

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Outer carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sporimune 50 mg/ml oral solution for cats and dogs
Ciclosporin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Ciclosporin 50 mg/ml

3. PHARMACEUTICAL FORM

Oral solution

4. PACKAGE SIZE

1 x25 ml
1 x 50 ml
1 x 100 ml

5. TARGET SPECIES

For cats and dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once opened, use by 6 months

11. SPECIAL STORAGE CONDITIONS

Do not refrigerate.
Store in the original container in order to protect from light.

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 sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Le Vet Beheer B.V.
The Netherlands

16. MARKETING AUTHORISATION NUMBER

Vm 41821/4017

17. MANUFACTURER'S BATCH NUMBER

LOT

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Brown glass bottle with 25 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sporimune 50 mg/ml oral solution for cats and dogs
Ciclosporin

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Ciclosporin 50 mg/ml

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

25 ml

4. ROUTE(S) OF ADMINISTRATION

Oral use

5. WITHDRAWAL PERIOD(S)

6. BATCH NUMBER

LOT

7. EXPIRY DATE

EXP (month/year)
Once opened, use by _____.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Brown glass bottle with 50 ml 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sporimune 50 mg/ml oral solution for cats and dogs
Ciclosporin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Ciclosporin 50 mg/ml

3. PHARMACEUTICAL FORM

Oral solution

4. PACKAGE SIZE

50 ml
100 ml

5. TARGET SPECIES

Cats and Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP (month/year)
Once opened, use by _____

11. SPECIAL STORAGE CONDITIONS

Do not refrigerate.
Store in the original container in order to protect from light.

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

Le Vet Beheer B.V.
The Netherlands

16. MARKETING AUTHORISATION NUMBER

Vm 41821/4017

17. MANUFACTURER'S BATCH NUMBER

LOT

B. PACKAGE LEAFLET

Do not use in dogs less than six months of age or less than 2 kg in weight.
Do not use in cases with a history of malignant disorders or progressive malignant disorders.
Do not vaccinate with a live vaccine during treatment or within a two-week interval before or after treatment.
Do not use in cats infected with FeLV or FIV.
See also section "Special warning(s)".

6. ADVERSE REACTIONS

Dogs

Gastrointestinal disturbances such as vomiting, mucoid or soft faeces and diarrhoea are observed very commonly. They are mild and transient and generally do not require the cessation of the treatment.

Other undesirable effects may be observed uncommonly: lethargy or hyperactivity, anorexia, mild to moderate gingival hyperplasia, skin lesions such as verruciform lesions or change of hair coat, red and swollen pinnae, muscle weakness or muscle cramps. These effects generally resolve spontaneously after treatment is stopped. In very rare cases diabetes mellitus has been observed, reported mainly in West Highland White Terriers.

Cats

In 2 clinical studies with 98 cats treated with ciclosporin the following undesirable effects were observed:

Very common: gastrointestinal disturbances such as vomiting and diarrhoea. These are generally mild and transient and do not require the cessation of the treatment.

Common: lethargy, anorexia, hypersalivation, weight loss and lymphopenia. These effects generally resolve spontaneously after treatment is stopped or following a decrease in the dosing frequency.

Side effects may be severe in individual animals.

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

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).

7. TARGET SPECIES

Dogs, cats.

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

For oral use.

To ensure administration of the correct dosage bodyweight should be determined as accurately as possible.

At first use: replace the original screw cap of the bottle with the separately delivered screw cap. Fill the correct dosing syringe by pulling the plunger until it reaches the graduation corresponding to the correct body weight of the cat or dog.

Dosage and method of administration

Dogs

The mean recommended dose of ciclosporin is 5 mg per kg bodyweight (0.25 ml oral solution per 2.5 kg bodyweight).

Cats

The recommended dose of ciclosporin is 7 mg/kg body weight (0.14 ml of oral solution per kg) and should initially be administered daily. The frequency of administration should subsequently be reduced depending on the response.

Duration and frequency of administration

The product will initially be given daily until a satisfactory clinical improvement is seen (assessed by intensity of pruritus and lesion severity - excoriations, miliary dermatitis, eosinophilic plaques and/or self-induced alopecia). This will generally be the case within 4-8 weeks. If no response is obtained within the first 8 weeks, the treatment should be stopped.

Once the clinical signs of atopic/allergic dermatitis are satisfactorily controlled, the preparation can then be given every other day as a maintenance dose. The veterinarian should perform a clinical assessment at regular intervals and adjust the frequency of administration to the clinical response obtained.

In some cases where the clinical signs are controlled with every-other-day dosing, the veterinarian can decide to give the veterinary medicinal product every 3 to 4 days. The lowest effective frequency of dosing should be used to maintain the remission of clinical signs.

Adjunct treatment (e.g. medicated shampoos, fatty acids) may be considered before reducing the dosing interval. Patients should be regularly re-evaluated and alternative treatment options reviewed.

Treatment may be stopped when the clinical signs are controlled. Upon recurrence of clinical signs, treatment should be resumed at daily dosing, and in certain cases repeated treatment courses may be required.

9. ADVICE ON CORRECT ADMINISTRATION

Before starting treatment, an evaluation of all alternative treatment options should be made.

After administration of the veterinary medicinal product close bottle tightly with cap, wash the measuring syringe with water and let it dry.

Dogs

The veterinary medicinal product should be given at least 2 hours before or after feeding.

The product should be administered directly into the dog's mouth on the back of the tongue using the graduated dosing syringe supplied (1 ml oral solution contains 50 mg ciclosporin) and delivering the entire dose.

Cats

The veterinary medicinal product can be given either mixed with food or directly into the mouth. If given with food, the solution should be mixed with half the normal amount of food consumed using the graduated dosing syringe supplied. (1 ml oral solution contains 50 mg ciclosporin), preferably after a sufficient period of fasting to ensure complete consumption by the cat. When the medicated feed is fully consumed the rest of the food may be given.

Should the cat not accept the product mixed with food, it should be given by inserting the syringe directly into the cat's mouth and delivering the entire dose. If the cat only partially eats the product mixed with food, administration of the product directly into the mouth using the graduated dosing syringe must only be continued the next day.

10. WITHDRAWAL PERIOD

Not applicable

11. SPECIAL STORAGE PRECAUTIONS

Do not refrigerate.

Store in the original container in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton after "EXP". The expiry date refers to the last day of that month.

Shelf-life after first opening the container: 6 months.

Keep out of the sight and reach of children.

The product contains fat components from natural origin which can become solid at lower temperatures. A turbidity or jelly-like formation may occur below 15°C which is however reversible at temperatures up to 25°C. However, this does not affect either the dosing or the efficacy and safety of the product.

12. SPECIAL WARNING(S)

Special warnings for each target species

Consideration should be given to the use of other measures and/or treatments to control moderate to severe pruritus when initiating therapy with ciclosporin.

Special precautions for use in animals

Clinical signs of atopic dermatitis and allergic dermatitis in cats such as pruritus and skin inflammation are not specific for this disease. Other causes of dermatitis such as ectoparasitic infestations, other allergies which cause dermatological signs (e.g. flea allergic dermatitis or food allergy) or bacterial and fungal infections should be

evaluated and eliminated where possible. It is good practice to treat flea infestations before and during treatment of atopic and allergic dermatitis.

A complete clinical examination should be performed before treatment.

Any infections should be properly treated before initiation of treatment. Infections occurring during treatment are not necessarily a reason for drug withdrawal, unless the infection is severe.

Particular attention must be paid to vaccination. Treatment with the veterinary medicinal product may interfere with vaccination efficacy. In the case of inactivated vaccines, it is not recommended to vaccinate during treatment or within a two-week interval before or after administration of the product. For live vaccines see also section "Contraindications".

It is not recommended to use other immunosuppressive agents concomitantly.

In laboratory animals, ciclosporin is liable to affect the circulating levels of insulin and to cause an increase in glycaemia. In the presence of suggestive signs of diabetes mellitus, the effect of treatment on glycaemia must be monitored. If signs of diabetes mellitus are observed following the use of the product, e.g. polyuria or polydipsia, the dose should be tapered or discontinued and veterinary care sought. The use of ciclosporin is not recommended in diabetic animals.

While ciclosporin does not induce tumours, it does inhibit T-lymphocytes and therefore treatment with ciclosporin may lead to an increased incidence of clinically apparent malignancy due to the decrease in antitumour immune response. The potentially increased risk of tumour progression must be weighed against the clinical benefit. If lymphadenopathy is observed in animals being treated with ciclosporin, further clinical investigations are recommended and treatment discontinued if necessary.

Dogs

Closely monitor creatinine levels in dogs with severe renal insufficiency.

Cats

Allergic dermatitis in cats can have various manifestations, including eosinophilic plaques, head and neck excoriation, symmetrical alopecia and/or miliary dermatitis.

The immune status of the cats to FeLV and FIV infections should be assessed before treatment.

Cats that are seronegative for *T. gondii* may be at risk of developing clinical toxoplasmosis if they become infected while under treatment. In rare cases this can be fatal. Potential exposure of seronegative cats or cats suspected to be seronegative to *Toxoplasma* should therefore be minimised (e.g. keep indoors, avoid raw meat or scavenging). Ciclosporin was shown to not increase *T. gondii* oocyte shedding in a controlled laboratory study. In cases of clinical toxoplasmosis or other serious systemic illness, stop treatment with ciclosporin and initiate appropriate therapy.

Clinical studies in cats have shown that decreased appetite and weight loss may occur during ciclosporin treatment. Monitoring of body weight is recommended.

Significant reduction in body weight may result in hepatic lipidosis. If persistent, progressive weight loss occurs during treatment it is recommended to discontinue treatment until the cause has been identified.

The efficacy and safety of ciclosporin has neither been assessed in cats less than 6 months of age nor weighing less than 2.3 kg.

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

Accidental ingestion of this product may lead to nausea and/or vomiting. To avoid accidental ingestion, the product must be used and kept out of reach of children. Do not leave unattended filled syringe in the presence of children. Any uneaten medicated cat food must be disposed of immediately and the bowl washed thoroughly. In case of accidental ingestion, particularly by a child, seek medical advice immediately and show the package leaflet or the label to the physician. Ciclosporin can trigger hypersensitivity (allergic) reactions. People with known hypersensitivity to ciclosporin should avoid contact with the product. Irritation to eyes is unlikely. As precautionary measure avoid contact with eyes. In case of contact, rinse thoroughly with clean water. Wash hands and any exposed skin after use

Pregnancy and lactation

In laboratory animals, at doses which induce maternal toxicity (rats at 30 mg/kg bw and rabbits at 100 mg/kg bw) ciclosporin was embryo- and foetotoxic, as indicated by increased pre- and postnatal mortality and reduced foetal weight together with skeletal retardations. In the well-tolerated dose range (rats at up to 17 mg/kg bw and rabbits at up to 30 mg/kg bw) ciclosporin was without embryo-lethal or teratogenic effects. The safety of the drug has neither been studied in breeding male cats or dogs nor in pregnant or lactating female cats or dogs. In the absence of such studies in the target species, it is recommended to use the drug in breeding cats or dogs only upon a positive risk/benefit assessment by the veterinarian.

Ciclosporin passes the placenta barrier and is excreted via milk. Therefore the treatment of lactating bitches or queens is not recommended.

Interaction with other medicinal products and other forms of interaction

Various substances are known to competitively inhibit or induce the enzymes involved in the metabolism of ciclosporin, in particular cytochrome P450 (CYP 3A 4). In certain clinically justified cases, an adjustment of the dosage of the veterinary medicinal product may be required. Ketoconazole is known to increase the blood concentration of ciclosporin in cats and dogs, which is considered to be clinically relevant. During concomitant use of ketoconazole and ciclosporin the veterinarian should consider as a practical measure to double the treatment interval if the animal is on a daily treatment regime.

Macrolides such as erythromycin may increase the plasma levels of ciclosporin up to twofold.

Certain inducers of cytochrome P450, anticonvulsants and antibiotics (e.g. trimethoprim/sulfadimidine) may lower the plasma concentration of ciclosporin.

Ciclosporin is a substrate and an inhibitor of the MDR1 P-glycoprotein transporter. Therefore, the co-administration of ciclosporin with P-glycoprotein substrates such as macrocyclic lactones (e.g. ivermectin and milbemycin) could decrease the efflux of such drugs from blood-brain barrier cells, potentially resulting in signs of CNS toxicity. In clinical studies with cats treated with ciclosporin and selamectin or milbemycin,

there did not appear to be an association between these drugs' concomitant use and neurotoxicity.

Ciclosporin can increase the nephrotoxicity of aminoglycoside antibiotics and trimethoprim. The concomitant use of ciclosporin is not recommended with these active ingredients.

Particular attention must be paid to vaccination (see section "Contraindications").

Concomitant use of immunosuppressive agents: see section "Special warning(s)".

Incompatibilities

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

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

There is no specific antidote and in case of signs of overdose the animal should be treated symptomatically.

Dogs:

No undesirable effects beyond those that were seen under recommended treatment have been observed in the dog with a single oral dose of up to 5 times of what is recommended.

In addition to what was seen under recommended dosage, the following adverse reactions were seen in case of overdose for 3 months or more at 4 times the mean recommended dosage: hyperkeratotic areas especially on the pinnae, callous-like lesions of the foot pads, weight loss or reduced weight gain, hypertrichosis, increased erythrocyte sedimentation rate, decreased eosinophil values. Frequency and severity of these signs are dose dependent.

The signs are reversible within 2 months following cessation of treatment.

Cats:

The following adverse events were seen in the case of repeated administration of the active substance for 56 days at 24 mg/kg (more than 3x the recommended dose) or for 6 months at up to 40 mg/kg (more than 5x the recommended dose): loose/soft faeces, vomiting, mild to moderate increases in absolute lymphocyte counts, fibrinogen, activated partial thromboplastin time (APTT), slight increases in blood glucose and reversible gingival hypertrophy. The frequency and severity of these signs were generally dose and time dependent. At 3x the recommended dose administered daily for nearly 6 months, changes in ECG (conduction disturbances) may occur in very rare cases. They are transient and not associated with clinical signs. Anorexia, recumbency, loss of skin elasticity, few or absent faeces, thin and closed eye lids may be observed in sporadic cases at 5x the recommended dose.

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 products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Brown glass bottles (type III) of 25, 50 or 100 ml, closed with a child resistant closure (PP screw cap with a Teflon inlay).

One bottle and a dispenser set (consisting of a child resistant HDPE screw cap and a 1 ml PP dosing syringe for cats and a 5 ml PP dosing syringe for dogs) packed in a cardboard box.

Not all pack sizes may be marketed.

A handwritten signature in black ink, consisting of several loops and a long horizontal stroke extending to the right.

Approved 10 December 2018