SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ALPHADERM Plus cutaneous spray solution for dogs
(in Austria, Bulgaria, Czech Republic, Hungary, Italy, Romania, Slovenia, Slovakia)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of product 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
Yellowish, slightly opal solution

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Treatment of acute dermatitis in dogs, when mixed infection caused by *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole is demonstrated.

4.3 Contraindications

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

4.4 Special warnings for each target species

Collar should be fixed on the treated dogs in order to prevent licking. Keep the animal to be treated separated from each other in order to prevent licking each other.
Bacterial and fungal dermatitis is often secondary in nature and appropriate diagnosis should be used to determine the primary factors involved.
Unnecessary use of the product in terms of any 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 active substances is no longer indicated due to the different characteristics of bacterial and fungal infections, the application of the product should be discontinued and replaced by an appropriate treatment option.

4.5 Special precautions for use

Special precautions for use in animals

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

Use of the veterinary medicinal product should be based on identification of infecting organisms and susceptibility testing and take into account official and local antimicrobial policies.

Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population. It is prudent to reserve fluoroquinolones for the treatment of clinical conditions, which have responded poorly or are expected to respond poorly to other classes of antibiotics.

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.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the quinolones and may decrease the effectiveness of treatment with other (fluoro) quinolones due to the potential for cross resistance.

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

Wear personal protective equipment, impermeable gloves when administering the product.

In case of skin exposition clean the contaminated skin with a water-soap solution.

In case eye contact, wash immediately with abundant water.

Seek medical advice if signs of cutaneous erithema, exanthema, or persistent ocular irritation appear after exposure. Swelling of face, lips and eyes, or respiratory difficulties are more serious signs that need urgent medical action.

Solution is inflammable, smoking and using naked flame is prohibited during administration.

4.6 Adverse reactions (frequency and seriousness)

Mild erythematous lesions have been observed following the application. The frequency of adverse reactions is very rare (less than 1 animal in 10,000 animals, including isolated reports).

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

- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, 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.

4.8 Interaction with other medicinal products and other forms of interaction

No data are available.

4.9 Amounts to be administered and administration route

Only for external use. Shake well before use.
The recommended dose level of the product for dogs is 2 squeezes of the application pump (two pumps are equivalent to app. 0.2 ml) two times per day, for 7-14 days. Spray from a distance of about 10 cm for 5 cm x 5 cm and from a distance of about 30 cm for about 10 cm x10 cm area of skin to be treated. Before the application of product the hair or dirt on the treated surface has to be removed.
Bacterial and fungal infections might require different treatment schedule. After 7 days of treatment, the veterinary surgeon should evaluate if it is necessary to extend the treatment with this product for another week or to continue the treatment with another product containing a smaller number of active substances.

4.10 Overdose (symptoms, emergency procedure, antidotes), if necessary
At 5 times the recommended dose, no local or general adverse reactions were observed.

4.11 Withdrawal periods
Not applicable.

5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group:
Dermatologicals. corticosteroids, weak, combinations with antibiotics
ATCvet code: QD07CA03

5.1 Pharmacodynamic properties
Marbofloxacin is a synthetic broad-spectrum bactericidal agent. It is classified as 2.2 generation fluoproquinolone. It has activity against wide range of Gram-positive and Gram-negative organism, as well as against mycoplasmas. The bactericidal action of marbofloxacin results from interference with the enzymes DNA topoisomerase II (DNA-gyrase) in Gram-negatives ad DNA topoisomerase IV in Gram-positives which are needed for the synthesis and maintenance of bacterial DNA. 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. It consists of significant post antibiotic effect (PAE).
Ketoconazole is a broad spectrum imidazole antifungal agent. It inhibits the ergosterol biosynthesis of the sensitive fungal strains. Lower concentrations of ketoconazole are fungistatic, however higher concentrations are fungicidal.
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
Systemic absorption of the active ingredients was determined in the course of target animal safety studies with the product. Following application of therapeutic levels of the product (i.e. app. 0.2 ml of test product, app. 0.44 mg ketoconazole twice daily, for 14 days) the active ingredients 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.
With regard to available data, following the therapeutic application the active ingredients of the product will not accumulate causing drug-related harmful action in treated dogs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Dimethyl sulfoxide (DMSO)
Polysorbate 80
Propylene-glycol
Ethanol (96%)
Water for injection

6.2 Major incompatibilities
None known.

6.3 Shelf life
Shelf life of the veterinary medicinal product as packaged for sale: 5 years (100 ml).
Shelf life of the veterinary medicinal product as packaged for sale: 3 years (30 ml).
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage
Store below 25 °C.

6.5 Nature and composition of immediate packaging
30 ml or 100 ml PET bottle with a spray pump in cardboard 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 AUTHORISATON HOLDER
ALPHA-VET Állatgyógyászati Kft., H-1194 Budapest, Hofherr A. u. 42., Hungary.
Tel.: +36-22-516-416
Fax: +36-22-516-419
E-mail: alpha-vet@alpha-vet.hu

8. MARKETING AUTHORIZATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE
Not applicable.

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE

PLASTIC BOTTLE WITH SPRAY PUMP - IMMEDIATE PACKAGING
CARDBOARD BOX - SECONDARY PACKAGING

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

In Austria, Bulgaria, Hungary, Italy, Romania, Slovenia, Slovakia:
ALPHADERM Plus cutaneous spray solution for dogs
Marbofloxacin, Ketoconazole, Prednisolone

In Czech Republic:
Alphaderm Plus, sprej pro zevní použití, roztok
(indikačním omezením)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml of product 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
100 ml

5. TARGET SPECIES

Dogs

6. INDICATION(S)

Treatment of acute dermatitis in dogs, when mixed infection caused by *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole is demonstrated.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Only for external use. Shake well before use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

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

Store below 25 C.

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 Állatgyógyászati Kft., Hofherr A. u. 42., Budapest, H-1194, Hungary
Tel.: +36-22-516-416
Fax: +36-22-516-419
E-mail: alpha-vet@alpha-vet.hu

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

NATIONAL ISSUE - ITALY

Manufacturer responsible for batch release:
ALPHA-VET Állatgyógyászati Kft., Köves János út 13., Bábolna, H-2943, Hungary

PACKAGE LEAFLET

ALPHADERM Plus 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 Állatgyógyászati Kft., Hofherr A. u. 42., Budapest, H-1194, Hungary

Manufacturer responsible for batch release:
ALPHA-VET Állatgyógyászati Kft., Köves János út 13., Bábolna, H-2943, Hungary

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

ALPHADERM Plus cutaneous spray solution for dogs
Marbofloxacin, Ketoconazole, Prednisolone
(in Austria, Bulgaria, Czech Republic, Hungary, Italy, Romania, Slovenia, Slovakia)

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

Each ml of product contains:
Active substances:
Marbofloxacin……. 1.025 mg
Ketoconazole……..….. 2.041 mg
Prednisolone …… 0.926 mg

4. INDICATION(S)

Treatment of acute dermatitis in dogs, when mixed infection caused by *Pseudomonas aeruginosa* or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole is demonstrated.

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Mild erythematous lesions have been observed following the application. The frequency of adverse reactions is very rare (less than 1 animal in 10,000 animals, including isolated reports).
The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

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

Only for external use. Shake well before use.
The recommended dose level of the product for dogs is 2 squeezes of the application pump (two pumps are equivalent to app. 0.2 ml) two times per day, for 7-14 days. Spray from a distance of about 10 cm for 5 cm x 5 cm and from a distance of about 30 cm for about 10 cm x10 cm area of skin to be treated. Before the application of product the hair or dirt on the treated surface has to be removed.
Bacterial and fungal infections might require different treatment schedule. After 7 days of treatment, the veterinary surgeon should evaluate if it is necessary to extend the treatment with this product for another week or to continue the treatment with another product containing a smaller number of active substances.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Store below 25 °C.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP.
Shelf life after first opening the container: 28 days.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Collar should be fixed on the treated dogs in order to prevent licking. Keep the animal to be treated separated from each other in order to prevent licking each other.

Bacterial and fungal dermatitis is often secondary in nature and appropriate diagnosis should be used to determine the primary factors involved.
Unnecessary use of the product in terms of any active substance should be avoided. Treatment is indicated only if mixed infection with bacteria and Malassezia spp. is demonstrated. If one of the active substances is no longer indicated due to the different characteristics of bacterial and fungal infections, the application of the product should be discontinued and replaced by an appropriate treatment option.

Special precautions for use in animals:
If hypersensitivity to any of the components occurs, treatment should be discontinued and appropriate therapy instituted.
Use of the veterinary medicinal product should be based on identification of infecting organisms and susceptibility testing and take into account official and local antimicrobial policies.
Heavy reliance on a single class of antibiotic may result in the induction of resistance in a bacterial population. It is prudent to reserve fluoroquinolones for the treatment of clinical conditions, which have responded poorly or are expected to respond poorly to other classes of antibiotics.
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.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to the quinolones and may decrease the effectiveness of treatment with other (fluoro) quinolones due to the potential for cross resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wear personal protective equipment, impermeable gloves when administering the product.
In case of skin exposition clean the contaminated skin with a water-soap solution.
In case eye contact, wash immediately with abundant water.
Seek medical advice if signs of cutaneous erythema, exanthema, or persistent ocular irritation appear after exposure. Swelling of face, lips and eyes, or respiratory difficulties are more serious signs that need urgent medical action.
Solution is inflammable, smoking and using naked flame is prohibited during administration.

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.

Interaction with other medicinal products and other forms of interaction:
No data are available.

Overdose (symptoms, emergency procedures, antidotes):
At 5 times the recommended dose, no local or general adverse reactions were observed.

Incompatibilities:
None known.

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

Ask your veterinary surgeon or pharmacist 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

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