ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, DE, DK, EL, HU, IT, LV, PL, PT, SK, ES:
Rifen 100 mg/ml solution for injection for horses, cattle and swine
CZ: Rifen 100 mg/ml - solution for inj.
SE: Rifen vet. 100 mg/ml solution for injection
FI: Ketovet vet 100 mg/ml – Solution for injection
FR, IE, NL, UK: Ketodale 100 mg/ml solution for injection for horses, cattle and swine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:

Active substance:
Ketoprofen 100 mg

Excipients:
Benzyl alcohol 10 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless to brownish-yellowish solution

4. CLINICAL PARTICULARS

4.1 Target species

Horse, cattle, swine

4.2 Indications for use, specifying the target species

Horse
Diseases affecting the osteoarticular and muscular-skeletal system associated with acute pain and inflammation:
- Lameness of traumatic origin
- Arthritis
- Osteitis, spavin
- Tendinitis, bursitis
- Naviculitis
- Laminitis
- Myositis

Ketoprofen is also indicated for post-surgical inflammation, symptomatic therapy of colic and fever.

Cattle
Diseases associated with inflammation, pain or fever:
- Respiratory diseases
- Mastitis
- Osteoarticular and muscular-skeletal disorders such as lameness, arthritis and to ease uprise post parturition
- Injuries

Swine
Diseases associated with inflammation, pain or fever:
- Treatment associated with the Mastitis Metritis Agalactia (MMA) Syndrome
- Respiratory tract infections
- Symptomatic treatment of fever

For the short-term relief of post operative pain associated with minor soft tissue surgery such as castration in piglets.

Where necessary ketoprofen should be combined with appropriate antimicrobial therapy.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance, or to any of the excipients. Do not use in animals suffering from gastrointestinal lesions, haemorrhagic diathesis, impaired hepatic, renal or cardiac function.

4.4 Special warnings for each target species

Treatment of piglets with ketoprofen before castration reduces post operative pain for 1 hour. To obtain pain relief during surgery co-medication with an appropriate anaesthetic/sedative is needed.

4.5 Special precautions for use

Special precautions for use in animals
Avoid intra-arterial injection. Do not exceed recommended dose or period of treatment. Special care should be taken when administering the product to animals with severe dehydration, hypovolaemia and hypotension.

The use of ketoprofen is not recommended in foals under the age of 15 days. Use in animals 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. See point 4.7 regarding the use of the product in pregnant mares and sows.

Sufficient drinking water must be supplied at all times during treatment.
In colic, a subsequent dose may be given only after a thorough re-examination.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. People with known hypersensitivity to ketoprofen or benzyl alcohol should avoid contact with the veterinary medicinal product.
Avoid splashes on the skin and eyes. Rinse thoroughly with water should this occur. If irritation persists seek medical advice. Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Due to the mechanism of action of NSAIDs (inhibition of prostaglandin synthesis), gastric and intestinal irritation or ulceration or renal intolerance may occur even after appropriate use.
Intramuscular injections may occasionally cause transient irritation.
Repeated administration to swine may result in reversible inappetence.
Allergic reactions may occur very rarely.

4.7 Use during pregnancy, lactation

Pregnancy:
The safety of ketoprofen has been investigated in pregnant laboratory animals and cattle and no adverse effects were noted. The product can be used in pregnant cows.

In absence of studies on swine use only according to the benefit/risk assessment by the responsible veterinarian. Do not use in pregnant mares.

Lactation:
Can be used in lactating cows.

4.8 Interaction with other medicinal products and other forms of interaction

The product must not be administered in conjunction with, or within 24 hours of administration of other NSAIDs and glucocorticoids. Concurrent administration of diuretics, nephrotoxic drugs and anticoagulative drugs should be avoided.

Ketoprofen is highly bound to plasma proteins, and may displace or be displaced by other highly protein bound medicines, such as anticoagulants. Due to the fact that ketoprofen may inhibit platelet aggregation and cause gastrointestinal ulceration, it should not be used with other medicines that have the same profile of adverse drug reactions.

4.9 Amounts to be administered and administration route

Horse:
2.2 mg ketoprofen/kg body weight/day intravenously once daily for up to 3 to 5 consecutive days, i.e. 1 ml per 45 kg body weight.

In order to treat colic one injection is normally sufficient. A second administration of ketoprofen requires a reassessment of the patient's clinical status. See point 4.5, Special precautions for use.

Cattle:
3 mg ketoprofen/kg body weight/day intravenously or deep intramuscularly once daily for up to 3 consecutive days, i.e. 3 ml per 100 kg body weight.

Swine:
3 mg ketoprofen/kg body weight as a single deep intramuscular injection, i.e. 3 ml per 100 kg body weight (= 0.03 ml/kg).

For reduction of post-operative pain the product should be injected 10 - 30 minutes before surgical intervention. Particular care should be taken with regard to the accuracy of dosing including the use of an appropriate dosing device (i.e.: low dose syringe) and proper determination of body weight.

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

Ketoprofen can lead to hypersensitivity reactions.
Overdose with NSAIDs can lead to gastrointestinal ulceration, loss of proteins, hepatic and renal impairment. In tolerance studies performed in pigs up to 25 % of the animals treated at three times the maximum recommended dose (9 mg/kg) for three days or at the recommended dose (3 mg/kg) for triple the maximum recommended time (9 days) showed erosive and/or ulcerative lesions in both the aglandular (pars oesophagica) and glandular parts of the stomach. Early signs of toxicity include loss of appetite and pasty faeces or diarrhoea. If overdose symptoms are observed, symptomatic treatment should be initiated. The occurrence of ulcers is dose dependent to a limited extent.

4.11 Withdrawal period(s)

Meat and offal: 4 days

Milk (cattle): Zero hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: anti-inflammatory and antirheumatic products, non-steroids
ATCvet code: QM01AE03

5.1 Pharmacodynamic properties

Ketoprofen is a non-steroidal anti-inflammatory drug. In addition to the anti-inflammatory effect, it also exerts an anti-pyretic and analgesic effect. The pharmacological mechanism of action of ketoprofen is based on the inhibition of the cyclo-oxygenase and lipoxygenase. Ketoprofen also prevents the formation of bradykinin and stabilises the cell membranes of lysosomes, which inhibits the release of lysosomal enzymes that mediate tissue destruction.

5.2 Pharmacokinetic particulars

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 swine 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Benzyl alcohol
- Arginine
- Citric acid monohydrate
- Water for injection

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

Keep the glass vial in the outer carton in order to protect from light.
After first opening the immediate packaging do not store above 25 °C.

6.5 Nature and composition of immediate packaging

50 ml, 100 ml, 10 x 50 ml, 10 x 100 ml
Amber glass vials type II, with brombutyl rubber stopper type I and aluminium caps.

Not all pack sizes may be marketed.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Richter Pharma AG
Feldgasse 19
A-4600 Wels

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<{DD/MM/YYYY}> <{DD month YYYY}>

10 DATE OF REVISION OF THE TEXT

{MM/YYYY} or <month YYYY>

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

AT, BE, DE, DK, EL, HU, IT, LV, PL, PT, SK, ES:
Rifen 100 mg/ml solution for injection for horses, cattle and swine
CZ: Rifen 100 mg/ml - solution for inj.
SE: Rifen vet. 100 mg/ml solution for injection
FI: Ketovet vet. 100 mg/ml – Solution for injection
FR, IE, NL, UK: Ketodale 100 mg/ml solution for injection for horses, cattle and swine

Ketoprofen

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml contains:
Ketoprofen 100 mg
Benzyl alcohol 10 mg

3. PHARMACEUTICAL FORM *- not required as it is already part of the name of the product*

-

4. PACKAGE SIZE

50 ml
100 ml
10 x 50 ml
10 x 100 ml

5. TARGET SPECIES

Horse, cattle, swine
- *Target species are not required in countries where they are already part of the name of the product.*

6. INDICATION(S)

Diseases associated with inflammation, pain or fever.
Post operative pain associated with minor soft tissue surgery such as castration in pigs.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Horse:
1 ml per 45 kg body weight IV once daily, up to 3 to 5 consecutive days

Cattle:
3 ml per 100 kg body weight IV or deep IM once daily, up to 3 consecutive days

Swine:
3 ml per 100 kg body weight (= 0.03 ml/kg) single deep IM

8. WITHDRAWAL PERIOD

Withdrawal period:

Meat and offal : 4 days

Milk (cattle): Zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

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

11. SPECIAL STORAGE CONDITIONS

Keep the glass vial in the outer carton in order to protect from light.
After first opening the immediate packaging do not store above 25 °C.

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 - to be supplied only on veterinary prescription.

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

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Richter Pharma AG, Wels, Austria

16. MARKETING AUTHORISATION NUMBER(S)

xxxxx

17. MANUFACTURER'S BATCH NUMBER

Batch{number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE:
50 ml, 100 ml
Amber glass vials type II, with brombutyl rubber stopper type I and aluminium caps

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, DE, DK, EL, HU, IT, LV, PL, PT, SK, ES:
Rifen 100 mg/ml solution for injection for horses, cattle and swine
CZ: Rifen 100 mg/ml - solution for inj.
SE: Rifen vet. 100 mg/ml solution for injection
FI: Ketovet vet. 100 mg/ml – Solution for injection
FR, IE, NL, UK: Ketodale 100 mg/ml solution for injection for horses, cattle and swine

Ketoprofen

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 ml contains:
Ketoprofen 100 mg
Benzyl alcohol 10 mg

3. PHARMACEUTICAL FORM *- not required as it is already part of the name of the product*

-

4. PACKAGE SIZE

50 ml
100 ml
10 x 50 ml
10 x 100 ml

5. TARGET SPECIES

Horse, cattle, swine
- *Target species are not required in countries where they are already part of the name of the product.*

6. INDICATION(S)

Read the package leaflet before use.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Horse:
1ml per 45 kg body weight IV once daily, up to 3 to 5 consecutive days

Cattle:
3 ml per 100 kg body weight IV or deep IM once daily, up to 3 consecutive days

Swine:
3 ml per 100 kg body weight (= 0.03 ml/kg) single deep IM

8. WITHDRAWAL PERIOD

Withdrawal period:

Meat and offal: 4 days

Milk (cattle): Zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

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

11. SPECIAL STORAGE CONDITIONS

Protect from light.
After first opening the immediate packaging do not store above 25 °C.

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 - to be supplied only on veterinary prescription.

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

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Richter Pharma AG, Wels, Austria

16. MARKETING AUTHORISATION NUMBER(S)

xxxxx

17. MANUFACTURER'S BATCH NUMBER

Batch{number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

AT, BE, DE, DK, EL, HU, IT, LV, PL, PT, SK, ES:
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FR, IE, NL, UK: Ketodale 100 mg/ml solution for injection for horses, cattle and swine

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

Marketing authorisation holder:
Richter Pharma AG, Feldgasse 19, A-4600 Wels

Manufacturer for the batch release:
Richter Pharma AG, Durisolstraße 14, A-4600 Wels

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

AT, BE, DE, DK, EL, HU, IT, LV, PL, PT, SK, ES:
Rifen 100 mg/ml solution for injection for horses, cattle and swine
CZ: Rifen 100 mg/ml - solution for inj.
SE: Rifen vet. 100 mg/ml solution for injection
FI: Ketovet vet. 100 mg/ml – Solution for injection
FR, IE, NL, UK: Ketodale 100 mg/ml solution for injection for horses, cattle and swine

Ketoprofen

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

1 ml contains:

Active substance:
Ketoprofen 100 mg

Excipients:
Benzyl alcohol 10 mg

Clear, colourless to brownish-yellowish solution

4. INDICATION(S)

Horse
Diseases affecting the osteoarticular and muscular-skeletal system associated with acute pain and inflammation:
- Lameness of traumatic origin
- Arthritis
- Osteitis, spavin

- Tendinitis, bursitis
- Naviculitis
- Laminitis
- Myositis

Ketoprofen is also indicated for post-surgical inflammation, symptomatic therapy of colic and fever.

Cattle

Diseases associated with inflammation, pain or fever:

- Respiratory diseases
- Mastitis
- Osteoarticular and muscular-skeletal disorders such as lameness, arthritis and to ease uprise post parturition
- Injuries

Swine

Diseases associated with inflammation, pain or fever:

- Treatment associated with the Mastitis Metritis Agalactia (MMA) Syndrome
- Respiratory tract infections
- Symptomatic treatment of fever

For the short-term relief of post operative pain associated with minor soft tissue surgery such as castration in piglets.

Where necessary ketoprofen should be combined with appropriate antimicrobial therapy.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance, or to any of the excipients. Do not use in animals suffering from gastrointestinal lesions, haemorrhagic diathesis, impaired hepatic, renal or cardiac function.

6. ADVERSE REACTIONS

Due to the mechanism of action of NSAIDs (inhibition of prostaglandin synthesis), gastric and intestinal irritation or ulceration or renal intolerance may occur even after appropriate use.
Intramuscular injections may occasionally cause transient irritation.
Repeated administration to swine may result in reversible inappetence.
Allergic reactions may occur very rarely.
If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Horse, cattle, swine

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

Horse:
2.2 mg ketoprofen/kg body weight/day intravenously once daily, for up to 3 to 5 consecutive days, i.e. 1 ml per 45 kg body weight.

In order to treat colic one injection is normally sufficient. A second administration of ketoprofen requires a reassessment of the patient's clinical status. See point 9, Advice on correct administration.

Cattle:
3 mg ketoprofen/kg body weight/day intravenously or deep intramuscularly once daily for up to 3 consecutive days, i.e. 3 ml per 100 kg body weight.

Swine:
3 mg ketoprofen/kg body weight as a single deep intramuscular injection, i.e. 3 ml per 100 kg body weight (= 0.03 ml/kg).

For reduction of post-operative pain the product should be injected 10 - 30 minutes before surgical intervention. Particular care should be taken with regard to the accuracy of dosing including the use of an appropriate dosing device (i.e.: low dose syringe) and proper determination of body weight.

9. ADVICE ON CORRECT ADMINISTRATION

Avoid intra-arterial injection. Do not exceed recommended dose or period of treatment. Special care should be taken when administering the product to animals with severe dehydration, hypovolaemia and hypotension.
The use of ketoprofen is not recommended in foals under the age of 15 days. Use in animals 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. See point 12 regarding the use of the product in pregnant mares and sows.
Sufficient drinking water must be supplied at all times during treatment.
In colic, a subsequent dose may be given only after a thorough re-examination.

10. WITHDRAWAL PERIOD

Meat and offal: 4 days

Milk (cattle): Zero hours

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Keep the vial in the outer carton in order to protect from light.
Do not use after the expiry date stated on the label.
After first opening the container do not store above 25 °C.
Shelf-life after first opening the container: 28 days.

12. SPECIAL WARNING(S)

Treatment of piglets with ketoprofen before castration reduces post operative pain for 1 hour. To obtain pain relief during surgery co-medication with an appropriate anaesthetic/sedative is needed.

Use during pregnancy and lactation
Can be used during pregnancy in cattle but should not be used in pregnant mares. In absence of studies on swine use only according to the benefit/risk assessment by the responsible veterinarian.
Can be used in lactating cows.

Interaction with other medicinal products
The product must not be administered in conjunction with, or within 24 hours of administration of other NSAIDs and glucocorticoids. Concurrent administration of diuretics, nephrotoxic drugs and anticoagulative drugs should be avoided.

Ketoprofen is highly bound to plasma proteins, and may displace or be displaced by other highly protein bound medicines, such as anticoagulants. Due to the fact that ketoprofen may inhibit platelet aggregation and cause gastrointestinal ulceration, it should not be used with other medicines that have the same profile of adverse drug reactions.

Overdose
Ketoprofen can lead to hypersensitivity reactions.
Overdose with NSAIDs can lead to gastrointestinal ulceration, loss of proteins, hepatic and renal impairment. Early signs of toxicity include loss of appetite and pasty faeces or diarrhoea. If overdose symptoms are observed, symptomatic treatment should be initiated.

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

To the user
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. People with known hypersensitivity to ketoprofen or benzyl alcohol should avoid contact with the veterinary medicinal product.
Avoid splashes on the skin and eyes. Rinse thoroughly with water should this occur. If irritation persists seek medical advice. Wash hands after use.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused product or waste material should be disposed of in accordance with national requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Month/YYYY

15. OTHER INFORMATION

Ketoprofen is a non-steroidal anti-inflammatory drug. In addition to the anti-inflammatory effect, it also exerts an anti-pyretic and analgesic effect. Ketoprofen is rapidly absorbed after intramuscular administration. Maximum plasma concentration is reached within 30 to 60 minutes. 80 % of the dose administered are eliminated within 12 hours.

Package sizes: 50 ml, 100 ml, 10 x 50 ml, 10 x 100 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.