ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Quadrisol 100 mg/ml oral gel for horses

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of Quadrisol oral gel contains:

Active substance:
Vedaprofen: 100 mg

Excipients:
Propylene glycol: 130 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral gel

4. CLINICAL PARTICULARS

4.1 Target species

Horse.

4.2 Indications for use, specifying the target species

Reduction of inflammation and relief of pain associated with musculo-skeletal disorders and soft tissue lesions (traumatic injuries and surgical trauma). In cases of anticipated surgical trauma, Quadrisol can be given prophylactically at least 3 hours prior to elective surgery.

4.3 Contraindications

Do not use in animals suffering from alimentary tract disorders, impaired heart, liver and kidney function. Do not use in foals under the age of 6 months. Do not use in lactating mares.
Do not use in the case of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

Horses intended for racing and competition should be treated according to local requirements. Appropriate precautions must be taken for such horses to ensure compliance with competition regulations. In case of doubt, it is advisable to test the urine.

4.5 Special precautions for use

Special precautions for use in animals

If side effects occur, treatment should be discontinued. Horses with oral lesions should be assessed clinically and the attending veterinarian should take a decision as to whether treatment should be continued. If oral lesions persist, treatment should be discontinued. Horses should be monitored for oral lesions during treatment. Avoid use in any dehydrated, hypovolaemic or hypotensive animals, as there may be potential risk of increased renal toxicity.

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

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Typical undesirable effects associated with NSAID use, such as lesions in the alimentary tract, soft faeces, urticaria and lethargy.
Side effects are reversible.

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy.
The safety of the veterinary medicinal product has not been established during lactation

4.8 Interaction with other medicinal products and other forms of interaction

Other NSAIDs, diuretics and substances with high protein binding may compete for binding and lead to toxic effects. Quadrisol must not be given with other NSAIDs or glucocorticosteroids.

4.9 Amounts to be administered and administration route

For oral use.
Twice daily administration. An initial dose of 2 mg/kg (2.0 ml/100 kg) is followed by a maintenance dose of 1 mg/kg (1.0 ml/100 kg) given every 12 hours. Treatment can be continued for a maximum of 14 consecutive days. In case of prophylactic treatment, a maximum duration of treatment of 7 consecutive days is sufficient.

Bodyweight and dosage must be accurately determined to avoid overdosing.

The gel is administered orally by inserting the nozzle of the syringe through the interdental space and depositing the required amount of gel on the back of the tongue. Before administration, the syringe should be adjusted to the calculated dosage by setting the ring on the plunger.

It is advisable to administer the product before feeding.

In cases of anticipated surgical trauma, Quadrisol can be given prophylactically at least 3 hours prior to elective surgery.

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

Lesions and bleedings in the alimentary tract, diarrhoea, urticaria, lethargy, inappetence. If symptoms occur, treatment should be discontinued. Symptoms are reversible. Overdosing may lead to death of treated animals.

4.11 Withdrawal period(s)

Meat and offal: 12 days
Not authorised for use in animals producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: non-steroidal anti-inflammatory drug
ATCvet code: QM01AE90

5.1 Pharmacodynamic properties

Vedaprofen is a non-steroidal anti-inflammatory drug (NSAID) belonging to the propionic acid derivate group. Vedaprofen inhibits the prostaglandin synthesis enzyme system (cyclo-oxygenase enzyme) and thus possesses anti-inflammatory, antipyretic and analgesic properties. Studies in the horse have demonstrated potent inhibition of prostaglandin E_2 (PG E_2) synthesis in exudate and thromboxane B_2 synthesis in serum and exudate. Vedaprofen contains an asymmetric carbon atom and, therefore, is a racemic mixture of a (+) enantiomer and a (-) enantiomer. Both enantiomers contribute to therapeutic actions of the compound. The (+) enantiomer is more potent in inhibiting prostaglandin synthesis. Both enantiomers are equipotent $PGF_{2\alpha}$ antagonists.

5.2 Pharmacokinetic particulars

Vedaprofen is rapidly absorbed following oral administration. Bioavailability after oral administration is 80-90%, but is reduced significantly if medication is administered with food. The terminal half-life following oral administration is 350-500 minutes and no accumulation occurs following repeated oral dosing. Steady state is reached quickly following onset of treatment. Vedaprofen is highly bound to plasma proteins and extensively metabolised. The most abundant metabolite is a monohydroxylated derivative. All metabolites of vedaprofen were shown to be less active than the parent compound as determined by a thromboxane B_2 formation inhibition assay. Approximately 70% of an orally administered dose is excreted in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water (minimum purified grade),
Propylene glycol,
Hydroxyethylcellulose,
Potassium hydroxide (E525),
Hydrochloric acid,
Chocolate flavour.

6.2 Major incompatibilities

None known.

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: 2 months.

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

A 30 ml adjustable multidose syringe consisting of high density polyethylene (white) and low density polyethylene (white and natural). The syringe is fitted with variable dose capability, adjustable in steps of 0.5 ml and graduated to 1 ml. The product is presented as a single syringe in a carton box or as a multipack of 3 syringes 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

GROVET B.V.
Centurionbaan 140
3769 AV Soesterberg
Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/97/005/001
EU/2/97/005/005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4 December 1997
Date of last renewal: 13 November 2007

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Provet A.E.
Nikiforou Foka & Agion Anargyron,
Thesi Vrago, Aspropyrgos, 193 00,
Greece

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

The active substance in Quadrisol is an allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010:

Pharmacologically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions
vedaprofen	vedaprofen	Equidae	1000 µg/kg 100 µg/kg 50 µg/kg 20 µg/kg	Kidney Liver Muscle Fat	

The excipients listed in section 6.1 of the SPC are either allowed substances for which table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this veterinary medicinal product.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

100 mg/ml oral gel for horses

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Quadrisol 100 mg/ml oral gel for horses

2. STATEMENT OF ACTIVE SUBSTANCES

Vedaprofen: 100 mg/ml

3. PHARMACEUTICAL FORM

Oral gel.

4. PACKAGE SIZE

Adjustable dose syringe, containing 30 ml gel
3 adjustable dose syringes, each containing 30 ml gel

5. TARGET SPECIES

Horse.

6. INDICATION(S)

Reduction of inflammation and relief of pain.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Meat and offal: 12 days.
Not authorised for use in lactating animals producing milk for human consumption.

9. SPECIAL WARNINGS, IF NECESSARY

If side effects occur, treatment should be discontinued.
Do not use in lactating mares.
For full contra-indications, see package leaflet.

10. EXPIRY DATE

EXP: {Month/year}

11. SPECIAL STORAGE CONDITIONS

No special precautions for storage.
Shelf-life after first opening the immediate packaging: 2 months.

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 SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GROVET B.V.
Centurionbaan 140
3769 AV Soesterberg
Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/97/005/001 (1 x 30 ml)
EU/2/97/005/005 (3 x 30 ml)

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{label on the syringe}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Quadrisol 100 mg/ml oral gel for horses

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Vedaprofen: 100 mg/ml
Propylene glycol: 130 mg/ml

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

30 ml

4. ROUTE(S) OF ADMINISTRATION

For oral use.

5. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Meat and offal: 12 days

6. BATCH NUMBER

Lot: {number}

7. EXPIRY DATE

EXP: {Month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Quadrisol 100 mg/ml oral gel for horses

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

Marketing authorisation holder:

GROVET B.V.
Centurionbaan 140
3769 AV Soesterberg
Netherlands
T: +3188582410

Manufacturers responsible for batch release:

Provet A.E.
Nikiforou Foka & Agion Anargyron,
Thesi Vrago, Aspropyrgos, 193 00,
Greece

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Quadrisol 100 mg/ml oral gel for horses.

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

Vedaprofen:	100 mg/ml
Propylene glycol:	130 mg/ml

4. INDICATION(S)

Reduction of inflammation and relief of pain associated with musculo-skeletal disorders and soft tissue lesions (traumatic injuries and surgical trauma). In cases of anticipated surgical trauma, Quadrisol can be given prophylactically at least 3 hours prior to elective surgery

5. CONTRAINDICATIONS

Do not use in animals suffering from alimentary tract disorders, impaired heart, liver and kidney function. Do not use in foals under the age of 6 months. Do not use in lactating mares.
Quadrisol must not be given with other NSAIDs or glucocorticosteroids.
Do not use in the case of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

Typical non-steroidal anti-inflammatory drugs (NSAIDs) side effects such as lesions and bleedings in the alimentary tract, diarrhoea, urticaria, lethargy, inappetence. If symptoms occur, treatment should be discontinued. Symptoms are reversible. Overdosing may lead to death of treated animals.

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 inform your veterinary surgeon.

7. TARGET SPECIES

Horse.

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

Quadrisol is intended for twice daily administration. The advised dosage is an initial dose of 2 mg/kg (2.0 ml/100 kg) followed by a maintenance dose of 1 mg/kg (1.0 ml/100 kg) given every 12 hours.

For oral use.

9. ADVICE ON CORRECT ADMINISTRATION

Treatment can be continued for a maximum of 14 consecutive days. Bodyweight and dosage rate must be accurately determined to avoid overdosing. In case of prophylactic treatment, a maximum duration of treatment of 7 consecutive days is sufficient.
The gel is administered orally by inserting the nozzle of the syringe through the interdental space and depositing the required amount of gel on the back of the tongue. Before administration, the syringe should be adjusted to the calculated dosage by setting the ring on the plunger.
It is advisable to administer the product before feeding.

10. WITHDRAWAL PERIOD(S)

Meat and offal: 12 days.
Not authorised for use in lactating animals producing milk for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
No special precautions for storage.
Shelf-life after first opening of the product: 2 months.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP.

12. SPECIAL WARNING(S)

The safety of the veterinary medicinal product has not been established during lactation. Quadrisol 100 mg/ml can be used during pregnancy.

Horses with oral lesions should be assessed clinically and the attending veterinarian should take a decision as to whether treatment should be continued. If oral lesions persist, treatment should be discontinued.

Horses should be monitored for oral lesions during treatment. Avoid the use in any dehydrated, hypovolaemic or hypotensive animals, as there may be potential risk of increased renal toxicity.

Horses intended for racing and competition should be treated according to local requirements. Appropriate precautions must be taken for such horses to ensure compliance with competition regulations. In case of doubt, it is advisable to test the urine.

In case of accidental ingestion by a person, seek medical advice immediately and show the package leaflet or the label to the physician.

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 product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/)

15. OTHER INFORMATION

For animal treatment only.