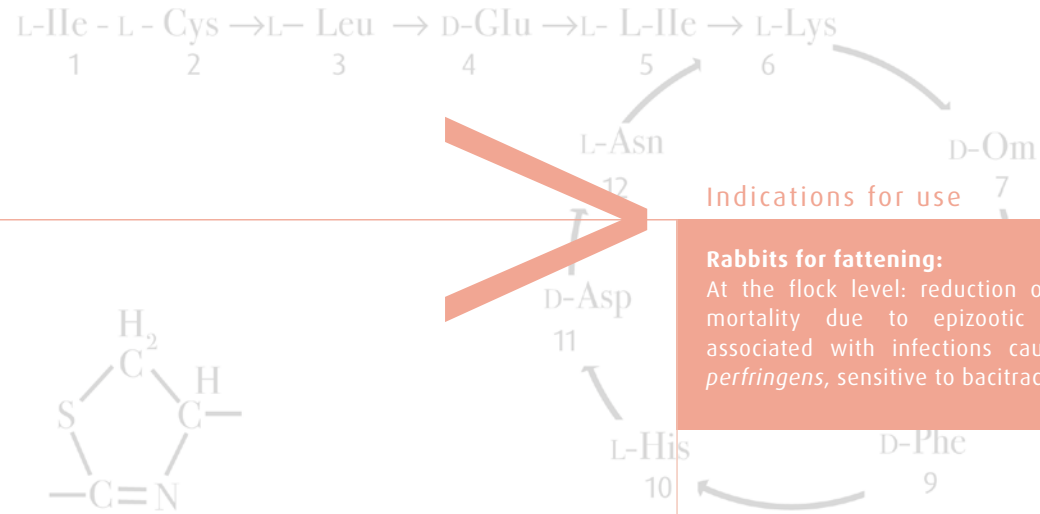
HUVEPHARMA®

Bacivet® S

POWDER FOR USE IN DRINKING WATER

INTRODUCTION



Thiazoline ring

Origin of the molecule

Bacitracin is a mixture of closely related peptides (A, B, C, D, E, F) produced by *Bacillus licheniformis*, first isolated in 1945.
Bacitracine A (C66H103 O16N17 S) is the main component.

Pharmacodynamics

Mode of action:

- Affects membrane permeability
- Inhibits cell wall synthesis
- Interacts with several enzyme systems

Bacitracin is a time-dependent antibiotic with bactericidal properties.
Its spectrum is includes primarily Gram-positive cocci and bacilli, particularly some species of Clostridiaceae.
There is no known cross-resistance and co-resistance with other antibiotics.

Pharmacokinetics

Bacitracin is hardly absorbed after oral administration in rabbits.

Efficacy

Efficacy of Bacivet® S was evaluated under field conditions in a blinded study. (Maertens *et al*, 2005)

Trial outline:

- 384 weaned rabbits (30 days of age) were randomly distributed
- Control group didn't receive any medication
- Treatment group received Bacivet®S for 21 days at the registered dose (420 IU / kg BW)

Results:

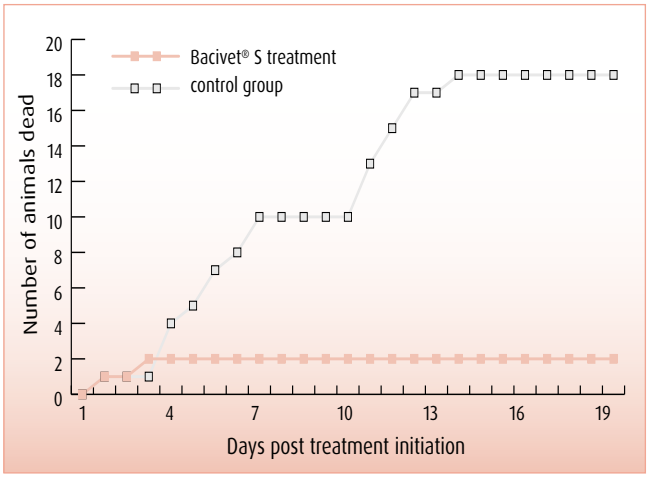


Figure 1. Cumulative ERE related mortality.

Indications for use

Rabbits for fattening:
At the flock level: reduction of clinical signs and mortality due to epizootic enterocolitis (ERE) associated with infections caused by *Clostridium perfringens*, sensitive to bacitracin.

Resistance

- Resistance is of the chromosomal type and is therefore acquired slowly and not transferable.
- There is no known cross-resistance and co-resistance.
- There are no Clinical and Laboratory Standards Institute (CLSI) interpretive criteria available for *Clostridium perfringens*, however:
  - MIC values of 2 µg/ml have been proposed as very susceptible
  - MIC values above 16 µg/ml as resistant.
- MIC90 is determined at 0.93 µg /ml.
- Field surveys showed no or very limited resistance was built up, even after several years of use. (Richez *et al*, 2008)

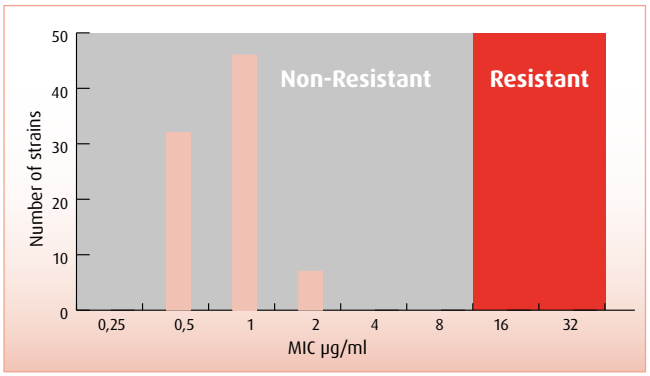


Figure 2. MIC's of Clostridium perfringens for bacitracin of 85 stains isolated from breeding facilities affected with ERE.

Product categorization and use

Bacivet® S is a water –soluble zinc bacitracin (4200 IU/g).
The zinc salt ensures the active remains stable.
Bacitracin is widely used and recognized in commercial rabbit farms because of its proven field efficacy against Clostridiosis and Epizootic Rabbit Enteropathy (ERE).

KEYPOINTS

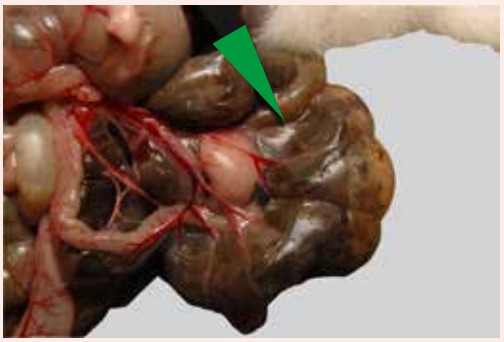
- **Efficacy**
  - Proven efficacy in the field
- **Alternative treatment**
  - No cross-resistance with for example tiamulin
- **Specific**
  - Does not pass intestinal barrier
- **Not contra-indicated or no known interactions**
  - With for example monovalent ionophores (salinomycin)

Epizootic Rabbit Enteropathy (ERE)

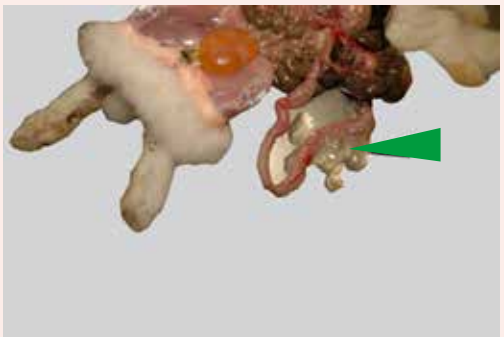
Epizootic Rabbit Enteropathy (ERE) is a complex gastro-intestinal disorder, of farmed rabbits aged between 6-14 weeks, usually occurring after weaning. The disease of which the exact aetiology is still unknown, characterized by a gut dysbiosis. *Clostridium perfringens* seems to be an important pathogen associated with it producing toxines. This intestinal disease has been present in Europe from 1996 on and without antimicrobial treatment it may produce mortality rates of up to 60% during the growing period.

The first sign of the disease is a reduction in feed intake. In the post-mortem examination a non-specific enteropathy can be observed, with no inflammatory lesions in the small intestine, heavily dilated stomach, caecal impaction, non-specific reaction in the gut associated lymphoid tissues, and often mucus into the colon.

Picture 1. Heavily dilated stomach.
The arrow indicates the demarcation line between fluid and gas.



Picture 2. Caecum filled with dry, impacted contents and gas.



Picture 3. Mucus in the colon.

Control and treatment

- Vetmulin® (tiamulin) is registered for the treatment and methaphylaxis of ERE.
- Bacivet® S has been proven to have excellent efficacy in the field

Important: Start as soon as the first clinical signs appear, often shortly after weaning.

Bacivet® S

Contraindications

Do not use in case of hypersensitivity to the active substance or to any of excipients.

Special warnings for each target species

Before installing a treatment, the management and sanitary conditions at the farm should be evaluated against the risk of an outbreak of the disease. The treatment should be installed if there is a known history of epizootic enterocolitis at the farm and as soon as the first case of mortality due to enterocolitis has been confirmed.

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.
Inappropriate use of the product may increase the prevalence of bacteria resistant to bacitracin zinc and may decrease the effectiveness of treatment with other classes of antimicrobials, due to the potential for cross resistance.
Special precautions to be taken by the person administering the veterinary medicinal product to animals. Bacitracin can occasionally cause hypersensitivity reactions after inhalation or skin contact. Do not manipulate this product in case of known allergy to bacitracin or when the person has received the recommendation to avoid working with this preparation.

Avoid inhalation of dust when incorporating the product, and to avoid all contact with it, follow the recommendations for use: it is recommended to wear a mask, security glasses, protection gloves and protection clothing. After preparation and administration of the solution, wash hands. In case of skin contact, rinse excessively with clear water.
In case of observations of symptoms such as skin eruptions after exposure to the product or a persistent eye irritation in case of projection, consult a medical doctor and show him this precaution text. Swelling of the face, lips or eyebrows and breathing difficulties are serious signs and need urgent medical care.

Adverse reactions (frequency and seriousness)

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.
Use during pregnancy, lactation or lay
Studies in laboratory animals (rats) did not show any teratogenic or embryotoxic effects of zinc bacitracin at a therapeutic dose. The safety of the product in pregnant or lactating breeding rabbits has not been demonstrated. The use of the product in these animals is not recommended.

Interaction with other medicinal products and other forms of interaction

None known

Bacivet® S, 4200 IU/g, powder for use in drinking water

Qualitative and quantitative composition

Active substance: Bacitracin zinc 4200 IU/g

Practical dosing and administration

Dosage: 420 IU /kg bodyweight (BW)
= 100 g of product (=1 sachet) per 1000 kilo rabbit for 14 days

In order to facilitate a correct dosing it is advised to dilute the powder first in a stock solution.
After evaluation of the therapeutic response, the duration of treatment can be prolonged by 7 days if necessary.
To ensure a correct dosage, body weight and water intake should be determined as accurately as possible to avoid underdosing.

Simulation for treatment:

Water consumption (ml) per day per kg BW	Gram Bacivet® S per 100 liter drinking water
100	100
110	91
120	83
130	77
140	71
150	67
160	63
170	59
180	56

Withdrawal period(s)

Meat and offal: 2 days

Overdose

No undesirable effects have been observed after administration of the product at 5 times the recommended dose level.

Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products

Shelf and storage

Shelf life of the veterinary medicinal product as packaged for sale: 2 years
Shelf life after first opening the immediate packaging: use immediately
Shelf life after dilution or reconstitution according to directions: 24 hours
Do not store above 30 °C.

Packaging

Low density polyethylene / aluminium / polyester bag.
Box containing 10 bags of 100 g.

* Used references can be obtained upon demand
* Please consult the local label and veterinary surgeon for exact indications and posology
* Use medicines responsibly.

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