ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketoprosol 100 mg/ml solution for injection for horses, cattle and pigs (DE)
Ketosol 100 mg/ml solution for injection for horses, cattle and pigs (IT, HU)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Ketoprofen 100.0 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)	10.0 mg
L-arginine	
Citric acid monohydrate (for pH adjustment)	
Water for injections	

Clear, light yellow solution for injection.

3. CLINICAL INFORMATION

3.1 Target species

Horses, cattle, pigs.

3.2 Indications for use for each target species

Horses:
- alleviation of inflammation and pain associated with musculoskeletal disorders
- alleviation of visceral pain associated with colic.

Cattle:
- supportive treatment of parturient paresis associated with calving
- reducing pyrexia and distress associated with bacterial respiratory disease when used in conjunction with an antimicrobial therapy, as appropriate
- improving the recovery rate in acute clinical mastitis, including acute endotoxin mastitis, caused by gram negative microorganisms, in conjunction with antimicrobial therapy
- reducing oedema of the udder associated with calving
- treatment of acute painful inflammatory conditions of the musculoskeletal system.

Pigs:
- reducing pyrexia and respiratory rate associated with bacterial or viral respiratory disease when used in conjunction with antimicrobial therapy, as appropriate
- supportive treatment of Mastitis Metritis Agalactia Syndrome in sows, in conjunction with antimicrobial therapy, as appropriate.

3.3 Contraindications

Do not use in horses, cattle or pigs that have previously shown a hypersensitivity to ketoprofen or to benzyl alcohol.
Do not administer other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.
Do not use in animals suffering from cardiac, hepatic or renal disease, where there is the possibility of gastrointestinal ulceration or bleeding, where there is evidence of a blood dyscrasia or hypersensitivity to the medicinal product.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use in any animal less than 6 weeks of age or in aged animals may involve additional risk. If such use cannot be avoided animals may require a reduced dosage and careful management.
Do not use in foals under the age of 15 days.
Avoid use in any dehydrated, hypovolemic or hypotensive animals as there is a potential risk of increased renal toxicity.
Avoid intra-arterial injection.
Do not exceed the stated dose or duration of treatment.

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

People with known hypersensitivity to ketoprofen or benzyl alcohol should avoid contact with the veterinary medicinal product. This product may cause dizziness and drowsiness. Avoid accidental self-injection and dermal exposure. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. However, do not drive! This product may cause skin and eye irritation. Avoid contact with skin and eyes. In case of spillage onto skin or eyes, wash the affected area thoroughly with water. If irritation persists, seek medical advice. Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Horses, cattle, pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reaction[1]
Undetermined frequency (cannot be estimated from the available data)	Injection site irritation[2] Gastric irritation, renal intolerance

[1] in case of occurrence the treatment should be stopped.
[2] following intramuscular injection.

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 and lactation:

The safety of ketoprofen has been investigated in pregnant laboratory animals (rats, rabbits) and cattle. Ketoprofen showed no teratogenic or embryotoxic effects. However, in the absence of specific data in pregnant mares and sows, the use of the product in these animals should be subject to a benefit/risk assessment by the responsible veterinarian.
It is indicated for use in lactating sows.

3.8 Interaction with other medicinal products and other forms of interaction

Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs which can lead to toxic effects.
Concurrent administration with nephrotoxic drugs should be avoided.
Concurrent administration of other steroidal or non-steroidal anti-inflammatory drugs, diuretics or anticoagulant agents may lead to potentiating adverse effects. A treatment free period, dependent on the product administered, should be observed between such treatments.

3.9 Administration routes and dosage

Intravenous use (horse, cattle).
Intramuscular use (cattle, pig).

Horse: intravenous use
For use in musculoskeletal conditions, the recommended dosage is 2.2 mg ketoprofen /kg body weight, corresponding to 1 ml of the veterinary medicinal product /45 kg body weight, administered by intravenous injection once daily for up to 3 to 5 days.
For use in equine colic, the recommended dosage is 2.2 mg ketoprofen /kg body weight corresponding to 1 ml of the veterinary medicinal product /45 kg body weight, given by intravenous injection for immediate effect.
Only after a thorough re-examination a second injection may be given if colic recurs.

Cattle: intravenous use, intramuscular use
The recommended dosage is 3 mg ketoprofen /kg body weight, corresponding to 1 ml of the veterinary medicinal product /33 kg body weight, administered by intravenous or deep intramuscular injection once daily for up to 3 days.

Pig: intramuscular use
The recommended dosage is 3 mg ketoprofen /kg body weight, corresponding to 1 ml of the veterinary medicinal product /33 kg body weight, administered once by deep intramuscular injection.
Do not administer more than 10 ml at each injection site.

The stopper cannot be punctured more than 20 times.

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

No clinical signs were observed when ketoprofen was administered to horses at 5 times the recommended dose for 15 days, to cattle at 5 times the recommended dose for 5 days, or to pigs at 3 times the recommended dose for 3 days.

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

Cattle:
Meat and offal: intravenous use: 1 day (24 hours).
intramuscular use: 4 days (96 hours).
Milk: Zero hours.

Pigs:
Meat and offal: 4 days (96 hours).

Horses:
Meat and offal: 1 day (24 hours).
Not authorised for use in mares producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QM01AE03

4.2 Pharmacodynamics

Ketoprofen is a derivative of phenylpropionic acid, and belongs to the non-steroidal anti-inflammatory group of drugs. Like all such substances, its principal pharmacological actions are anti-inflammatory, analgesic and antipyretic. The mechanism of action is related to the ability of ketoprofen to interfere with the synthesis of prostaglandins from precursors such as arachidonic acid.
Ketoprofen inhibits the biosynthesis of PGE2 and PGF2α without influencing the relationship between PGE2/PGF2α and thromboxanes. Even though ketoprofen inhibits cyclooxygenase, the lysosomes cell membranes are stabilized and bradykinin effect antagonized.

4.3 Pharmacokinetics

Ketoprofen is rapidly absorbed after intramuscular administration. Maximum plasma concentration is reached within 30 to 60 minutes. Absolute bioavailability after intramuscular administration in cattle and pigs is 90 - 100%, in the horse 70%. The volume of distribution and clearance are approximately 0.17 L/kg and 0.3 L/kg respectively. Linear kinetics prevails.
The plasma half-life after intramuscular administration is 2 to 3 hours. Ketoprofen binds 95% to plasma proteins and is metabolised by reduction to the secondary alcohol. It is excreted rapidly; mainly via the urine i.e. 80% of the dose administered are eliminated within 12 hours. The reduced ketoprofen metabolite prevails in cattle, the glucuronidated conjugate in horses.

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: 3 years.
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.

5.4 Nature and composition of immediate packaging

Amber type II glass vials closed with a red chlorobutyl rubber stopper, sealed with an aluminum cap and packaged in a cardboard box.

Pack sizes:
Cardboard box with 1 vial of 50 ml solution for injection.
Cardboard box with 1 vial of 100 ml solution for injection.

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

CP-Pharma Handelsges. mbH

7. MARKETING AUTHORISATION NUMBER(S)

< To be completed nationally>

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

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Administration by a veterinary surgeon or under their direct responsibility.
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

Ketoprosol 100 mg/ml solution for injection (DE)
Ketosol 100 mg/ml solution for injection (IT, HU)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Ketoprofen 100.0 mg

3. PACKAGE SIZE

50 ml
100 ml

4. TARGET SPECIES

Horses, Cattle, Pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Horses: intravenous use
Cattle: intravenous use, intramuscular use
Pigs: intramuscular use

7. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:
Meat and offal: intravenous use: 1 day (24 hours).
intramuscular use: 4 days (96 hours).
Milk: Zero hours.

Pigs:
Meat and offal: 4 days (96 hours).

Horses:
Meat and offal: 1 day (24 hours).
Not authorised for use in mares producing milk for human consumption.

8. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life after first opening the immediate packaging: 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"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

CP-Pharma Handelsges. mbH

14. MARKETING AUTHORISATION NUMBERS

<to be completed nationally>

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

100 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketoprosol 100 mg/ml solution for injection (DE)
Ketosol 100 mg/ml solution for injection (IT, HU)"

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Ketoprofen 100.0 mg

3. TARGET SPECIES

Horses, cattle and pigs

4. ROUTES OF ADMINISTRATION

Horses: intravenous use
Cattle: intravenous use, intramuscular use
Pigs: intramuscular use

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal periods:

Cattle:
Meat and offal: intravenous use: 1 day (24 hours).
intramuscular use: 4 days (96 hours).
Milk: Zero hours.

Pigs:
Meat and offal: 4 days (96 hours).

Horses:
Meat and offal: 1 day (24 hours).
Not authorised for use in mares producing milk for human consumption.

6. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life after first opening the immediate packaging: 28 days.
Once broached, use by …

7. SPECIAL STORAGE PRECAUTIONS

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

8. NAME OF THE MARKETING AUTHORISATION HOLDER

CP-Pharma Handelsges. mbH

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketoprosol (DE)
Ketosol (IT, HU)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Ketoprofen 100 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life after first opening the immediate packaging: 28 days.
Once broached, use by …

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Ketoprosol 100 mg/ml solution for injection for horses, cattle and pigs (DE)
Ketosol 100 mg/ml solution for injection for horses, cattle and pigs (IT, HU)

2. Composition

Each ml contains:

Active substance:
Ketoprofen: 100.0 mg

Excipient:
Benzyl alcohol (E1519) 10.0 mg

Clear, light yellow solution for injection.

3. Target species

Horses, cattle and pigs.

4. Indications for use

Horses:
- alleviation of inflammation and pain associated with musculoskeletal disorders
- alleviation of visceral pain associated with colic.

Cattle:
- supportive treatment of parturient paresis associated with calving
- reducing pyrexia and distress associated with bacterial respiratory disease when used in conjunction with an antimicrobial therapy, as appropriate
- improving the recovery rate in acute clinical mastitis, including acute endotoxin mastitis, caused by gram negative microorganisms, in conjunction with antimicrobial therapy
- reducing oedema of the udder associated with calving
- treatment of acute painful inflammatory conditions of the musculoskeletal system.

Pigs:
- reducing pyrexia and respiratory rate associated with bacterial or viral respiratory disease when used in conjunction with antimicrobial therapy, as appropriate
- supportive treatment of Mastitis Metritis Agalactia Syndrome in sows, in conjunction with antimicrobial therapy, as appropriate.

5. Contraindications

Do not use in horses, cattle or pigs that have previously shown a hypersensitivity to ketoprofen or to benzyl alcohol.

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

Do not use in animals suffering from cardiac, hepatic or renal disease, where there is the possibility of gastrointestinal ulceration or bleeding, where there is evidence of a blood dyscrasia or hypersensitivity to the medicinal product.

6. Special warnings

Special precautions for safe use in the target species:

Use in any animal less than 6 weeks of age or in aged animals may involve additional risk. If such use cannot be avoided animals may require a reduced dosage and careful management.
Do not use in foals under the age of 15 days.

Avoid use in any dehydrated, hypovolemic or hypotensive animals as there is a potential risk of increased renal toxicity.
Avoid intra-arterial injection.
Do not exceed the stated dose or duration of treatment.

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

People with known hypersensitivity to ketoprofen or benzyl alcohol should avoid contact with the veterinary medicinal product. This product may cause dizziness and drowsiness. Avoid accidental self-injection and dermal exposure. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. However, do not drive! This product may cause skin and eye irritation. Avoid contact with skin and eyes. In case of spillage onto skin or eyes, wash the affected area thoroughly with water. If irritation persists, seek medical advice. Wash hands after use.

Pregnancy and lactation:

The safety of ketoprofen has been investigated in pregnant laboratory animals (rats, rabbits) and cattle. Ketoprofen showed no teratogenic or embryotoxic effects. However, in the absence of specific data in pregnant mares and sows, the use of the product in these animals should be subject to a benefit/risk assessment by the responsible veterinarian. It is indicated for use in lactating sows.

Interaction with other medicinal products and other forms of interaction:

Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs which can lead to toxic effects.
Concurrent administration with nephrotoxic drugs should be avoided.
Concurrent administration of other steroidal or non-steroidal anti-inflammatory drugs, diuretics or anticoagulant agents may lead to potentiating adverse effects. A treatment free period, dependent on the product administered, should be observed between such treatments.

Overdose:

No clinical signs were observed when ketoprofen was administered to horses at 5 times the recommended dose for 15 days, to cattle at 5 times the recommended dose for 5 days, or to pigs at 3 times the recommended dose for 3 days.

Major incompatibilities:

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

7. Adverse events

Horses, cattle, pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reaction[1]
Undetermined frequency (cannot be estimated from the available data)	Injection site irritation[2] Gastric irritation, renal intolerance

[1] in case of occurrence the treatment should be stopped.
[2] following intramuscular injection.

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 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

Intravenous use (horse, cattle).
Intramuscular use (cattle, pig).

Horse: intravenous use
For use in musculoskeletal conditions, single intravenous injection at a dose of 2.2 mg ketoprofen /kg body weight (1 ml/45 kg), administered daily for up to 3 to 5 days.
For use in equine colic, single intravenous injection at a dose of 2.2 mg ketoprofen /kg body weight (1 ml/45 kg), for immediate effect. Only after a thorough re-examination a second injection may be given if colic recurs.

Cattle: intravenous use, intramuscular use
Single intravenous or deep intramuscular injection at a dose of 3 mg ketoprofen /kg body weight (1 ml/33 kg), administered daily for up to 3 days.

Pig: intramuscular use
Single, deep intramuscular injection at a dose of 3 mg ketoprofen /kg body weight (1 ml/33 kg).

Do not administer more than 10 ml at each injection site.

9. Advice on correct administration

The stopper must not be punctured more than 20 times.

10. Withdrawal periods

Cattle:
Meat and offal: intravenous use: 1 day (24 hours).
intramuscular use: 4 days (96 hours).
Milk: Zero hours.

Pigs:
Meat and offal: 4 days (96 hours).

Horses:
Meat and offal: 1 day (24 hours).
Not authorised for use in mares producing milk for human consumption.

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.
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: 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

Administration by a veterinary surgeon or under their direct responsibility.
Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Amber type II glass vials closed with a red chlorobutyl rubber stopper, sealed with an aluminum cap and packaged in a cardboard box.

Pack sizes:
Carboard box with 1 vial of 50 ml solution for injection.
Carboard box with 1 vial of 100 ml solution for injection.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{DD month 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:

CP-Pharma Handelsges. mbH
Ostlandring 13
31303 Burgdorf
Germany
Tel: +49-(0)5136-6066-0

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.