ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box of 5, 15, 30, 50 or 60 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclavance 100 mg/ml oral solution
Ciclosporin

2. STATEMENT OF ACTIVE SUBSTANCES

Ciclosporin 100 mg/ml

3. PHARMACEUTICAL FORM

Oral solution

4. PACKAGE SIZE

5 ml
15 ml
30 ml
50 ml
60 ml

5. TARGET SPECIES

Dogs, cats

6. INDICATION(S)

Treatment of chronic manifestations of atopic dermatitis in dogs.
Symptomatic treatment of chronic allergic dermatitis in cats.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

9. SPECIAL WARNING(S), IF NECESSARY

Wash hands after administration.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician. People with known hypersensitivity to ciclosporin should avoid contact with the product.

10. EXPIRY DATE

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

11. SPECIAL STORAGE CONDITIONS

Keep the bottle in the outer carton.
Do not refrigerate.

After first opening: Do not store above 25°C.

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

VIRBAC
1ère avenue – 2065 m – L.I.D.
06516 Carros
FRANCE

16. MARKETING AUTHORISATION NUMBER

Vm 05653/5045

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Bottle of 60 ml (packaging type 1)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclavance 100 mg/ml oral solution
Ciclosporin

2. STATEMENT OF ACTIVE SUBSTANCES

Ciclosporin 100 mg/ml

3. PHARMACEUTICAL FORM

Oral solution

4. PACKAGE SIZE

60 ml

5. TARGET SPECIES

Dogs, cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
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 within 6 months.

11. SPECIAL STORAGE CONDITIONS

Keep the bottle in the outer carton.
Do not refrigerate.
After first opening: Do not store above 25°C.

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.

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

VIRBAC
1ère avenue – 2065 m – L.I.D.
06516 Carros
FRANCE

16. MARKETING AUTHORISATION NUMBER

Vm 05653/5045

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Bottle of 5, 15, 30
Bottle of 50 ml (packaging type 2)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclavance 100 mg/ml oral solution for dogs and cats
Ciclosporin

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Ciclosporin 100 mg/ml

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

5 ml
15 ml
30 ml
50 ml

4. ROUTE(S) OF ADMINISTRATION

Oral use.

5. WITHDRAWAL PERIOD

6. BATCH NUMBER

Lot: {number}

7. EXPIRY DATE

EXP : {month/year}

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET FOR:

Cyclavance 100 mg/ml oral solution for dogs and cats

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

Marketing authorisation holder:
VIRBAC – 1ère avenue – 2065 m – L.I.D. – 06516 Carros – France

Manufacturer responsible for batch release:
LABIANA LIFE SCIENCES SAU - Venus 26, Pol. Ind. Can Parellada, 08228 Tarrasa - Barcelone, Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclavance 100 mg/ml oral solution for dogs and cats
Cyclance vet 100 mg/ml oral solution for dogs and cats (FI, NO, SE)

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

Each ml contains:

Active substance:	
Ciclosporin	100 mg
Excipients:	
All-rac-α-tocopherol (E-307)	1.00 mg

Clear to slightly yellow solution

4. INDICATION(S)

Treatment of chronic manifestations of atopic dermatitis in dogs.
This is a type of allergic skin disease in dogs and is caused by allergens such as house dust mites or pollens which stimulate an excessive immune response. Ciclosporin reduces the inflammation and itching associated with atopic dermatitis.

Symptomatic treatment of chronic allergic dermatitis in cats.

5. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in cases with a history of malignant disorders (cancer) or progressive malignant disorders (cancer).
Do not vaccinate with a live vaccine during treatment or within a two-week interval before or after treatment.

Do not use in dogs less than six months of age or less than 2 kg in weight.

Do not use in cats infected with Feline Leukemia Virus (FeLV) or Feline Immunodefiency Virus (FIV).

6. ADVERSE REACTIONS

Regarding malignancy, please see sections “Contraindications” and “Special warning(s)” of the Package Leaflet.

Dogs:

The occurrence of adverse reactions is uncommon. The most commonly observed undesirable effects are gastrointestinal disturbances such as vomiting, mucoid or soft faeces and diarrhoea. 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 (decreased appetite), mild to moderate gingival hyperplasia (thickened areas on the gums), skin reactions such as verruciform lesions or change of hair coat, red and swollen pinnae (visible part of the ear), muscle weakness or muscle cramps.
Mild and transient salivation can be observed following treatment administration.

These effects generally resolve spontaneously after treatment is stopped.

In very rare cases diabetes mellitus has been observed, especially in West Highland White Terriers.

Cats:

In cats treated with ciclosporin the following undesirable effects were observed:
Very common: gastrointestinal disturbances such as vomiting and diarrhoea, accompanied by weight loss. These are generally mild and transient and do not require the cessation of the treatment. Increased appetite was also commonly observed.
Common: lethargy (tiredness), anorexia (appetite decrease), hypersalivation, hyperactivity, polydipsia, gingival hyperplasia and lymphopaenia (low level of lymphocytes). 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.

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.

7. TARGET SPECIES

Dogs, cats.

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

For oral use.

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

Before administration, the body weight of animals has to be accurately determined.

Dogs:

The recommended dose of ciclosporin is 5 mg/kg body weight (0.05 ml of oral solution per kg BW) and should initially be administered daily. The frequency of administration should subsequently be reduced depending on the response.

The product should initially be given daily until a satisfactory clinical improvement is seen. 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 (a type of allergic skin disease) dermatitis are satisfactorily controlled, the product can then be given every second day. 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 second day dosing, the veterinary surgeon can decide to give the product every 3 to 4 days. The lowest effective frequency of dosing should be used to maintain the remission of clinical signs.

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

Dosages for dogs:

At standard dosage of 5mg/kg

Weight (kg)		**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Dosage (ml)		0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Weight (kg)	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
Dosage (ml)	0.55	0.6	0.65	0.7	0.75	0.8	0.85	0.9	0.95	1
Weight (kg)	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**
Dosage (ml)	1.05	1.1	1.15	1.2	1.25	1.3	1.35	1.4	1.45	1.5
Weight (kg)	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**
Dosage (ml)	1.55	1.6	1.65	1.7	1.75	1.8	1.85	1.9	1.95	2
Weight (kg)	**41**	**42**	**43**	**44**	**45**	**46**	**47**	**48**	**49**	**50**
Dosage (ml)	2.05	2.1	2.15	2.2	2.25	2.3	2.35	2.4	2.45	2.5
Weight (kg)	**51**	**52**	**53**	**54**	**55**	**56**	**57**	**58**	**59**	**60**
Dosage (ml)	2.55	2.6	2.65	2.7	2.75	2.8	2.85	2.9	2.95	3
Weight (kg)	**61**	**62**	**63**	**64**	**65**	**66**	**67**	**68**	**69**	**70**
Dosage (ml)	3.05	3.1	3.15	3.2	3.25	3.3	3.35	3.4	3.45	3.5
Weight (kg)	**71**	**72**	**73**	**74**	**75**	**76**	**77**	**78**	**79**	**80**
Dosage (ml)	3.55	3.6	3.65	3.7	3.75	3.8	3.85	3.9	3.95	4

PACKAGING TYPE 1
For the 30 and 60 ml bottles, either the 1 ml oral syringe (graduated every 0.05 ml) or the 2 ml oral syringe (graduated every 0.1 ml) can be used to achieve the dose stated above, determined according to bodyweight.

PACKAGING TYPE 2
For the 30 and 50 ml bottles, either the 1 ml oral syringe (graduated every 0.05 ml) or the 3 ml oral syringe (graduated every 0.1 ml) can be used to achieve the dose stated above, determined according to bodyweight.

Cats:

The recommended dose of ciclosporin is 7 mg/kg body weight (0.07 ml of oral solution per kg) and should initially be administered daily.

The frequency of administration should subsequently be reduced depending on the response.

The product should 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. Severe prolonged pruritus may induce a state of anxiety and subsequent excessive grooming behaviour. In such cases, despite an improvement in pruritus upon administration of the treatment, the resolution of self-induced alopecia may be delayed.

Once the clinical signs of allergic dermatitis are satisfactorily controlled, the product can then be given every second day. In some cases where the clinical signs are controlled with every second day dosing, the veterinary surgeon can decide to give the product every 3 to 4 days. The lowest effective frequency of dosing should be used to maintain the remission of clinical signs.
Patients should be regularly re-evaluated and alternative treatment options reviewed. The duration of treatment should be adjusted according to treatment response. 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.

The product can be given either mixed with food or directly into the mouth. If given with food, the solution should be mixed with a small amount of food, preferably after a sufficient period of fasting to ensure complete consumption by the cat. Should the cat not accept the product mixed with food, it should be given by inserting the oral syringe directly into the cat’s mouth and delivering the entire dose. In case the cat only partially consumes the product mixed with food, administration of the product with the oral syringe should be resumed only the next day. Any uneaten medicated cat food must be disposed of immediately and the bowl washed thoroughly.

The efficacy and tolerability of this product was demonstrated in clinical studies with a duration of 4.5 months.

Dosage for cats:

As the efficacy and safety of ciclosporin have not been assessed in cats weighing less than 2.3 kg (see section *Special precautions for use in animals*), administration of the product to cats weighing less than 2.3 kg should be according to a benefit-risk assessment by the responsible veterinarian.

At standard dosage of 7 mg/kg

Weight (kg)	**2.1**	**2.9**	**3.6**	**4.3**	**5.0**	**5.7**	**6.4**	**7.1**
Dosage (ml)	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5

Weight (kg)	**7.9**	**8.6**	**9.3**	**10.0**	**10.7**	**11.4**	**12.1**	**12.8**	**13.6**	**14.3**
Dosage (ml)	0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95	1.00

PRIMARY PACKAGING TYPE 1
For the 30 and 60 ml bottles, either the 1 ml oral syringe (graduated every 0.05 ml) or the 2 ml oral syringe (graduated every 0.1 ml) can be used to achieve the dose stated above, determined according to bodyweight..

PRIMARY PACKAGING TYPE 2
For the 30 and 50 ml bottles, either the 1 ml oral syringe (graduated every 0.05 ml) or the 3 ml oral syringe (graduated every 0.1 ml) can be used to achieve the dose stated above, determined according to bodyweight.

9. ADVICE ON CORRECT ADMINISTRATION

The veterinary product will be administered by owner.

Dogs: The veterinary medicinal product should be given at least 2 hours before or after feeding. Insert the oral syringe directly into the dog’s mouth.
Cats: The product can be given either mixed with food or directly into the mouth in cats.

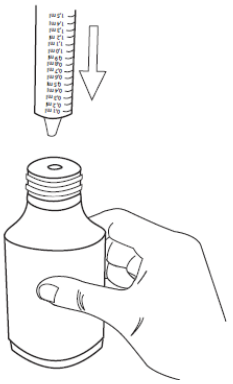
[Depending on the type of primary packaging retained, only one of the following descriptions will be included on the leaflet.]

[PRIMARY PACKAGING TYPE 1]

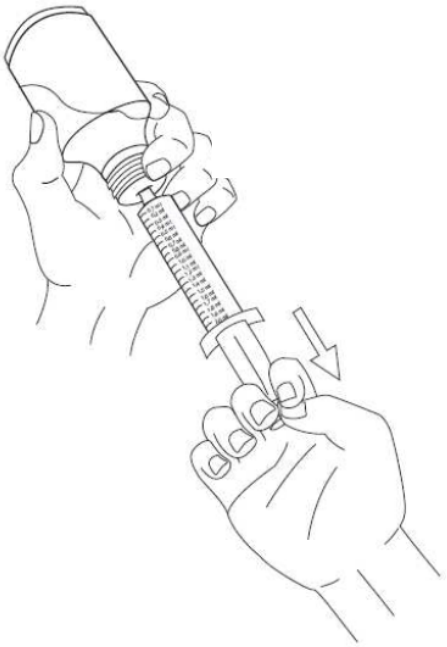
1 Push and turn the child-resistant screw cap to open the bottle.

Always close the bottle with the child-resistant screw cap after use.

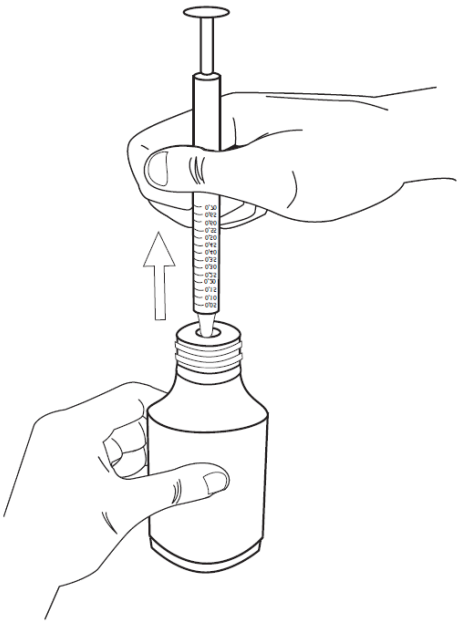
2 Keep the bottle upright and insert the oral dosing syringe firmly into the plastic adapter.



3 Turn the bottle upside down and slowly pull the plunger up so that the oral dosing syringe fills with the product.
Withdraw the dose of medicine prescribed by your veterinarian.



4 Return the bottle to its upright position and remove the oral dosing syringe by gently twisting it out of the plastic adapter.



5 You can now introduce the syringe in the mouth of your animal and push the medicine out of the syringe.
Do not rinse or clean the oral dosing syringe between uses.

Note: If the prescribed dose is more than the maximum volume marked on the oral dosing syringe, you will need to reload the syringe to withdraw the full dose.

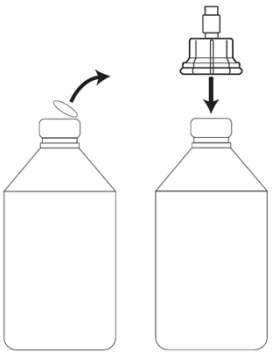
Note: For cats, you can also give the product mixed with food

6 Always close the bottle with the child-resistant screw cap after use.
To provide a child-resistant closure, push down on the child-resistant screw cap as you turn it.

Keep out of the sight and reach of children

[PRIMARY PACKAGING TYPE 2]

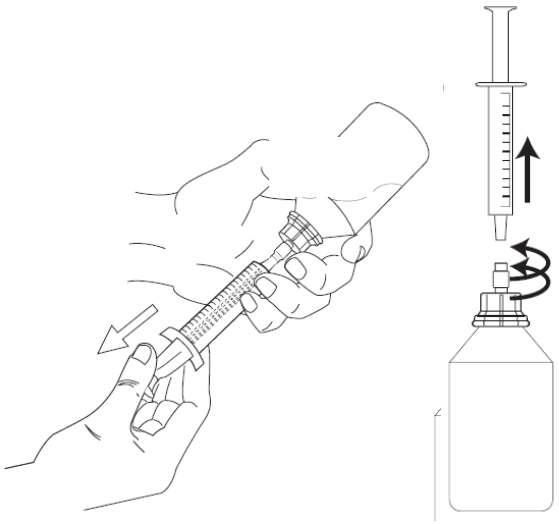
1 Retrieve the plastic cap and insert firmly the plastic dispenser.



The plastic dispenser should remain in place.

2 Keep the bottle upright and insert the oral dosing syringe firmly into the plastic dispenser.

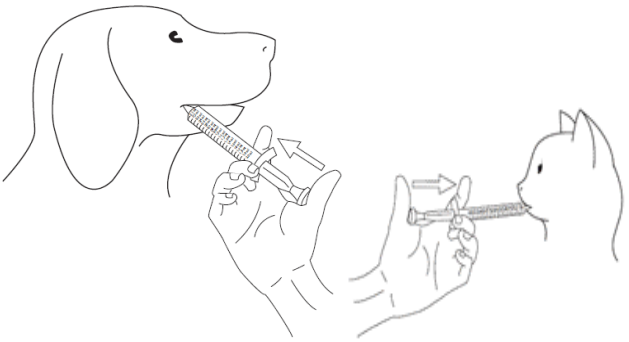
3 Turn the bottle upside down and slowly pull the plunger up so that the oral dosing syringe fills with the product.
Withdraw the dose of medicine prescribed by your veterinarian.



Return the bottle to its upright position and remove the oral dosing syringe by gently twisting it out of the plastic dispenser.

4 You can now introduce the syringe in the mouth of your animal and push the medicine out of the syringe.

Do not rinse or clean the oral dosing syringe between uses.



Note: If the prescribed dose is more than the maximum volume marked on the oral dosing syringe, you will need to reload the syringe to withdraw the full dose.

Note: For cats, you can also give the product mixed with food

Keep out of the sight and reach of children

If necessary, the user can wipe the outside of the oral syringe with a dry tissue and dispose of used tissue immediately.

Prescription recommendations:

Dosage	mg/kg	ml/kg	ml/animal

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

Every Day	Morning	Evening	With food	Before meal	After meal	Duration

NOTE: The package leaflet that will be marketed will mention either packaging type 1 or packaging type 2 but not both.

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Keep the bottle in the outer carton.
Do not refrigerate.
A jelly-like formation may occur below 15°C which is however reversible at temperatures up to 25°C without affecting the quality of the product.
After first opening: Do not store above 25°C.

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and bottle label, after “EXP”. The expiry date refers to the last day of that month.
Shelf life after first opening the container: 6 months.
When the bottle is opened for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the bottle should be discarded should be worked out. This discard date should be written in the space provided on the carton.

12. SPECIAL WARNING(S)

Special precautions for use in animals:

Clinical signs of atopic dermatitis in dogs and allergic dermatitis in cats such as pruritus and skin inflammation are not specific for these diseases. 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 ruled out before treatment is started. It is good practice to treat flea infestations before and during treatment of atopic or allergic dermatitis.

A complete clinical examination should be performed by a veterinary surgeon prior to treatment. 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.

It is recommended to clear bacterial and fungal infections before administering the veterinary medicinal product. However, infections occurring during treatment are not necessarily a reason for drug withdrawal, unless the infection is severe.

If signs of diabetes mellitus are observed following the use of the product, e.g. polyuria (increased production of urine), polydipsia (increased thirst), the dose should be tapered or discontinued and veterinary care sought.
In the presence of suggestive signs of diabetes mellitus, the effect of treatment on glycaemia must be monitored. The use of ciclosporin is not recommended in diabetic animals.

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.

Dogs:
Closely monitor creatinine levels with severe renal insufficiency.

Cats:

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

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

Cats that are tested negative 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 negative cats or cats suspected to be negative to Toxoplasma should therefore be minimised (e.g. keep indoors, avoid raw meat or scavenging). However, in a controlled laboratory study, treatment with ciclosporin did not reactivate oocyst shedding in cats previously exposed to *T. gondii*. 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 (fatty liver syndrome). 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 oral syringes 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. This product may cause irritation in case of eye contact. Avoid contact with eyes. In case of contact, rinse thoroughly with clean water. Wash hands and any exposed skin after use.

Pregnancy, lactation and fertility:
The safety of the drug has neither been studied in male dogs or cats used for breeding nor in pregnant or lactating bitches and queens. In the absence of such studies, it is recommended to use the drug in breeding animals only upon a positive benefit/risk assessment by the responsible veterinarian.

The treatment of pregnant bitches and queens as well as lactating bitches and queens is not recommended.

Interactions 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 certain clinically justified cases, an adjustment of the dosage of the veterinary medicinal product may be required.

The compound class of azoles (e.g. ketoconazole) is known to increase the blood concentration of ciclosporin in dogs and cats, which is considered to be clinically relevant. Ketoconazole at 5-10 mg/kg is known to increase the blood concentration of ciclosporin in dogs up to five-fold. During concomitant use of ketoconazole and ciclosporin the veterinarian should consider as a practical measure to double the treatment interval if the dog 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.

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 and to concomitant use of other immunosuppressive agents.

Overdose (symptoms, emergency procedures, antidotes):

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 6 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: areas with thickened skin especially on the pinnae, callous-like lesions of the foot pads, weight loss or reduced weight gain, excessive hair growth, 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 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 neutrophil counts, fibrinogen, activated partial thromboplastin time (APTT), slight increases in blood glucose and reversible gingival hypertrophy. Increased appetite was observed for both dose regimens. A transient increase followed by a decrease in the lymphocyte counts is observed in treated cats, combined with a greater occurrence of palpable small peripheral lymph nodes. This may reflect immunosuppression following prolonged exposure to ciclosporin. APTT was prolonged in cats administered at least twice the recommended dose of ciclosporin. 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) commonly occur. 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.

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

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

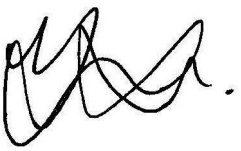
14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

April 2024

15. OTHER INFORMATION

5 ml bottle with a 1 ml oral syringe
15 ml bottle with a 1 ml oral syringe
30 ml bottle with a 1 ml and 2 ml oral syringes
30 ml bottle with a 1 ml and 3 ml oral syringes
50 ml bottle with a 1 ml and 3 ml oral syringes
60 ml bottle with a 1 ml and 2 ml oral syringes

Not all pack sizes may be marketed.



Approved: 04 April 2024