum Inhibitory Concentrations (MIC) have been determined for benzylpenicillin in target bacteria isolated from diseased animals according to European Committee on Antimicrobial Susceptibility Testing, version 8.1, 2018:

Organisms	MIC range ($\mu\text{g/ml}$)	MIC ₉₀ ($\mu\text{g/ml}$)
<i>Listeria spp.</i>	$\leq 1-1$	≤ 0.5
<i>Mannheimia haemolytica</i>	ND	ND
<i>Pasteurella multocida</i>	$\leq 0.5-0.5$	≤ 0.25
<i>Staphylococcus spp.</i>	$\leq 0.125-0.125$	ND
<i>Streptococcus spp.</i>	$\leq 0.25-0.25$	ND
<i>Trueperella pyogenes</i>	ND	ND
<i>Erysipelothrix rhusiopathiae</i>	ND	ND

ND: not determined.

5.2 Pharmacokinetic particulars

In pigs after a single intramuscular dose of 10 mg/kg body weight (bw), maximum plasma concentrations of 2.78 $\mu\text{g/mL}$ were reached after 1 hour; the terminal elimination half-life ($t_{1/2}$) 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 ($t_{1/2}$) was 5.91 hours.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lecithin
Sodium methyl parahydroxybenzoate (E219)
Sodium citrate
Disodium edetate
Povidone
Carmellose sodium
Citric acid monohydrate
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: 3 years.
Shelf life after first opening the immediate packaging: 28 days at 2°C-8°C.

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

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.

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

Laboratorios SYVA, S.A.U
Avda. Párraco Pablo Díez
49-57 León
24010
Spain

8 MARKETING AUTHORISATION NUMBER(S)

VPA10495/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 03 May 2019

10 DATE OF REVISION OF THE TEXT