[Version 8.1,01/2017]

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Triderm cutaneous spray solution for dogs (CY, ES, EL, HR, LT, LV, MT, PT)
Tripoflox cutaneous spray solution for dogs (PL)

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 opal solution

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Treatment of acute dermatitis when mixed infection caused by *Pseudomonas aeruginos*a or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole is demonstrated. The veterinary medicinal product should be used based on susceptibility testing on the bacteria isolated from the animal.

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 animals 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 pharmacologically active substance in terms of any pharmacologically active substance should be avoided. Treatment is indicated only if mixed infection with *Pseudomonas aeruginos*a 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.

4.5 Special precautions for use

Special precautions for use in animals

If hypersensitivity to any of the active components occurs, treatment should be discontinued and appropriate therapy should be 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. However, microbiological diagnosis and sensitivity test must be performed.

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 animals.

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

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

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

Do not inhale spray mist. Use only in well ventilated areas

Several components of the product may cause hypersensitivity reactions as well as skin and/or eye irritation.

People with known hypersensitivity to (fluoro)quinolones, ketoconazole, prednisolone or any of the excipients should avoid contact with the veterinary medicinal product.

Avoid contact with skin or eyes. In case of accidental spillage, skin or eyes should be rinsed immediately with plenty of water.

Wash hands after use.

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.

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

Treated animals should not be handled, and children should not be allowed to play with treated animals until the fur is dry.

Animals treated should not be allowed to sleep with owners, especially children.

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 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.

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

4.9 Amounts to be administered and administration route
Cutaneous use. Shake well before use.
The recommended dosage is 2.26-9.18 µg of marbofloxacin, 4.52-18.36 µg of ketoconazole and 2.08-8.45 µg of prednisolone per cm^2 of affected skin per day. This dosage can be achieved with two pump spray activations (equivalent to approximately 0.2 ml/ treatment) over a surface to be treated equivalent to a square of 5 cm x 5 cm when spraying from a distance of about 10 cm; of 10 cm x 10 cm when spraying from a distance of about 30 cm. Repeat the application twice a day for 7-14 days, depending on clinical and microbiological healing. Before the application of the veterinary medicinal product the hair or dirt on the treated surface has to be removed.
Period of treatment depends on clinical convalescence of skin inflammations of bacterial and of fungal origin. In case the dog treated doesn't recover until 7^{th} day the treatment should be followed until 14^{th} day. In those cases when the dog still didn't recover within 14 days, it is recommendable to change to another, adequate veterinary medicinal product.

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

4.11 Withdrawal periods
Not applicable.

5. PHARMACOLOGICAL PROPERTIES
Pharmacotherapeutic group: antibiotics and chemotherapeutics, combinations. Marbofloxacin, Ketoconazole, Prednisolone.
ATCvet code: QD06C

5.1 Pharmacodynamic properties

Marbofloxacin is a synthetic, bactericidal antimicrobial, belonging to the fluoroquinolone group which acts by the inhibition of DNA gyrase and topoisomerase IV. 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 µg/ml are susceptible and with a MIC ≥4 µg/ml are resistant to marbofloxacin (CLSI document VET01S, 2015).

Resistance to fluoroquinolones occurs by chromosomal mutations with the following mechanisms: decrease in bacterial cell wall permeability, expression change of genes coding for efflux pumps or mutations in genes encoding enzymes responsible for molecule binding. Plasmid-mediated resistance to fluoroquinolones, which confers reduced susceptibility, 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 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.
According to our preclinical efficacy study carried out in 2017-2018:

Microorganism	MIC_{90} (µg/ml)
Malassezia pachydrematis	0.063

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.
With regard to available data, following the therapeutic application the active ingredients of the product will not absorb from skin and 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
Not applicable.

6.3 Shelf life
Shelf life of the veterinary medicinal product as packaged for sale: 4 years.
Shelf life after first opening the immediate packaging: 28 days.

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
Pack size: Box with 1 bottle of 30 ml.

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.

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
Organit Kft., Homoksor 7., Székesfehérvár, H-8000, Hungary.
Tel.: +36-22-516-419
Fax: +36-22-516-416
E-mail: phv@organit.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
CARDBOARD BOX - SECONDARY PACKAGING

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

TRIDERM cutaneous spray solution for dogs (CY, ES, EL, HR, LT, LV, MT, PT)
TRIPOFLOX cutaneous spray solution for dogs (PL)
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
Yellowish-slightly opal solution.

4. PACKAGE SIZE

30 ml

5. TARGET SPECIES

Dogs

6. INDICATION(S)

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

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

Organit Kft., Homoksor 7., Székesfehérvár, H-8000, Hungary.
Tel.: +36-22-516-419
Fax: +36-22-516-416
E-mail: phv@organit.hu

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
TRIDERM cutaneous spray solution for dogs
TRIPOFLOX 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: Organit Kft., Homoksor 7., Székesfehérvár, H-8000, 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

TRIDERM cutaneous spray solution for dogs (CY, ES, EL, HR, LT, LV, MT, PT)
TRIPOFLOX cutaneous spray solution for dogs (PL)
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
Excipients: q.s

Yellowish-slightly opal solution.

4. INDICATION(S)

Treatment of acute dermatitis when mixed infection caused by *Pseudomonas aeruginos*a or *Staphylococcus pseudintermedius* susceptible to marbofloxacin and *Malassezia pachydermatis* susceptible to ketoconazole is demonstrated. The veterinary medicinal product should be used based on susceptibility testing on the bacteria isolated from the animal.

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 treated, including isolated reports).
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.
The recommended dosage is 2.26-9.18 µg of marbofloxacin, 4.52-18.36 µg of ketoconazole and 2.08-8.45 µg of prednisolone per cm2 of affected skin per day. This dosage can be achieved with two pump spray activations (equivalent to approximately 0.2 ml/ treatment) over a surface to be treated equivalent to a square of 5 cm x 5 cm when spraying from a distance of about 10 cm; of 10 cm x 10 cm when spraying from a distance of about 30 cm. Repeat the application twice a day for 7-14 days, depending on clinical and microbiological healing. Before the application of the veterinary medicinal product the hair or dirt on the treated surface has to be removed.
Period of treatment depends on clinical convalescence of skin inflammations of bacterial and of fungal origin. In case the dog treated doesn't recover until 7th day the treatment should be followed until 14th day. In those cases in which the treatment was extended to 14 days and dog still didn’t recover within 14 days, it is recommendable to change to another, adequate veterinary medicinal product.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.
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)

None.

Special warnings for each target species:
Collar should be fixed on the treated dogs in order to prevent licking. Keep the animals 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 pharmacologically active substance in terms of any active substance should be avoided. Treatment is indicated only if mixed infection with *Pseudomonas aeruginos*a 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.

Special precautions for use in animals:
If hypersensitivity to any of the active components occurs, treatment should be discontinued and appropriate therapy should be 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. However, microbiological diagnosis and sensitivity test must be performed.
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 is must be avoided.
During the administration do not bath or shampoo the animals.

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

As with all medicinal formulation operators are advised to use the product according to label instructions.

Flammable solution. Do not spray on naked flame or any incandescent material.
Do not smoke, drink or eat while handling the product.
Do not inhale spray mist. Use only in well ventilated areas
Several components of the product may cause hypersensitivity reactions as well as skin and/or eye irritation.
People with known hypersensitivity to (fluoro)quinolones, ketoconazole, prednisolone or any of the excipients should avoid contact with the veterinary medicinal product.
Avoid contact with skin or eyes. In case of accidental spillage, skin or eyes should be rinsed immediately with plenty of water.
Wash hands after use.
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.
In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.
Treated animals should not be handled, and children should not be allowed to play with treated animals until the fur is dry.
Animals treated should not be allowed to sleep with owners, especially children.

Product should be kept out of sight and reach of children.

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 available.

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

Incompatibilities:
Not applicable.

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

Medicines should not be disposed of via wastewater or household waste.
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

Pack size:
Box 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.