

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Profexx 50 mg/ml solution for injection for cattle (AT, BE, BG, CY, CZ, DE, EE, EL, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SI, SK, UK(NI))

Profexx Vet 50 mg/ml solution for injection for cattle (DK, FI, IS, NO, SE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Carprofen 50 mg

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Benzyl alcohol (E1519)	10 mg
Ethanol 96%	0.104 ml
Ethanolamine	
Macrogol 400	
Poloxamer 188	
Water for injections	

Clear, colourless to yellow coloured solution for injection.

3. CLINICAL INFORMATION

3.1 Target species

Cattle

3.2 Indications for use for each target species

An adjunct to antimicrobial therapy to reduce clinical signs in acute infectious respiratory disease and acute mastitis in cattle.

3.3 Contraindications

Do not use in animals suffering from cardiac, hepatic or renal impairment.

Do not use in animals suffering from gastro-intestinal ulceration or bleeding.

Do not use where there is evidence of a blood dyscrasia.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Avoid use in any dehydrated, hypovolaemic or hypotensive animal, as there is a potential risk of increased renal toxicity. Concurrent administration of potentially nephrotoxic drugs should be avoided. Do not exceed the stated dose or the duration of treatment.

Do not administer other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.

As NSAID therapy can be accompanied by gastro-intestinal or renal impairment, adjunctive fluid therapy should be considered especially in the case of acute mastitis treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Carprofen, in common with other NSAIDs, has been shown to exhibit photosensitising potential in laboratory studies. Benzyl alcohol and macrogol may cause hypersensitivity (allergic) reactions. People with known (hyper)sensitivity to carprofen, NSAIDs, benzyl alcohol or macrogol should administer the veterinary medicinal product with caution. Avoid contact with skin. Wash off any splashes immediately with clean, running water. Seek medical attention if irritation persists. Take care to avoid self-injection. In case of accidental self-injection, seek medical advice and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data)	Injection site reaction*
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* transient local reaction

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

Pregnancy:

The safety of the veterinary medicinal product has not been established during pregnancy. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

In common with other NSAIDs, carprofen should not be administered simultaneously with another veterinary medicinal product of the NSAID or glucocorticoid class.

NSAIDs are highly bound to plasma proteins and may compete with other highly bound drugs, such that concomitant administration may result in toxic effects.

However during clinical studies in cattle four different antibiotic classes (macrolides, tetracyclines, cephalosporins and potentiated penicillins) were used in combination with a carprofen containing veterinary medicinal product without known interactions.

3.9 Administration routes and dosage

For subcutaneous or intravenous use.

Single injection at a dosage of 1.4 mg carprofen/ kg body weight (corresponding to 1 ml of the veterinary medicinal product/35 kg bodyweight) in combination with antibiotic therapy, as appropriate.

The stopper should not be breached more than 16 times. For the highest vial sizes and when treating groups of animals in one run, the use of a multidose syringe is recommended. To refill the syringe use a draw-off needle to avoid excessive breaching of the stopper. The draw-off needle has to be removed after treatment.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

In clinical studies with a carprofen containing veterinary medicinal product, no adverse signs were reported after intravenous and subcutaneous administration of up to 5 times the recommended dose. There is no specific antidote for carprofen overdosage but general supportive therapy, as applied to clinical overdosage with NSAIDs, should be applied.

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: 21 days

Milk: zero hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QM01AE91

4.2 Pharmacodynamics

Carprofen is a member of the 2-arylpropionic acid group of NSAID's and possesses anti-inflammatory, analgesic and antipyretic activity.

Carprofen, like most other NSAIDs is an inhibitor of the enzyme cyclo-oxygenase of the arachidonic acid cascade. However, the inhibition of prostaglandin synthesis by carprofen is slight in relation to its anti-inflammatory and analgesic potency. The precise mode of action is unclear.

Studies have shown that carprofen has potent antipyretic activity and significantly reduces the inflammatory response in lung tissue in cases of acute, pyrexia infectious respiratory disease in cattle. Studies in cattle with experimentally induced acute mastitis have shown that carprofen administered intravenously has potent antipyretic activity and improves heart rate and rumen function.

4.3 Pharmacokinetics

Following a single subcutaneous dose of 1.4 mg carprofen/kg the maximum plasma concentration (C_{max}) of 15.4 µg/ml was reached after (T_{max}) 7-19 hours.

The highest carprofen concentrations are found in bile and plasma and more than 98% of carprofen is bound to plasma proteins. Carprofen was well distributed in the tissues with the highest concentrations found in kidney and liver followed by fat and muscle.

Carprofen (parent compound) is the main component in all tissues. Carprofen (parent compound) is slowly metabolised primarily by ring hydroxylation, hydroxylation at the α -carbon and by conjugation

of the carboxylic acid group with glucuronic acid. The 8-hydroxylated metabolite and unmetabolized carprofen predominate in the faeces. Bile samples are comprised of conjugated carprofen.

Carprofen has a plasma elimination half-life of 70 hours. Carprofen is primarily excreted in the faeces, indicating that the biliary secretion plays an important role.

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: 30 months.

Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Keep the vial in the outer carton in order to protect from light.

This veterinary medicinal product does not require any special temperature storage condition.

5.4 Nature and composition of immediate packaging

One clear glass (type II) vial with a grey bromobutyl rubber stopper and aluminium cap in a cardboard box.

Pack sizes:

Cardboard box with 1 vial of 50 ml.

Cardboard box with 1 vial of 100 ml.

Cardboard box with 1 vial of 250 ml.

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 BV

7. MARKETING AUTHORISATION NUMBER

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 OUTER PACKAGE**CARTON BOX****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Profexx 50 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Carprofen 50 mg/ml

3. PACKAGE SIZE

50 ml

100 ml

250 ml

4. TARGET SPECIES

Cattle

5. INDICATIONS**6. ROUTES OF ADMINISTRATION**

SC, IV

7. WITHDRAWAL PERIODS

Withdrawal period:

Meat and offal: 21 days

Milk: zero hours

8. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

Once broached use by...

9. SPECIAL STORAGE PRECAUTIONS

Keep the vial in the outer carton in order to protect from light.

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”
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Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland BV

14. MARKETING AUTHORISATION NUMBERS
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15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Glass vial 100 ml and 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Profexx 50 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Carprofen 50 mg/ml

3. TARGET SPECIES**4. ROUTES OF ADMINISTRATION**

SC, IV

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:

Meat and offal: 21 days

Milk: zero hours

6. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

7. SPECIAL STORAGE PRECAUTIONS

Keep the vial in the outer carton in order to protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Alfasan Nederland BV

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Glass vial 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Profexx 50 mg/ml

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

carprofen 50 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Profexx 50 mg/ml solution for injection for cattle

2. Composition

Each ml contains:

Active substance:

Carprofen 50 mg

Excipients:

Benzyl alcohol 10 mg

Ethanol 96% 0.104 ml

Clear, colourless to yellow coloured solution for injection.

3. Target species

Cattle

4. Indications for use

An adjunct to antimicrobial therapy to reduce clinical signs in acute infectious respiratory disease and acute mastitis in cattle.

5. Contraindications

Do not use in animals suffering from cardiac, hepatic or renal impairment.

Do not use in animals suffering from gastro-intestinal ulceration or bleeding.

Do not use where there is evidence of a blood dyscrasia.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special precautions for safe use in the target species:

Avoid use in any dehydrated, hypovolaemic or hypotensive animal, as there is a potential risk of increased renal toxicity. Concurrent administration of potentially nephrotoxic drugs should be avoided.

Do not exceed the stated dose or the duration of treatment.

Do not administer other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.

As NSAID therapy can be accompanied by gastro-intestinal or renal impairment, adjunctive fluid therapy should be considered especially in the case of acute mastitis treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

Carprofen, in common with other NSAIDs, has been shown to exhibit photosensitising potential in laboratory studies. Benzyl alcohol and macrogol may cause hypersensitivity (allergic) reactions.

People with known (hyper)sensitivity to carprofen, NSAIDs, benzyl alcohol or macrogol should administer the veterinary medicinal product with caution. Avoid contact with skin. Wash off any splashes immediately with clean, running water. Seek medical attention if irritation persists.

Take care to avoid self-injection. In case of accidental self-injection, seek medical advice and show the package leaflet or the label to the physician.

Pregnancy:

The safety of the veterinary medicinal product has not been established during pregnancy. Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

In common with other NSAIDs, carprofen should not be administered simultaneously with another veterinary medicinal product of the NSAID or glucocorticoid class.

NSAIDs are highly bound to plasma proteins and may compete with other highly bound drugs, such that concomitant administration may result in toxic effects.

However during clinical studies in cattle four different antibiotic classes (macrolides, tetracyclines, cephalosporins and potentiated penicillins) were used in combination with a carprofen containing veterinary medicinal product without known interactions.

Overdose:

In clinical studies with a carprofen containing veterinary medicinal product, no adverse signs were reported after intravenous and subcutaneous administration of up to 5 times the recommended dose. There is no specific antidote for carprofen overdosage but general supportive therapy, as applied to clinical overdosage with NSAIDs, should be applied.

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 the available data)	Injection site reaction*
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* transient local reaction

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 the local representative of the marketing authorisation holder 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

For subcutaneous or intravenous use.

Single injection at a dosage of 1.4 mg carprofen/ kg body weight (corresponding to 1 ml of the veterinary medicinal product/35 kg bodyweight) in combination with antibiotic therapy, as appropriate.

9. Advice on correct administration

The stopper should not be breached more than 16 times. For the highest vial sizes and when treating groups of animals in one run, the use of a multidose syringe is recommended. To refill the syringe use a draw-off needle to avoid excessive breaching of the stopper. The draw-off needle has to be removed after treatment.

10. Withdrawal periods

Meat and offal: 21 days

Milk: zero hours

11. Special storage precautions

Keep out of the sight and reach of children.

Keep the vial in the outer carton in order to protect from light.

This veterinary medicinal product does not require any special temperature storage conditions. Do not use this veterinary medicinal product after the expiry date which is stated on the carton after Exp. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging: 28 days.

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

One clear glass (type II) vial with a grey bromobutyl rubber stopper and aluminium cap in a cardboard box.

Pack sizes:

Cardboard box with 1 vial of 50 ml.

Cardboard box with 1 vial of 100 ml.

Cardboard box with 1 vial of 250 ml.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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 BV
Kuipersweg 9
3449 JA Woerden
The Netherlands

Local representatives and contact details to report suspected adverse reactions:

17. Other information

