SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Calcibel 240/60/60 mg/ml solution for infusion for horses, cattle, sheep, goats and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Calcium gluconate	240 mg	(equivalent to 21.5 mg calcium)
Magnesium chloride hexahydrate	60 mg	(equivalent to 7.2 mg magnesium)
Boric acid	60 mg	

For the full list of excipients, see section 6.1

Excipient(s):
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for infusion
Clear, colourless to slightly yellowish solution

4. CLINICAL PARTICULARS

4.1 Target species

Horse, cattle, sheep, goat, pig.

4.2 Indications for use, specifying the target species

For the treatment of acute hypocalcaemia.

4.3 Contraindications

Do not use in cases of:

- hypercalcaemia and hypermagnesaemia,
- idiopathic hypocalcaemia in foals,
- calcinosis in cattle and small ruminants,
- septicaemia in the course of acute mastitis in cattle,
- chronic renal insufficiency or cases of circulatory or cardiac disorders.

Do not use following application of high doses of vitamin D3 preparations.

Do not use concomitantly or immediately following application of inorganic phosphorous solutions.
Do not use in cases of known hypersensitivity to the active substances.

4.4 Special warnings for each target species

In case of acute hypomagnesaemia, the administration of a solution with a higher concentration of magnesium may be necessary.

4.5 Special precautions for use

Special precautions for use in animals
During infusion, the product must be administered slowly and at body temperature.
During infusion, cardiac rate and rhythm and circulation must be monitored. If any sign of overdose (disturbances of the cardiac rhythm decrease in blood pressure, restlessness) appears, the infusion should be stopped immediately.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Care should be taken to avoid accidental self-injection as this may cause irritation at site of injection. In case of accidental self-injection, seek medical advice immediately and show the label to the physician.

This product can cause slight skin and eye-irritation due to the low pH of the product formulation. Avoid contact with skin and eyes. Wear protective gloves and glasses. When the product comes into contact with the skin or eyes, rinse immediately with water.

This veterinary medicinal product contains boric acid, and should not be administered by pregnant women and users trying to conceive.

4.6 Adverse reactions (frequency and seriousness)

Transient hypercalcaemia with the following symptoms may occur in very rare cases:

- initial bradycardia,
- restlessness, muscle tremor, salivation,
- increase in respiratory rate.

An increase of heart rate following an initial bradycardia may indicate overdose. In this case, stop the infusion immediately. Delayed undesirable effects may appear in form of disturbances of the general state of health and symptoms of hypercalcaemia up to 6 – 10 hours after administration and must not be diagnosed as a relapse of hypocalcaemia.
See also “Overdose”.

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

4.8 Interaction with other medicinal products and other forms of interaction

Calcium increases the efficacy of cardiac glycosides.
Calcium increases the cardiac effects of β-adrenergic drugs and methylxanthines.
Glucocorticoids increase the renal excretion of calcium by vitamin D antagonism.

4.9 Amounts to be administered and administration route

For intravenous use.

Cattle:
For slow intravenous infusion

Adult cattle:
40-50 ml of this product per 50 kg body weight
(equivalent to 17.2 – 21.5 mg Ca^{2+} and 5.8 – 7.2 mg Mg^{2+} per kg b.w.).

Calf:
30 ml of this product per 50 kg body weight
(equivalent to 12.9 mg Ca^{2+} and 4.3 mg Mg^{2+} per kg body weight).

Sheep, goat, pig:
For slow intravenous infusion
30 ml of this product per 50 kg body weight
(equivalent to 12.9 mg Ca^{2+} and 4.3 mg Mg^{2+} per kg body weight).

Adult cattle, calf, sheep, goat and pig:
The intravenous infusion must be executed slowly over a period of 20-30 minutes.

Horse:
For slow intravenous infusion.
30 ml of this product per 50 kg body weight
(equivalent to 12.9 mg Ca2+ and 4.3 mg Mg2+ per kg body weight).

Infusion in horses should not exceed a rate of 4-8 mg/kg/h calcium (equivalent to 0.18-0.36 ml/kg/h of this product). It is recommended to dilute the required dose of this product 1:4 with isotonic saline or dextrose and to infuse over at least two hours.

The dosage instructions are given for guidance and must be adapted to the individual deficit and actual circulatory conditions.

After a minimum of 6 hours after treatment, a second treatment may be administered. Additional treatments every 24 hours can be administered if it is clear that on-going symptoms are due to hypocalcaemia.

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

Overdose and intravenous infusion that is too fast may result in initial bradycardia with subsequent tachycardia, cardiac rhythm disturbances and, in severe cases, ventricular fibrillation' with cardiac arrest.
Additional symptoms of hypercalcaemia are: motor weakness, muscle tremors, increased excitability, agitation, sweating, polyuria, fall in blood pressure, depression and coma.

Exceeding the maximum infusion rate may result in hypersensitivity reactions due to the release of histamine. Symptoms of hypercalcaemia may persist for 6-10 hours after infusion. It is important that these symptoms are not incorrectly diagnosed as a relapse of hypocalcaemia.

4.11 Withdrawal period(s)

Cattle, sheep, goats, horses:

Meat and offal:	Zero days
Milk:	Zero hours
Pig: Meat and offal:	Zero days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:	Calcium, combinations with vitamin D and/or other drugs
ATCvet code:	QA12AX

5.1 Pharmacodynamic properties

Calcium
Calcium is an essential element that is required for normal nerve and musculoskeletal function, cell membrane and capillary permeability and activation of enzymatic reactions. Only free ionised calcium in the blood is biologically active. Especially in times of increased requirement of calcium, e.g. post-partum, hypocalcaemia may develop.

Magnesium
Magnesium is a cofactor in a number of enzyme systems. It also plays a role in muscular excitement and neurochemical transmission. In the heart magnesium leads to delayed conduction. Magnesium stimulates the secretion of parathyroid hormone and therefore regulates serum calcium levels. In ruminants, especially after intake of young, protein-rich grass, hypomagnesaemia may develop.

The product contains calcium in an organic compound and magnesium in form of magnesium chloride as active substances. By the addition of boric acid, calcium borogluconate is formed, which increases its solubility and tissue tolerability. The main indication for its use is hypocalcaemic conditions. The addition of magnesium antagonises possible cardiac effects of calcium, especially following overdose or

rapid infusion, and helps correct hypomagnesaemia, which frequently occurs in combination with hypocalcaemia.

5.2 Pharmacokinetic particulars

Calcium

More than 90% of total body calcium is found in bone. Only about 1% is free to be exchanged with the calcium in serum and interstitial fluid. In the serum, 35 – 40% of calcium is bound to proteins, 5 – 10% is complexed with anions and 40 – 60% is in the ionized form. Calcium is eliminated mainly through the faeces with small amounts eliminated in the urine.

Magnesium

In adult animals, around 50% of magnesium is found in bone, 45% in the intracellular space and 1% in the extracellular space, of which 30% is bound to proteins and the remainder exists as free ions. The amount of magnesium utilized from the nutrition varies between 15 and 26 % in adult cattle. Approximately 80% is absorbed through the rumen. When grazing on young protein-rich grass pasture, the absorption may decrease to 8%.
Magnesium is excreted by the kidneys at a rate proportional to the serum concentration and glomerular filtration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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: Use immediately

6.4 Special precautions for storage

Do not refrigerate or freeze.

6.5 Nature and composition of immediate packaging

Bottle for infusion made of polypropylene with scaling, closures made of bromobutyl rubber stopper, aluminium caps with tear-off.
Pack sizes:

1 x 500 ml,
6 x 500 ml,

12 x 500 ml,
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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bela-Pharm GmbH & Co. KG
Lohner Straße 19
49377 Vechta
Germany

8. MARKETING AUTHORISATION NUMBER

Vm 41816/4002

9. DATE OF FIRST AUTHORISATION

25 April 2016

10. DATE OF REVISION OF THE TEXT

June 2021

Approved 04 June 2021