[Version 8, 10/2012]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Acticarp 50 mg/ml Solution for Injection for Cattle [PL]
CARPROLIVE 50 mg/ml Soluzione iniettabile per bovini [IT]
CarproRes 50 mg/ml Solución inyectable para bovino [ES]
Acticarp Cattle 50 mg/ml oplossing voor injectie voor runderen [NL]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per ml:

Active substance:
Carprofen 50 mg

Excipients:
Ethanol anhydrous 0.1 ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, pale straw yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle.

4.2 Indications for use, specifying the target species

The product is indicated as an adjunct to antimicrobial therapy to reduce clinical signs in acute infectious respiratory disease and acute mastitis in cattle.

4.3 Contraindications

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

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
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 NSAID's concurrently or within 24 hours of each other.

As NSAID therapy can be accompanied by GI 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.
Avoid contact with skin and eyes. Should this occur, wash the affected areas immediately. Seek medical attention if irritation persists.
Care should be taken to avoid accidental self-injection. In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Studies in cattle have shown that a transient local reaction may form at the site of the injection.

4.7 Use during pregnancy, lactation or lay

In the absence of any specific studies in pregnant cattle, use only after a risk/benefit assessment has been performed by the attending veterinary surgeon.

4.8 Interaction with other medicinal products and other forms of interaction

No significant drug interactions have been reported for carprofen. During clinical studies in cattle four different antibiotic classes were used, macrolides, tetracyclines, cephalosporins and potentiated penicllins without known interactions. However, in common with other NSAIDs, carprofen should not be administered simultaneously with another product of the NSAID or glucocorticoid class. Animals should be carefully monitored if carprofen is administered simultaneously with an anticoagulant.

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

4.9 Amounts to be administered and administration route

The product should be given as a single subcutaneous or intravenous injection at a dosage of 1.4 mg carprofen/kg body weight (1 ml/35 kg) in combination with antibiotic therapy, as appropriate.

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

In clinical studies, 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 NSAID's, should be applied.

4.11 Withdrawal period(s)

Meat and offal: 21 days.
Milk: zero hours.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-inflammatory and Anti-rheumatic products, non-steroids
ATCvet code: QM01AE91

5.1 Pharmacodynamic properties

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

Carprofen, like most other NSAID's 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, pyrexic 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.

5.2 Pharmacokinetic particulars

Absorption:
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.

Distribution:
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.

Metabolism:
Carprofen (parent) 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.

Elimination:
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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol anhydrous
Macrogol 400
Poloxamer 188
Ethanolamine (for pH adjustment)
Water for injections

6.2 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: 28 days.

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

50 ml amber glass (Type I) vial closed with Flurotec (coated chlorobutyl) rubber stopper and aluminium flip off. One vial in a carton box.

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

Accord Healthcare B.V
Winthontlaan 200,
3256 KV Utrecht,
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard Box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Acticarp 50 mg/ml Solution for Injection for Cattle
NL: Acticarp Cattle 50 mg/ml oplossing voor injectie voor runderen
IT: CARPROLIVE 50 mg/ml Soluzione iniettabile per bovini
ES: CarproRes 50 mg/ml Solución inyectable para bovino

Carprofen

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml solution for injection contains 50 mg carprofen and ethanol anhydrous.

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

1 vial of 50 ml

5. TARGET SPECIES

Cattle

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or intravenous use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 21 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 of the container: 28 days.

Once broached use by…

11. SPECIAL STORAGE CONDITIONS

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS 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.

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 SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Accord Healthcare B.V
Winthontlaan 200,
3256 KV Utrecht,
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial Label

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Acticarp 50 mg/ml Solution for Injection for Cattle
NL: Acticarp Cattle 50 mg/ml oplossing voor injectie voor runderen
IT: CARPROLIVE 50 mg/ml Soluzione iniettabile per bovini
ES: CarproRes 50 mg/ml Solución inyectable para bovino

Carprofen

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

1 ml solution for injection contains 50 mg carprofen and ethanol anhydrous.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

50 ml

4. ROUTE(S) OF ADMINISTRATION

SC / IV

5. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 21 days.
Milk: zero hours.

6. BATCH NUMBER

Lot:

7. EXPIRY DATE

EXP {month/year}
Once broached use by 28 days.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:
Acticarp 50 mg/ml Solution for Injection for Cattle
NL: Acticarp Cattle 50 mg/ml oplossing voor injectie voor runderen
IT: CARPROLIVE 50 mg/ml Soluzione iniettabile per bovini
ES: CarproRes 50 mg/ml Solución inyectable para bovino

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

Marketing authorisation holder:
Accord Healthcare B.V
Winthontlaan 200,
3256 KV Utrecht,
The Netherlands

Manufacturer responsible for batch release:
Laboratori Fundació DAU
C/ De la letra C 12-14, Polígono industrial de la Zona Franca
08040 Barcelona
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Acticarp 50 mg/ml Solution for Injection for Cattle
NL: Acticarp Cattle 50 mg/ml oplossing voor injectie voor runderen
IT: CARPROLIVE 50 mg/ml Soluzione iniettabile per bovini
ES: CarproRes 50 mg/ml Solución inyectable para bovino

Carprofen

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

Per ml:

Active substance:
Carprofen 50 mg

Excipients:
Ethanol anhydrous

The product is a clear, pale straw yellow solution.

4. INDICATION(S)

The product is indicated as 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 cases of hypersensitivity to the active substance or to any of the excipients.
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.

6. ADVERSE REACTIONS

Studies in cattle have shown that a transient local reaction may form at the site of the injection.
If you notice any serious effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle.

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

The product should be given as a single subcutaneous or intravenous injection at a dosage of 1.4 mg carprofen/kg body weight (1 ml/35 kg) in combination with antibiotic therapy, as appropriate.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD

Meat and offal: 21 days.
Milk: zero hours.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.
Do not use this veterinary medicinal product after the expiry date which is stated on the outer carton and immediate label. The expiry date refers to the last day of that month.
Shelf life after first opening of the container: 28 days.

12. SPECIAL WARNING(S)

Special precautions for use in animals:
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 NSAID's concurrently or within 24 hours of each other.

Special precautions to be taken by the person administering the product:
Carprofen, in common with other NSAIDs, has been shown to exhibit photosensitising potential in laboratory studies.
Avoid contact with skin and eyes. Should this occur, wash the affected areas immediately. Seek medical attention if irritation persists.
Care should be taken to avoid accidental self-injection. In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician.

Use during pregnancy:
In the absence of any specific studies in pregnant cattle, use only after a risk/benefit assessment has been performed by the attending veterinary surgeon.

Interaction with other medicinal products and other forms of interaction:
No significant drug interactions have been reported for carprofen. During clinical studies in cattle four different antibiotic classes were used, macrolides, tetracyclines, cephalosporins and potentiated penicllins without known interactions. However, in common with other NSAIDs, carprofen should not

be administered simultaneously with another product of the NSAID or glucocorticoid class. Animals should be carefully monitored if carprofen is administered simultaneously with an anticoagulant.
As NSAID therapy can be accompanied by GI or renal impairment, adjunctive fluid therapy should be considered especially in the case of acute mastitis treatment.

NSAID's are highly bound to plasma proteins and may compete with other highly bound drugs, such that concomitant administration may result in toxic effects.
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

Overdose (symptoms, emergency procedures, antidotes):
In clinical studies, 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 NSAID's, should be applied.

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

1 vial of 50 ml.

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