# ANNEX III

# LABELLING AND PACKAGE LEAFLET

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**
**[Outer Package / Cardboard box for multi-unit packages]**

**6 x 500 ml, 12 x 500 ml**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

Calcium gluconate, magnesium chloride hexahydrate, boric acid

## 2. STATEMENT OF ACTIVE SUBSTANCES

1 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 | |

## 3. PHARMACEUTICAL FORM

Solution for infusion.

## 4. PACKAGE SIZE

6 x 500 ml
12 x 500 ml

## 5. TARGET SPECIES

Horse, cattle, sheep, goat, pig.

## 6. INDICATION(S)

*[Not requested]*

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD

Withdrawal periods:
Cattle, sheep, goats, horses:

| | |
|---|---|
| Meat and offal: | Zero days |
| Milk: | Zero hours |

Pig: Meat and offal: Zero days

## 9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

## 10. EXPIRY DATE

EXP: {month/year}
Once broached, use immediately

## 11. SPECIAL STORAGE CONDITIONS

Do not refrigerate or freeze.

## 12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: Read the package leaflet

## 13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription.

## 14. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the sight and reach of children.

## 15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

## 16. MARKETING AUTHORISATION NUMBER(S)

Vm 41816/4002

## 17. MANUFACTURER'S BATCH NUMBER

Batch No.:

# B. PACKAGE LEAFLET

# PACKAGE LEAFLET

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

## 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
Bela-Pharm GmbH & Co. KG
Lohner Straße 19
49377 Vechta
Germany

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

Calcium gluconate, magnesium chloride hexahydrate, boric acid

## 3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

1 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 | |

Clear, colourless to slightly yellowish solution.

## 4. INDICATION(S)

For the treatment of acute hypocalcaemia.

## 5. 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.

## 6. ADVERSE REACTIONS

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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

Alternatively you can report via your national reporting system {national system details}. For details regarding national system please contact NCA.

## 7. TARGET SPECIES

Horse, cattle, sheep, goat, pig.

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

*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.

## 9. ADVICE ON CORRECT ADMINISTRATION

The intravenous infusion must be executed slowly over a period of 20-30 minutes.

## 10. WITHDRAWAL PERIOD

Cattle, sheep, goats, horses:

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

## 11. SPECIAL STORAGE PRECAUTIONS

Once broached, use immediately.
Keep out of the sight and reach of children.
Do not refrigerate or freeze.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after “EXP”.
The expiry date refers to the last day of that month.

## 12. SPECIAL WARNING(S)

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.

Special precautions for use in animals
During intravenous 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.

Pregnancy and Lactation
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.

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.

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.

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

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

April 2021

## 15. OTHER INFORMATION

**Pack size:**
500 ml

Pack sizes:
1 x 500 ml
6 x 500 ml
12 x 500 ml

Not all pack sizes may be marketed.

## B. COMBINED LABELLING

Full information of package leaflet and label are provided on the 500 ml bottle.

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET**

**Bottle**

## 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE , IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
Bela-Pharm GmbH & Co. KG
Lohner Straße 19
49377 Vechta
Germany

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

Calcium gluconate, magnesium chloride hexahydrate, boric acid

## 3. STATEMENT OF THE ACTIVE SUBSTANCE (S) AND OTHER INGREDIENTS

1 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 | |

Clear, colourless to slightly yellowish solution.

## 4. PHARMACEUTICAL FORM

Solution for infusion

## 5. PACKAGE SIZE

Pack sizes:
500 ml

## 6. INDICATION(S)

For the treatment of acute hypocalcaemia.

## 7. 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.

## 8. ADVERSE REACTIONS

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).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.
Alternatively you can report via your national reporting system {national system details}.
For details regarding national system please contact NCA.

## 9. TARGET SPECIES

Horse, cattle, sheep, goat, pig.

## 10. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

*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 $Ca^{2+}$ and 4.3 mg $Mg^{2+}$ 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.

## 11. ADVICE ON CORRECT ADMINISTRATION

The intravenous infusion must be executed slowly over a period of 20-30 minutes.

## 12. WITHDRAWAL PERIOD(S)

Withdrawal period(s):

Cattle, sheep, goats, horses:

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

## 13. SPECIAL STORAGE PRECAUTIONS

Do not use this veterinary medicinal product after the expiry date which is stated on the label after “EXP”. The expiry date refers to the last day of that month.

Do not refrigerate or freeze.

## 14. SPECIAL WARNING(S)

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.

Special precautions for use in animals:
During intravenous 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.

Pregnancy and lactation:
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.

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.

Overdose (symptoms, emergency procedures, antidotes):
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.

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

## 15. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

## 16. DATE ON WHICH THE LABEL WAS LAST APPROVED

April 2021

## 17. OTHER INFORMATION

1 x 500 ml
6 x 500 ml
12 x 500 ml

Not all pack sizes may be marketed.

## 18. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

## 19. THE WORDS “KEEP OUT OF THE REACH AND SIGHT OF CHILDREN”

Keep out of the sight and reach of children.

## 20. EXIRY DATE

EXP {month/year}

Once broached, use immediately.

## 21. MARKETING AUTHORISATION NUMBER(S)

Vm 41816/4002

## 22. MANUFACTURER'S BATCH NUMBER

<Batch> <Lot> <BN> {number}

Approved 04 June 2021