1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Addimag 240 mg/ml + 126 mg/ml solution for infusion for cattle (AT, BE, BG, CY, CZ, DE, EE, EL, ES, HU, HR, IE, IT, LT, LU, LV, NL, PL, PT, RO, SI, SK, UK(NI)
Addimag forte solution for infusion for cattle (FR)
Addimag vet 240 mg/ml + 126 mg/ml solution for infusion for cattle (DK, FI, IS, NO, SE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Calcium gluconate monohydrate	240 mg
(equivalent to 21,5 mg or 0.54 mmol calcium)	
Magnesium chloride hexahydrate	126 mg
(equivalent to 15.1 mg or 0.62 mmol magnesium)	

Excipients:

Boric acid (E284)	48 mg
Glucose monohydrate	165 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion
Clear, yellow to brownish solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle

4.2 Indications for use, specifying the target species

For the treatment of clinical hypomagnesaemia (grass tetany) accompanied by deficiency of calcium and for the treatment of clinical hypocalcaemia (milk fever) complicated by deficiency of magnesium.

4.3 Contraindications

Do not use in cases of hypercalcaemia and hypermagnesemia.
Do not use in cases of calcinosis in cattle.
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 cases of septicaemic processes in the course of acute mastitis in cattle.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

The medicinal product must be administered slowly, at body temperature.

During infusion, the heart rate, rhythm and circulation must be monitored. In case of symptoms of overdosing (bradycardia, 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

Not applicable

4.6 Adverse reactions (frequency and seriousness)

Too rapid administration of the product may cause the following effects:
Calcium may cause a transient hypercalcaemia with the following symptoms: initial bradycardia followed by tachycardia, arrhythmia (especially ectopic ventricular beats), muscle tremors, salivation and increased respiratory rate. Increase in heart rate following initial bradycardia may indicate that overdosing has occurred. In this case the administration should be stopped immediately.

4.7 Use during pregnancy and lactation

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. 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 and arrhythmias may occur if these drugs are given together.
Calcium amplifies the cardiac effects of β-adrenergic drugs and methylxanthines.
Glucocorticoids increase the renal excretion of calcium by way of vitamin D antagonism.
Do not administer inorganic phosphate solutions simultaneously or shortly after the infusion.

4.9 Amounts to be administered and administration route

Slow intravenous use.
These dosage instructions are given for guidance and must be adapted to the individual deficit and actual circulatory conditions.

Administer approximately 15 - 20 mg Ca^{2+} (0.37 – 0.49 mmol Ca^{2+}) and 10 – 13 mg Mg^{2+} (0.41 - 0.53 mmol Mg^{2+}) per kg bodyweight corresponding to approximately 0.7 - 0.9 ml of product per kg bodyweight.

If the animal's weight cannot be determined accurately, but has to be estimated, the following approach might be used:

Bottle size (ml)	Weight (kg)	Ca^{2+} (mg/kg)	Mg^{2+} (mg/kg)
500	500-725	14.8 – 21.5	10.4 – 15.1
750	750-1000	16.1 – 21.5	11.3 – 15.1

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

After a minimum of 6 hours after treatment, a second treatment may be administered. The administration can be repeated twice at 24-hour intervals, if the hypocalcaemic condition is persisting.

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

When the intravenous administration is performed too rapidly, hypercalcaemia and/or hypermagnesemia with cardiotoxic symptoms such as initial bradycardia with subsequent tachycardia, cardiac arrhythmia and in severe cases ventricular fibrillation with cardiac arrest may occur.

Additional symptoms of hypercalcaemia are: motor weakness, muscle tremors, increased excitability, agitation, sweating, polyuria, fall in blood pressure, depression and coma.
Symptoms of hypercalcaemia may persist 6 – 10 hours after the infusion and must not be incorrectly diagnosed as symptoms of hypocalcaemia.

4.11 Withdrawal periods

Meat and offal: Zero days
Milk: Zero hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Calcium, combinations with vitamin D and/or other drugs
ATC vet 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.

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.

5.2 Pharmacokinetic particulars

Calcium
Approximately 99% of total body calcium is found in bone and teeth. The remaining 1% is found mainly in the extra-cellular fluid. Of circulating calcium, approximately 50% is bound to serum proteins or complexed with anions and 50% is in the ionized form. Total serum calcium is dependent on serum protein concentrations. Calcium crosses the placenta and is distributed into milk. Calcium is eliminated mainly through the faeces with small amounts eliminated in the urine.

Magnesium
In adult animals, around 60% of magnesium is found in bone where it is relatively difficult to mobilize. Magnesium is about 30 – 35% bound to proteins and the remainder exists as free ions. It is excreted by the kidneys at a rate proportional to the serum concentration and glomerular filtration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Boric acid (E-284)
Glucose monohydrate
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: 2 years.
Shelf life after first opening the immediate packaging: once broached, use immediately.

6.4. Special precautions for storage

Do not store above 30°C.
Do not refrigerate or freeze.

6.5 Nature and composition of immediate packaging

500 and 750 ml square shaped clear polypropylene (PP) bottle with a bromobutyl rubber stopper and an aluminium screw cap.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

500 ml and 750 ml bottles

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Addimag 240 mg/ml + 126 mg/ml solution for infusion for cattle
calcium gluconate monohydrate + magnesium chloride hexahydrate

2. STATEMENT OF ACTIVE SUBSTANCES

Calcium gluconate monohydrate	240 mg/ml (equivalent to 21,5 mg or 0.54 mmol calcium)
Magnesium chloride hexahydrate	126 mg/ml (equivalent to 15.1 mg or 0.62 mmol magnesium)

3. PHARMACEUTICAL FORM

Solution for infusion

4. PACKAGE SIZE

500 ml
750 ml

5. TARGET SPECIES

Cattle

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Slow intravenous use
Read the package leaflet before use.

8. WITHDRAWAL PERIODS

Withdrawal periods:

Meat and offal:	Zero days
Milk:	Zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

Shelf life after first opening the container: once broached, use immediately.

11. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.
Do not refrigerate or freeze.

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

Disposal: read package leaflet

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

Addimag 240 mg/ml + 126 mg/ml solution for infusion for cattle

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

Marketing authorisation holder:
Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

Manufacturer responsible for batch release:
Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

Bela-pharm GmbH & Co. KG
Lohner Str. 19
49377 Vechta
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Addimag 240 mg/ml + 126 mg/ml solution for infusion for cattle
calcium gluconate monohydrate + magnesium chloride hexahydrate

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

Each ml contains:

Active substance:
Calcium gluconate monohydrate 240 mg
(equivalent to 21,5 mg or 0.54 mmol calcium)
Magnesium chloride hexahydrate 126 mg
(equivalent to 15.1 mg or 0.62 mmol magnesium)

Excipients:
Boric acid (E-284) 48 mg
Glucose monohydrate 165 mg

Solution for infusion
Clear, yellow to brownish solution

4. INDICATION(S)

For the treatment of clinical hypomagnesaemia (grass tetany) accompanied by deficiency of calcium and for the treatment of clinical hypocalcaemia (milk fever) complicated by deficiency of magnesium

5. CONTRAINDICATIONS

Do not use in cases of hypercalcaemia and hypermagnesemia.

Do not use in cases of calcinosis in cattle.
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 cases of septicaemic processes in the course of acute mastitis in cattle.

6. ADVERSE REACTIONS

Too rapid administration of the product may cause the following effects:
Calcium may cause a transient hypercalcaemia with the following symptoms: initial bradycardia followed by tachycardia, arrhythmia (especially ectopic ventricular beats), muscle tremors, salivation and increased respiratory rate. Increase in heart rate following initial bradycardia may indicate that overdosing has occurred. In this case the administration should be stopped immediately.

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.

7. TARGET SPECIES

Cattle

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

Slow intravenous use.
These dosage instructions are given for guidance and must be adapted to the individual deficit and actual circulatory conditions.

Administer approximately 15 - 20 mg Ca^{2+} (0.37 – 0.49 mmol Ca^{2+}) and 10 – 13 mg Mg^{2+} (0.41 - 0.53 mmol Mg^{2+}) per kg bodyweight corresponding to approximately 0.7 - 0.9 ml of product per kg bodyweight.

If the animal's weight cannot be determined accurately, but has to be estimated, the following approach might be used:

Bottle size (ml)	Weight (kg)	Ca^{2+} (mg/kg)	Mg^{2+} (mg/kg)
500	500-725	14.8 – 21.5	10.4 – 15.1
750	750-1000	16.1 – 21.5	11.3 – 15.1

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

After a minimum of 6 hours after treatment, a second treatment may be administered. The administration can be repeated twice at 24-hour intervals, if the hypocalcaemic condition is persisting.

9. ADVICE ON CORRECT ADMINISTRATION

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

10. WITHDRAWAL PERIODS

Meat and offal: Zero days
Milk: Zero hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not store above 30°C.
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.
Shelf life after first opening the container: once broached, use immediately.

12. SPECIAL WARNING(S)

Special precautions for use in animals:
The medicinal product must be administered slowly, at body temperature.
During infusion, the heart rate, rhythm and circulation must be monitored. In case of symptoms of overdosing (bradycardia 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:
Not applicable

Pregnancy and Lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation. Use only according 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 and arrhythmias may occur if these drugs are given together.
Calcium amplifies the cardiac effects of β-adrenergic drugs and methylxanthines.
Glucocorticoids increase the renal excretion of calcium by way of vitamin D antagonism.
Do not administer inorganic phosphate solutions simultaneously or shortly after the infusion.

Overdose (symptoms, emergency procedures, antidotes):
When the intravenous administration is performed too rapidly, hypercalcaemia and/or hypermagnesemia with cardiotoxic symptoms such as initial bradycardia with subsequent tachycardia, cardiac arrhythmia and in severe cases ventricular fibrillation with cardiac arrest may occur.
Additional symptoms of hypercalcaemia are: motor weakness, muscle tremors, increased excitability, agitation, sweating, polyuria, fall in blood pressure, depression and coma.
Symptoms of hypercalcaemia may persist 6 – 10 hours after the infusion and must not be incorrectly diagnosed as symptoms 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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack sizes: 500 ml and 750 ml.

Not all pack sizes may be marketed.
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.