1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Probencil 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

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	
Povidone	
Carmellose sodium	
Sodium citrate	
Disodium edetate	
Citric acid monohydrate	
Water for injections	

White suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and pigs.

3.2 Indications for use for each target species

For the treatment of systemic infections in cattle and pigs caused by bacteria sensitive to penicillin.

3.3 Contraindications

Do not inject intravenously.
Do not use in 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.

3.4 Special warnings

After absorption, benzylpenicillin poorly penetrates biological membranes (e.g., blood-brain barrier)

since it is ionised and poorly lipid soluble. Use of the 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 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 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 the 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.

Do not handle this product if you know 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 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.

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 shock [1]
Undetermined frequency (cannot be estimated from the available data):	- Hypersensitivity reaction (allergic reaction)[2]

[1] Which may be caused by the content of povidone.
[2] May occasionally be serious.

Pigs:

Rare (1 to 10 animals / 10,000 animals treated):	- Pyrexia[1] - Vomiting[1] - Shivering[1] - Listless[1] - Incoordination[1] - Vaginal discharge[3]
Undetermined frequency (cannot be estimated from the available data):	- Hypersensitivity reaction (allergic reaction)[2]

[1] May be caused by the release of procaine.
[2] May occasionally be serious.
[3] Could be associated with abortion

Systemic toxic effects have been observed in young piglets, which are transient but can be potentially lethal, especially at higher doses.

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 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

Pregnancy and lactation:
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.

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

For intramuscular use. Shake well before use.
The recommended dosage rate is 10 mg/kg bodyweight procaine benzylpenicillin equivalent to 1 ml per 30 kg bodyweight daily. The treatment duration is 3 to 7 days.

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.

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 distinct 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.

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).

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, 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.

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 8.1, 2018:

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

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

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

Organisms	**MIC range (µg/ml)**	**MIC_{90} (µg/ml)**
Listeria spp.	≤ 1-1	≤0.5
Mannheimia haemolytica	ND	ND
Pasteurella multocida	≤ 0.5-0.5	≤0.25
Staphylococcus spp.	≤ 0.125-0.125	ND
Streptococcus spp.	≤ 0.25-0.25	ND
Trueperella pyogenes	ND	ND
Erysipelothrix rhusiopathiae	ND	ND

ND: not determined.

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.

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 of the immediate packaging: 28 days.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Colourless polyethylene terephthalate (PET) vial with type I bromobutyl rubber stoppers and flip-off caps.

Pack sizes:
Carton box with 1 vial of 100 ml
Carton box with 1 vial 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 <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 applicable national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

MEVET S.A.U.

7. MARKETING AUTHORISATION NUMBER

VPA2209/001/001

8. DATE OF FIRST AUTHORISATION

03/05/2019

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

18/12/2024

10. CLASSIFICATION OF 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).