

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

GEFRIDERM cutaneous spray solution for dogs (ES, DE, IE, UK, EE)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Marbofloxacin.....	1.025 mg
Ketoconazole.....	2.041 mg
Prednisolone	0.926 mg

Excipients:

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cutaneous spray, solution

Yellowish, slightly opaque solution

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Treatment of acute superficial dermatitis caused by mixed infections with *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole. The indication is limited to focal skin infections (e.g. hot spots, intertrigo, superficial folliculitis).

4.3 Contraindications

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

4.4 Special warnings for each target species

Bacterial and fungal dermatitis is often secondary in nature and appropriate diagnosis should be used to determine the primary factors involved. The unnecessary use of any pharmacologically active substance should be avoided. Treatment is indicated only if mixed infection with *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* and *Malassezia pachydermatis* has been proved. If one of the pharmacologically active substances is no longer indicated due to the different characteristics of bacterial and fungal infections, the application of pharmacologically active substance should be discontinued and replaced by an appropriate treatment option.

The indication is limited to focal skin infections not exceeding 25 cm². The treatment is 2 pumps of the application pump to each treated animal when the affected area is under 25 cm², and above this value the treated area has to be partitioned 25 cm² zones, maximum 4

treatment areas at the same time. Cross-resistance has been shown between quinolones. The product should not be used when antimicrobial susceptibility testing has shown resistance to quinolones because its effectiveness may be reduced.

4.5 Special precautions for use

Special precautions for use in animals

Animals should be prevented from licking the application site (e.g., by the fixation of a collar). Keep the animals to be treated separated from each other in order to prevent licking each other. Use of the veterinary medicinal product should be based on identification of infecting organisms and susceptibility testing.

Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly to other classes of antimicrobials. However, microbiological diagnosis and susceptibility test must be performed. Official and local antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may reduce effectiveness of treatment with other quinolones due to the potential for cross-resistance. Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population.

Direct contact of product with eyes must be avoided.

If hypersensitivity to any of the active components occurs, treatment should be discontinued and appropriate therapy should be initiated.

Prolonged and intensive use of topical corticosteroids preparation is known to trigger local and systemic effects, including suppression of adrenal function, thinning of the epidermis and delayed healing.

Spraying on open lesions and wounds must be avoided.

During the administration do not bath or shampoo the animal.

The hair coat should be kept short during treatment to assist optimal contact of antimicrobial agents with the skin surface. Use only on altered parts of skin.

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

This product may be harmful to children after accidental ingestion (gastrointestinal disturbances, insomnia, and restlessness). Do not leave the bottle out of its child resistant container except when applying the product to the animal. The bottle must be closed and placed in the child resistant container immediately after application and kept in a safe place out of the sight and reach of the children. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Ketoconazole and prednisolone may affect the unborn child and negatively influence male reproductive functions. Excessive exposure to the product may lead to foetal defects, or reduced sperm viability. The product should not be administered by pregnant women, or those trying to conceive.

Marbofloxacin, ketoconazole and prednisolone may cause hypersensitivity (allergy) reactions. People with known hypersensitivity to (fluoro)quinolones, ketoconazole, prednisolone, or DMSO should avoid contact with the product.

This product may be irritating to skin and mucosal membranes. Avoid contact with the skin including hand-to-mouth contact. Wear single-use impermeable gloves when handling and administering the product. If contact occurs, wash hands or the exposed area thoroughly with clean water.

Seek medical advice in case of hypersensitivity reactions or if irritation persists. Swelling of face, lip and eyes, or respiratory difficulties are more serious signs that need urgent medical action.

This product may be irritating to the eyes. Avoid contact with the eyes including hand-to eye contact. If contact occurs, rinse with clean water. If eye irritation persists, seek medical advice and show the package leaflet or label to the physician.

This product may be harmful after inhalation. Spray animals in the open air or in well-ventilated area. Avoid breathing in the spray-mist.

Do not smoke, drink or eat while handling the product.

Flammable solution. Do not spray on naked flame or any incandescent material.

Avoid prolonged contact with the treated animals. Treated animals should not be handled and children should not be allowed to play with treated animals until the application site is dry (at least 20 minutes). It is therefore recommended that animals are not treated during the day, but should be treated during the early morning and evening.

Treated animals should not be allowed to sleep with owners, especially children.

Treated areas should not be touched during the treatment period; any fur, or other areas that do not require this treatment, that may have been sprayed, should be thoroughly cleaned using a disinfectant wipe to prevent contamination. Any wipes and gloves used should be disposed of immediately.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases mild erythematous lesions have been reported in the literature after cutaneous application of the active substances.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. The use is not recommended during pregnancy and lactation. Studies with ketoconazole in laboratory animals have shown evidence of teratogenic and embryotoxic effects.

4.8 Interaction with other medicinal products and other forms of interaction

Concomitant use of products with a low pH might have an inhibitory effect on the activity of marbofloxacin and are to be avoided. No interaction studies have been provided to confirm acceptability of use of products in combination and so the safety/efficacy of such combined product use is uncertain.

4.9 Amounts to be administered and administration route

Cutaneous use. Shake well before use.

Before application of the veterinary medicinal product, the affected area should be cleaned mechanically or by irrigation taking care to avoid further damage to the skin. Any excess exudate, hair or debris on the treated area should be carefully removed prior to application.

Apply 2 pumps of the pump spray bottle per 25 cm² area of affected skin twice daily for 7 days, up to a maximum of 14 days. Hold the pump spray bottle at a distance of 10 cm from the affected skin during application.

When spraying from a distance of about 10 cm, 2 pumps (approximately 0.2 ml) corresponds to a recommended treatment dosage is 8.20 µg of marbofloxacin, 16.33 µg of ketoconazole and 7.4 µg of prednisolone per cm² area of affected skin.

Treatment area(s):

The indication is limited to focal skin infections.

- A single area of affected skin for treatment covers an area of 25 cm². This area of skin is equivalent to an irregular shape of 5 cm x 5 cm.
- When the affected area of skin covers an area larger than 25 cm², the treated area should be divided into multiple 25 cm² zones. A maximum of 4 treatment areas may be treated at the same time.
- It is the responsibility of the practitioner to determine the maximum treated surface taking into account size of the dog, age, concomitant diseases and any other influencing factors.

The length of the treatment period:

Length of treatment depends on the speed of clinical and microbiological healing (i.e. clinical recovery of bacterial and fungal skin lesions).

- Application to the affected skin area should continue twice daily for 7 days.
- If dermatitis lesions have not clinically resolved by the 7th day of treatment, product application should be continued until the 14th day of treatment (see also section 4.4).
- If there are still signs of skin infection after 14 days of treatment, the dermatitis lesions should be re-evaluated by the veterinarian. If continued medical treatment is required, a change to another appropriate veterinary medicinal product is recommended.

This veterinary medicinal product must not be used exceeding the recommended dose per administration (0.2 ml/treatment, twice daily) nor beyond a 14-day period.

The used product has to be disposed after finishing the treatment (see also section 6.6).

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

At 5 times the recommended dose of 0.2 ml in one area per dog (i.e. product overdose volume of 1.0 ml) administered for a maximum treatment period of 14 days, no local or general adverse reactions were observed. No overdose studies in more than one area per dog at the same time were performed.

4.11 Withdrawal periods

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Dermatologicals, Corticosteroids, combination with antibiotics, prednisolone and antibiotics

ATCvet code: QD07CA03

5.1 Pharmacodynamic properties

The preparation combines three active ingredients, marbofloxacin, ketoconazole and prednisolone. Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the

fluoroquinolone antibiotics, which act by inhibiting DNA gyrase in gram-negative bacteria, or DNA topoisomerase IV in gram-positive bacteria. It is effective against *Pseudomonas aeruginosa* and *Staphylococcus pseudintermedius*. Such impairment disrupts replication of the bacterial cell, leading to rapid cell death. The rapidity and extent of killing are directly proportional to the drug concentration. Marbofloxacin is a concentration-dependent antibiotic with significant post antibiotic effect.

Marbofloxacin clinical breakpoints for *Staphylococcus* spp. in dogs (skin, soft tissue, UTI) are available. Strains with a MIC ≤ 1 $\mu\text{g/ml}$ are susceptible and with a MIC ≥ 4 $\mu\text{g/ml}$ are resistant to marbofloxacin (CLSI document VET01S, 2018).

Resistance to fluoroquinolones occurs by chromosomal mutations with the following mechanisms: (1) decrease in bacterial cell wall permeability, (2) expression change of genes coding for efflux pumps or (3) mutations in genes encoding enzymes responsible for molecule binding (i.e. bacterial DNA gyrase and DNA topoisomerase IV). Plasmid-mediated resistance to fluoroquinolones, which confers reduced susceptibility (i.e. Qnr protein that binds to and protects both DNA gyrase and topoisomerase IV), has also been described.

Depending on the underlying resistance mechanism, cross-resistance to other (fluoro)quinolones and co-resistance to other antimicrobial classes can occur.

Ketoconazole is an imidazole antifungal agent against *Malassezia pachydermatis*. It targets the ergosterol biosynthetic pathway by inhibition of a key enzyme, the lanosterol 14 α -demethylase, encoded by the ERG11 gene. Lower concentrations of ketoconazole are fungistatic, however higher concentrations are fungicidal.

Mechanism of resistance to azoles can be divided to four categories: (1) decrease in azole affinity of their target (e.g. by mutations in ERG11), (2) increase in azole target copy number (by ERG11 upregulation), (3) alteration of ergosterol biosynthetic pathway after azoles action, and (4) decrease in intracellular azole accumulation (e.g. by upregulation of multidrug transporter genes). In highly resistant clinical isolates, mechanisms of resistance can be combined as well.

Prednisolone is a synthetic corticosteroid. It inhibits the synthesis of eicosanoid molecules during the inflammatory processes due to the inhibition of phospholipase A2 enzyme. It demonstrates pronounced local and systemic anti-inflammatory properties.

5.2 Pharmacokinetic particulars

Following application of recommended dose of the veterinary medicinal product (i.e. app. 0.2 ml of test veterinary medicinal product, app. 0.21 mg marbofloxacin, 0.41 mg ketoconazole and 0.19 mg prednisolone twice daily, for 7-14 days) the pharmacologically active substances appeared in plasma samples only at very low concentration. The concentrations remained very low during the whole study. The highest levels of marbofloxacin, ketoconazole and prednisolone in plasma were 4.8 ng/l, 2.8 ng/l, and 4.4 ng/l, respectively. The above levels declined rapidly after the cessation of application.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dimethyl sulfoxide (DMSO)

Polysorbate 80

Propylene glycol Ethanol (96 per cent)

Water for injections

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 48 months.

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

6.4 Special precautions for storage

Do not refrigerate or freeze.

6.5 Nature and composition of immediate packaging

The material of the bottle is polyethylene terephthalate. The bottle closure system is a spraying pump. The materials of the pump are: polyethylene, polypropylene, solvent resistant thermoplastic elastomer, polyoxymethylene and stainless steel.

Approximately 0.1 ml solution is delivered per one spray.

Pack size:

Child resistant polyethylene container with 1 bottle of 30 ml.

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

Alpha-Vet Veterinary Ltd., Hofherr A. str. 42, Budapest, H-1194, Hungary

Tel.: +36-22-516-419

Fax: +36-22-516-416

E-mail: alpha-vet@alpha-vet.hu

8. MARKETING AUTHORIZATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}.

10. DATE OF REVISION OF THE TEXT

{DD month YYYY}

PROHIBITION OF SALE, SUPPLY AND/OR USE

Dispensing conditions: Veterinary medicinal product subject to veterinary prescription.

Administration conditions: Administration under the control or direct responsibility of a veterinary surgeon.

LABELLING AND PACKAGE LEAFLET

A. LABELLING

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE

PLASTIC BOTTLE WITH SPRAY PUMP - IMMEDIATE PACKAGING

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

GEFRIDERM cutaneous spray solution for dogs (ES, DE, IE, UK, EE)
Marbofloxacin / Ketoconazole / Prednisolone

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:

Active substances:

Marbofloxacin..... 1.025 mg
Ketoconazole..... 2.041 mg
Prednisolone 0.926 mg

3. PHARMACEUTICAL FORM

Cutaneous spray, solution

4. PACKAGE SIZE

30 ml

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

Once opened use within 28 days.

Use by: ...

11. SPECIAL STORAGE CONDITIONS

Do not refrigerate or freeze.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material 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

Alpha-Vet Veterinary Ltd., Hofherr A. str. 42, Budapest, H-1194, Hungary

Tel.: +36-22-516-419

Fax: +36-22-516-416

E-mail: alpha-vet@alpha-vet.hu

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE

CHILD RESISTANT CONTAINER- SECONDARY PACKAGING

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

GEFRIDERM cutaneous spray solution for dogs (ES, DE, IE, UK, EE)
Marbofloxacin / Ketoconazole / Prednisolone

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:

Active substances:

Marbofloxacin..... 1.025 mg
Ketoconazole..... 2.041 mg
Prednisolone 0.926 mg

3. PHARMACEUTICAL FORM

Cutaneous spray, solution

4. PACKAGE SIZE

30 ml

5. TARGET SPECIES

Dogs

6. INDICATION(S)

Treatment of acute superficial dermatitis caused by mixed infections with *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole. The indication is limited to focal skin infections (e.g. hot spots, intertrigo, superficial folliculitis).

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use. Shake well before use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

Once opened use within 28 days.

Use by: ...

11. SPECIAL STORAGE CONDITIONS

Do not refrigerate or freeze.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material 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

Alpha-Vet Veterinary Ltd., Hofherr A. str. 42, Budapest, H-1194, Hungary

Tel.: +36-22-516-419

Fax: +36-22-516-416

E-mail: alpha-vet@alpha-vet.hu

16. MARKETING AUTHORISATION NUMBER(S)**17. MANUFACTURER’S BATCH NUMBER**

Batch {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
GEFRIDERM cutaneous spray solution for dogs

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

Marketing authorisation holder: Alpha-Vet Veterinary Ltd., Hofherr A. str. 42, Budapest, H-1194, Hungary

Manufacturer responsible for batch release: Alpha-Vet Veterinary Ltd., Köves János str. 13, Bábolna, H-2943, Hungary

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

GEFRIDERM cutaneous spray solution for dogs (ES, DE, IE, UK, EE)
Marbofloxacin, Ketoconazole, Prednisolone

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

Each ml contains:

Active substances:

Marbofloxacin..... 1.025 mg
Ketoconazole..... 2.041 mg
Prednisolone 0.926 mg

Yellowish, slightly opaque solution

4. INDICATION(S)

Treatment of acute superficial dermatitis caused by mixed infections with *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole. The indication is limited to focal skin infections (e.g. hot spots, intertrigo, superficial folliculitis).

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

In very rare cases mild erythematous lesions have been reported in the literature after cutaneous application of the active substances.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1.000 animals treated)
- rare (more than 1 but less than 10 animals in 10.000 animals treated)
- very rare (less than 1 animal in 10.000 animals treated, including isolated reports).

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. Alternatively you

can report via your national reporting system. For details regarding the national system please contact NCA.

7. TARGET SPECIES

Dogs

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

Cutaneous use. Shake well before use.

Before application of the veterinary medicinal product, the affected area should be cleaned mechanically or by irrigation taking care to avoid further damage to the skin. Any excess exudate, hair or debris on the treated area should be carefully removed prior to application.

Apply 2 pumps of the pump spray bottle per 25 cm² area of affected skin twice daily for 7 days, up to a maximum of 14 days. Hold the pump spray bottle at a distance of 10 cm from the affected skin during application.

When spraying from a distance of about 10 cm, 2 pumps (approximately 0.2 ml) corresponds to a recommended treatment dosage is 8.20 µg of marbofloxacin, 16.33 µg of ketoconazole and 7.4 µg of prednisolone per cm² area of affected skin.

Treatment area(s):

The indication is limited to focal skin infections.

- A single area of affected skin for treatment covers an area of 25 cm². This area of skin is equivalent to an irregular shape of 5 cm x 5 cm.
- When the affected area of skin covers an area larger than 25 cm², the treated area should be divided into multiple 25 cm² zones. A maximum of 4 treatment areas may be treated at the same time.
- It is the responsibility of the practitioner to determine the maximum treated surface taking into account size of the dog, age, concomitant diseases and any other influencing factors.

The length of the treatment period:

Length of treatment depends on the speed of clinical and microbiological healing (i.e. clinical recovery of bacterial and fungal skin lesions).

- Application to the affected skin area should continue twice daily for 7 days.
- If dermatitis lesions have not clinically resolved by the 7th day of treatment, product application should be continued until the 14th day of treatment.
- If there are still signs of skin infection after 14 days of treatment, the dermatitis lesions should be re-evaluated by the veterinarian. If continued medical treatment is required, a change to another appropriate veterinary medicinal product is recommended.

This veterinary medicinal product must not be used exceeding the recommended dose per administration (0.2 ml/treatment, twice daily) nor beyond a 14-day period.

The used product has to be disposed after finishing the treatment.

9. ADVICE ON CORRECT ADMINISTRATION

This product is supplied in child resistant PE container as secondary packaging. To open it, press the ribbed part of the cap firmly with two fingers and screw it in the direction as

indicated by the arrows (counterclockwise). Press the ribbed part continuously while screwing.

The bottle must be closed/capped immediately after every use and stored in the child resistant container with cap.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not refrigerate or freeze. Do not use this veterinary medicinal product after the expiry date which is stated on the label, and carton after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 28 days

12. SPECIAL WARNING(S)

Special warnings for each target species:

Bacterial and fungal dermatitis is often secondary in nature and appropriate diagnosis should be used to determine the primary factors involved.

The unnecessary use of any pharmacologically active substance should be avoided.

Treatment is indicated only if mixed infection with *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* and *Malassezia pachydermatis* has been proved. If one of the pharmacologically active substances is no longer indicated due to the different characteristics of bacterial and fungal infections, the application of pharmacologically active substance should be discontinued and replaced by an appropriate treatment option.

The indication is limited to focal skin infections not exceeding 25 cm². The treatment is 2 pumps of the application pump to each treated animal when the affected area is under 25 cm², and above this value the treated area has to be partitioned 25 cm² zones, maximum 4 treatment areas at the same time. Cross-resistance has been shown between quinolones. The product should not be used when antimicrobial susceptibility testing has shown resistance to quinolones because its effectiveness may be reduced.

Special precautions for use in animals:

Animals should be prevented from licking the application site (e.g., by the fixation of a collar). Keep the animals to be treated separated from each other in order to prevent licking each other.

Use of the veterinary medicinal product should be based on identification of infecting organisms and susceptibility testing.

Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly to other classes of antimicrobials. However, microbiological diagnosis and susceptibility test must be performed. Official and local antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the fluoroquinolones and may reduce effectiveness of

treatment with other quinolones due to the potential for cross-resistance. Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population.

Direct contact of product with eyes must be avoided.

If hypersensitivity to any of the active components occurs, treatment should be discontinued and appropriate therapy should be initiated.

Prolonged and intensive use of topical corticosteroids preparation is known to trigger local and systemic effects, including suppression of adrenal function, thinning of the epidermis and delayed healing.

Spraying on open lesions and wounds must be avoided.

During the administration do not bath or shampoo the animal.

The hair coat should be kept short during treatment to assist optimal contact of antimicrobial agents with the skin surface. Use only on altered parts of skin.

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

This product may be harmful to children after accidental ingestion (gastrointestinal disturbances, insomnia, and restlessness). Do not leave the bottle out of its child resistant container except when applying the product to the animal. The bottle must be closed and placed in the child resistant container immediately after application and kept in a safe place out of the sight and reach of the children. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Ketoconazole and prednisolone may affect the unborn child and negatively influence male reproductive functions. Excessive exposure to the product may lead to foetal defects, or reduced sperm viability. The product should not be administered by pregnant women, or those trying to conceive.

Marbofloxacin, ketoconazole and prednisolone may cause hypersensitivity (allergy) reactions. People with known hypersensitivity to (fluoro)quinolones, ketoconazole, prednisolone, or DMSO should avoid contact with the product.

This product may be irritating to skin and mucosal membranes. Avoid contact with the skin including hand-to-mouth contact. Wear single-use impermeable gloves when handling and administering the product. If contact occurs, wash hands or the exposed area thoroughly with clean water.

Seek medical advice in case of hypersensitivity reactions or if irritation persists. Swelling of face, lip and eyes, or respiratory difficulties are more serious signs that need urgent medical action.

This product may be irritating to the eyes. Avoid contact with the eyes including hand-to eye contact. If contact occurs, rinse with clean water. If eye irritation persists, seek medical advice and show the package leaflet or label to the physician.

This product may be harmful after inhalation. Spray animals in the open air or in well-ventilated area. Avoid breathing in the spray-mist.

Do not smoke, drink or eat while handling the product.

Flammable solution. Do not spray on naked flame or any incandescent material.

Avoid prolonged contact with the treated animals. Treated animals should not be handled and children should not be allowed to play with treated animals until the application site is dry (at least 20 minutes). It is therefore recommended that animals are not treated during the day, but should be treated during the early morning and evening.

Treated animals should not be allowed to sleep with owners, especially children.

Treated areas should not be touched during the treatment period; any fur, or other areas that do not require this treatment, that may have been sprayed, should be thoroughly cleaned

using a disinfectant wipe to prevent contamination. Any wipes and gloves used should be disposed of immediately.

Pregnancy and lactation:

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. The use is not recommended during pregnancy and lactation. Studies with ketoconazole in laboratory animals have shown evidence of teratogenic and embryotoxic effects.

Interaction with other medicinal products and other forms of interaction:

Concomitant use of products with a low pH might have an inhibitory effect on the activity of marbofloxacin and are to be avoided. No interaction studies have been provided to confirm acceptability of use of products in combination and so the safety/efficacy of such combined product use is uncertain.

Overdose (symptoms, emergency procedures, antidotes):

At 5 times the recommended dose of 0.2 ml in one area per dog (i.e. product overdose volume of 1.0 ml) administered for a maximum treatment period of 14 days, no local or general adverse reactions were observed. No overdose studies in more than one area per dog at the same time were performed.

Incompatibilities:

Not applicable.

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

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

The material of the bottle is polyethylene terephthalate. The bottle closure system is a spraying pump. The materials of the pump are: polyethylene, polypropylene, solvent resistant thermoplastic elastomer, polyoxymethylene and stainless steel.

Approximately 0.1 ml solution is delivered per one spray.

Pack size:

Child resistant polyethylene container with 1 bottle of 30 ml.

Dispensing conditions: Veterinary medicinal product subject to veterinary prescription.

Administration conditions: Administration under the control or direct responsibility of a veterinary surgeon.

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