SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Procapen, 300 mg/ml, Suspension for injection for cattle, pigs and horses [BG, CY, CZ, DE, DK, EE, EL, ES, FI, HU, IT, LV, LT, MT, NL, PL, PT, RO, SK]
Livipen, 300 mg/ml, Suspension for injection for cattle, pigs and horses [AT, SI]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains

Active substance:

Benzylpenicillin, procaine monohydrate	300.00 mg

Excipients:

Methyl parahydroxybenzoate (E 218)	2.84 mg
Propyl parahydroxybenzoate	0.32 mg
Sodium thiosulfate	> 1.00 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection
White to yellowish suspension

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, pigs (adult pigs) and horses

4.2 Indications for use, specifying the target species

For the treatment of bacterial infectious diseases, caused by pathogens susceptible to benzylpenicillin.

Cattle, calves, and horses:
General bacterial infections (septicaemias)
Infections of the

- respiratory system
- urinary and genital apparatus
- skin, claws and hooves
- joints

Pigs (adult pigs):
Infections of the

- urogenitary tract (infections with beta-haemolytic *Streptococcus* spp.)
- musculoskeletal system (infections with *Streptococcus suis*)
- skin (infections with *Erysipelotrix rhusiopathiae*)

4.3 Contraindications

Do not use in case of:

- hypersensitivity to penicillins or cephalosporins, procain, benzylpenicillin or to any of the excipients
- severe disturbances of kidney functions with anuria or oliguria

Do not administer intravenously.

4.4 Special warnings for each target species

None.

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 the benzylpenicillin and may decrease the effectiveness of treatment with other penicillins and selected 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 hypersensitivity (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 may occasionally be serious.
Do not handle this product if you know you are sensitised to penicillins or cephalosporins or if you have been advised not to work with such preparations.
Handle this product with great care to avoid self-injection and exposure by accidental contact with the skin or eyes. Persons developing a reaction after contact with the product should avoid handling the product (and other penicillin and cephalosporin containing products) in future.
It is recommended to wear gloves when handling or administering the product. Wash exposed skin after use. In case of any eye contact, wash the eyes thoroughly with copious amounts of clean running water.
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 with breathing are more serious symptoms and require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

All species
In very rare cases allergic reactions may occur in penicillin-sensitive animals.
In case of side effects the animal has to be treated symptomatically.

Cattle
Because of the excipient polyvidon, in very rare cases anaphylactic shocks may occur.

Horses
Because of the active substance procain, symptoms like restlessness, loss of coordination and muscle tremors occur, in rare cases with fatal outcome.

Pigs
Vomitus, coughing and a little swelling at the injection site may occur. Signs of intolerance such as elevation of body temperature, trembling, vomiting, incoordination, and inappetence may occur within 24 hours after injection of benzylpenicillin procain, which may be caused by the release of procain. In pregnant sows abortion may occur. In very rare cases adverse reactions include haemolytic anaemia and thrombocytopenia.

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

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use during pregnancy and lactation only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

The bactericidal efficacy of penicillin pose antagonism with bacteriostatic antimicrobials such as macrolides and tetracyclines and synergism with aminoglycosides.

The excretion of benzylpenicillin is extended due to phenylbutazon and acetylsalicylacid.
Inhibitors of the cholinesterase delay the degradation of procain.

4.9 Amounts to be administered and administration route

For intramuscular use.
Shake well before use.

Cattle:
20 mg benzylpenicillin, procaine per kg bodyweight,
corresponding to 1 ml of the product for 15 kg bodyweight.
Per each injection site not more than 20 ml of injectable suspension should be applied.

Calves:
15 - 20 mg benzylpenicillin, procaine per kg bodyweight
corresponding to 0.75 - 1 ml of the product for 15 kg bodyweight.
Per each injection site not more than 20 ml of injectable suspension should be applied.

Pigs:
20 mg benzylpenicillin, procaine per kg bodyweight
corresponding to 1 ml of the product for 15 kg bodyweight.
Per each injection site not more than 10 ml of injectable suspension should be applied.

Horses:
15 mg benzylpenicillin, procaine per kg bodyweight
corresponding to 0.5 ml of the product for 10 kg bodyweight.
Per each injection site not more than 20 ml of injectable suspension should be applied.

Administer alternatively on the left and right side.

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

The duration of treatment is 3 days, one injection to be administered every 24 hours. A clinical response is normally observed within 24 hours. It is important to continue treatment for 2 more days. If no distinct clinical response is seen within 3 days, then a check of the diagnosis and eventually a change of treatment are required.

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

In the case of overdosing central nervous excitations and convulsions may occur. The use of the veterinary medicinal product has to be terminated immediately and a symptomatic treatment (e.g. barbiturates) should be initiated.

A premature termination of the treatment with this veterinary medicinal product should be done only after consultation of the veterinarian to avoid the development of resistant bacterial strains.

4.11 Withdrawal period(s)

Cattle:
Meat and offal 14 days
Milk 6 days

Pigs (adult pigs):
Meat and offal 15 days

Horse:
Meat and offal 14 days
Not authorised for use in mares producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactamase sensitive penicillins
ATCvet-code: QJ01CE09

5.1 Pharmacodynamic properties

Benzylpenicillin, procaine is a depot penicillin which is not easily dissolved in water and which releases benzylpenicillin and procaine in the organism by means of dissociation. The free benzylpenicillin is primarily effective against gram-positive pathogens. Penicillins have a bactericidal effect on proliferating pathogens by inhibiting cell wall synthesis. Benzylpenicillin is acid-labile and is inactivated by bacterial beta-lactamases.

The clinical breakpoints for Benzylpenicillin (Penicillin G) proposed in 2015 by CLSI (Clinical and Laboratory Standards Institute) can be summarised as follows:

	Target species	**Tissue**	**Clinical Breakpoints (µg/ml)**		
			Susceptible	**Intermediate**	**Resistant**
Streptococcus spp.	Horse	Respiratory tract Soft tissue	≤ 0.5	1	≥ 2
Streptococcus suis	Pig	-	≤ 0.25	0.5	≥ 1
Staphylococcus spp.	Horse	Respiratory tract Soft tissue	≤ 0.5	1	≥ 2
Pasteurella multocida	Pig	-	≤ 0.25	0.5	≥ 1
Pasteurella multocida	Cattle	Respiratory tract	≤ 0.25	0.5	≥ 1
Mannheimia haemolytica	Cattle	Respiratory tract	≤ 0.25	0.5	≥ 1
Histophilius somni	Cattle	Respiratory tract	≤ 0.25	0.5	≥ 1

Mechanisms of resistance:
The most frequent mechanism of resistance is production of beta-lactamases (more specifically penicillinase especially in *S.* aureus), which cleave the beta-lactam ring of penicillins making them inactive. Modification of penicillin-binding proteins is another mechanism of acquired resistance

5.2 Pharmacokinetic particulars

As benzylpenicillin procaine is a depot penicillin, absorption is delayed when compared to easy water soluble penicillin salts and therapeutic serum levels are maintained over a prolonged period.
In pigs, maximum serum levels are reached within 30 min after parenteral injection of benzylpenicillin procaine.

Environmental properties
Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Methyl parahydroxybenzoate (E 218)
Propyl parahydroxybenzoate
Lecithin
Povidone K 25
Sodium citrate
Sodium thiosulphate
Propylene glycol
Disodium edetate
Potassium dihydrogen phosphate
Water for injections

6.2 Major incompatibilities

The mixing with other drugs in one syringe has to be avoided because of possible chemical-physical incompatibilities.
Water-soluble penicillins are not compatible with metal ions, aminoacids, ascorbin acid, heparin and the vitamins of the B-complex.

6.3 Shelf life
Shelf-life of the veterinary medicinal product as packaged for sale:

Glass bottle:	4 years
PP-bottle:	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)
Keep the container in the outer carton in order to protect from light

6.5 Nature and composition of immediate packaging
1 vial/bottle with 100 ml or 250 ml suspension for injection.
12 vials/bottles with 100 ml or 250 ml suspension for injection.

Siliconised bottle of glass type II/ PP-bottle with bromobutyl rubber stopper and aluminium flip-off seal.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER
aniMedica GmbH

Im Südfeld 9
48308 Senden-Bösensell
Germany

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<{DD/MM/YYYY}> <{DD month YYYY}>…

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE
Not applicable.