

## **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Calcibel Forte, 380/60/50 mg/ml solution for infusion for horses, cattle, sheep, goats and pigs.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

### Active substance:

Calcium gluconate for injection	380 mg	(equivalent to 34.0 mg calcium)
Magnesium chloride hexahydrate	60 mg	(equivalent to 7.2 mg magnesium)
Boric acid	50 mg	

For the full list of excipients, see section 6.1

## 3. PHARMACEUTICAL FORM

Solution for infusion

Clear, slightly, yellow-brownish solution, free from visible particles

Strongly hypertonic solution

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Horses, cattle, sheep, goats, pigs.

### 4.2 Indications for use, specifying the target species

Acute hypocalcaemic conditions.

### 4.3 Contraindications

Do not use in cases of hypercalcaemia and hypermagnesaemia.

Do not use in cases of idiopathic hypocalcaemia in foals.

Do not use in cases of calcinosis in cattle and small ruminants.

Do not use following administration of high doses of vitamin D3.

Do not use in cases of chronic kidney insufficiency or in cases of circulatory or cardiac disorders.

Do not use in cattle suffering septicemic processes in the course of acute mastitis in cattle.

Do not administer inorganic phosphate solutions simultaneously or shortly after the infusion.

Do not use in case of known hypersensitivity to the active substances.

### 4.4 Special warnings for each target species

None known.

## 4.5 Special precautions for use

### Special precautions for use in animals

The medicinal product must be administered only slowly intravenously.

The solution should be warmed to body temperature before administration.

During infusion, heart rate, rhythm and circulation must be monitored.

In case of symptoms of overdosing (cardiac arrhythmia, fall in blood pressure, agitation), 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 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 has been reported very rarely in spontaneous reports:

- initial bradycardia,
- restlessness, muscle tremor, hypersalivation,
- 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 recurring hypocalcaemia.

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 product has not been established during pregnancy.

Use only according 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  $\beta$ -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 slow intravenous infusion

### Cattle:

Acute hypocalcaemic conditions:

20-30 ml of this product per 50 kg body weight

(equivalent to 0.34 – 0.51 mmol Ca<sup>2+</sup> and 0.12 – 0.18 mmol Mg<sup>2+</sup> per kg body weight).

Horse, calf, sheep, goat, pig:

15-20 ml of this product per 50 kg body weight  
(equivalent to 0.26 – 0.34 mmol Ca<sup>2+</sup> and 0.09 – 0.12 mmol Mg<sup>2+</sup> per kg body weight).

Infusion in horses should not exceed a rate of 4-8 mg/kg/h calcium (equivalent to 0.12-0.24 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 intravenous infusion must be executed slowly over a period of 20-30 minutes.

Dosage instructions above serve as guidance, but must be adapted to the existing individual deficit and condition of the circulatory system.

After a minimum of 6 hours after treatment, a second treatment may be administered. Additional treatments every 24 hours can be administered if persisting symptoms are clearly related to due to hypocalcaemia.

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

In case of overdose or if infusion has been carried out too rapidly, hypercalcaemia or hypermagnesaemia with cardiotoxic symptoms as initial bradycardia with subsequent tachycardia, disturbances of the cardiac rhythm, and in severe cases ventricular fibrillation may occur. Other symptoms of hypercalcaemia are: motoric weakness, muscle tremor, increased excitability, restlessness, transpiration, polyuria, decrease in blood pressure, depression and coma.

Exceeding the maximum infusion rate may result in hypersensitivity reactions due to the release of histamine.

If the symptoms described above are observed, the infusion has to be stopped immediately.

Symptoms of hypercalcaemia may persist for 6-10 hours after infusion. It is important that these symptoms are not incorrectly diagnosed as a recurring hypocalcaemia.

#### **4.11 Withdrawal period(s)**

Cattle, sheep, goats, horses:	Meat and offal:	Zero days
	Milk:	Zero hours
Pigs:	Meat and offal:	Zero days

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: alimentary tract and metabolism, mineral supplements, calcium, combinations with vitamin D and/or other drugs.

ATCvet code: QA12AX.

### 5.1 Pharmacodynamic properties

#### Calcium

Calcium is among the most essential cations in the organism. Only free ionized calcium in the blood is biologically active and regulates calcium metabolism. Free calcium participates in many functions in the body, e.g. release of hormones and neurotransmitters, second message cascade in blood coagulation and formation of action potentials in sensitive membranes as well as muscle contraction. Physiological calcium concentration in animals is in the range of 2.3 and 3.4 mmol/L. In case of increased calcium needs, e.g. post partum, hypocalcaemia may develop. The symptoms of an acute hypocalcaemia are characterized by tetany or paresis.

#### Magnesium

Magnesium is another important cation in the organism. It contributes as a cofactor to numerable enzyme systems and transport processes and is of importance in polarization and conduction in nerves and muscle cells. In the neuromotoric excitation at the motoric end-plate magnesium decreases the liberation of acetylcholin. Magnesium ions may influence the release of transmitters at synapses of the CNS and vegetative ganglions. In the heart magnesium leads to a delayed conduction. Magnesium stimulates the secretion of parathormone and acts therefore regulating on the serum calcium level. The physiological serum levels of magnesium are different in the animal species and vary between 0.75 and 1.1 mmol/l. At magnesium serum concentrations below 0.5 mmol/l symptoms of an acute hypomagnesaemia occur. Especially in ruminants disturbances in magnesium metabolism appear, as in these animal species the absorption is less than in monogastric animals, especially after intake of young, protein-rich grass. As a consequence of hypomagnesaemia an increase of neuromuscular excitation in form of hyperaesthesia, ataxia, muscle tremor, tetany, recumbency, increasing loss in consciousness, and arrhythmia up to cardiac arrest may be observed.

The product contains calcium in an organic compound as calcium gluconate 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. The blood level is maintained within narrow limits by hormonal regulation involving parathormone, calcitonin, and dihydrocholecalciferol. 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. The amount of magnesium sourced from

diet varies between 15 and 26 % in adult cattle. Approximately 80 % is absorbed from 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**

Graduated, polypropylene bottle for infusion with bromobutyl rubber stopper and aluminium cap.

1 x 500 ml,

12 x 500 ml, packaged in a cardboard box

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

### **Distributor**

*[To be completed nationally]*

## **8. MARKETING AUTHORISATION NUMBER(S)**

*[Item to be completed by the Marketing Authorisation Holder once the Marketing Authorisation has been granted.]*

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

{DD/MM/YYYY}

**10 DATE OF REVISION OF THE TEXT**

{MM/YYYY}

**PROHIBITION OF SALE, SUPPLY AND/OR USE**