[Version 9,1,11/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

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:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Boric acid (E284)	48 mg
Glucose monohydrate	165 mg
Hydrochloric acid (for pH adjustment)	
Sodium hydroxide (for pH adjustment)	
Water for injections	

Clear, yellow to brown solution

3. CLINICAL INFORMATION

3.1 Target species

Cattle.

3.2 Indications for use for each 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.

3.3 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.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
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.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cattle:

Undetermined frequency (cannot be estimated from available data)	Hypercalcaemia[1,2]; Bradycardia[2,3] Arrhythmia[2,4] Increased respiratory rate[2]; Muscle tremor[2] Increased salivation[2]

[1] transient
[2] as result of too rapid administration.
[3] initial, followed by tachycardia which may indicate that overdosing has occurred. In this case the administration should be stopped immediately.
[4] especially ectopic ventricular beats.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Pregnancy and lactation:
Use only according to the benefit/risk assessment by the responsible veterinarian.

3.8 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.

3.9 Administration routes and dosage

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 veterinary medicinal 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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and 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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Meat and offal: Zero days
Milk: Zero hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QA12AX

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: use immediately.

5.3 Special precautions for storage

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

5.4 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.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

<Date of first authorisation:> {DD/MM/YYYY}

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{DD/MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

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

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

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)

3. PACKAGE SIZE

500 ml
750 ml

4. TARGET SPECIES

Cattle

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Slow intravenous use.

7. WITHDRAWAL PERIODS

Withdrawal periods:

Meat and offal:	Zero days
Milk:	Zero hours

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use immediately.

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland B.V.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. 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

Clear, yellow to brown solution.

3. Target species

Cattle

4. Indications for use

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. Special warnings

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.

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.

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

7. Adverse events

Cattle:

Undetermined frequency (cannot be estimated from available data)	Hypercalcaemia (high level of calcium in the blood)[1,2]; Bradycardia (slow heart rate)[2,3] Arrhythmia (irregular heart rate)[2,4] Increased respiratory rate[2]; Muscle tremor[2] Increased salivation[2]

[1] transient
[2] as result of too rapid administration.
[3] initial, followed by tachycardia (rapid heart rate) which may indicate that overdosing has occurred. In this case the administration should be stopped immediately.
[4] especially ectopic ventricular beats.

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or its local representative using the contact details at the end of this leaflet, or via your national reporting system. {national system details}

8. Dosage for each species, routes 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 veterinary medicinal product per kg bodyweight.

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

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500	500-725	14.8 – 21.5	10.4 – 15.1
750	750-1000	16.1 – 21.5	11.3 – 15.1

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 immediate packaging: use immediately.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

<Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.>

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Pack sizes: 500 ml and 750 ml.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{DD/MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:
Alfasan Nederland B.V.
Kuipersweg 9
3449 JA Woerden
The Netherlands

Manufacturer responsible for batch release:
Bela-pharm GmbH & Co. KG
Lohner Str. 19
49377 Vechta
Germany

17. Other information