PACKAGE LEAFLET FOR
VETERINARY MEDICINAL PRODUCT

This medicine is dispensed with
a veterinarian's prescription only

For veterinary use only

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Atopica 100 mg/ml oral solution for cats and dogs
Veterinary

2. Active substance:

Each ml contains 100 mg ciclosporin

3. WHAT IS THE MEDICINE INTENDED FOR

Symptomatic treatment of chronic allergic dermatitis in cats.
Treatment of chronic manifestations of atopic dermatitis in dogs.
Therapeutic group: Selective immunosuppressant

Allergic dermatitis and atopic dermatitis are common skin diseases in cats and dogs, respectively. They are caused by allergens such as house dust mites or pollens which stimulate an exaggerated immune response. The diseases are chronic and recurrent. Ciclosporin selectively acts on the immune cells involved in the allergic reaction. Ciclosporin reduces the inflammation and itching associated with allergic dermatitis.

4. CONTRAINDICATIONS

Do not use in animals with hypersensitivity to the active substance or to any of the excipients.
Do not use in cats infected with FeLV or FIV.
Do not use in animals 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 dogs less than six months of age or less than 2 kg in weight.

5. ADVERSE REACTIONS

Cats:
The most frequently observed undesirable effects are gastrointestinal disturbances such as vomiting and diarrhea. These effects are generally mild and transient and do not require cessation of the treatment.

Other undesirable effects observed in clinical studies included: lethargy, anorexia, hypersalivation, weight loss and low levels of white blood cells. 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.

Dogs:
The occurrence of adverse reactions is uncommon. The most frequently observed undesirable effects are gastrointestinal problems such as hypersalivation, vomiting, mucoid or soft faeces and diarrhea. These effects are mild and transient and do not generally require cessation of the treatment.

Other undesirable effects that are observed infrequently may include lethargy or hyperactivity, anorexia, mild to moderate gingival hyperplasia (overgrowth of gums), skin reactions such as wart-like lesions or change of hair coat, red and swollen ear flaps, muscle weakness or muscle cramps. These effects generally resolve spontaneously after treatment is stopped.

Very rarely diabetes mellitus has been observed, reported mainly in West Highland White Terriers.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals developing adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 in 100 animals)
- uncommon (more than 1 but less than 10 in 1,000 animals)
- rare (more than 1 but less than 10 in 10,000 animals)
- very rare (less than 1 in 10,000 animals, including isolated reports).

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.
You can report side effects to the Ministry of Health by clicking on the link “Report adverse effects and problems associated with medications and drugs” found on the homepage of the Ministry of Health website (www.health.gov.il), which will direct you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

6. TARGET SPECIES

Cats
Dogs (weighing more than 2 kg)

7. METHOD OF ADMINISTRATION AND DOSAGE

This product is intended for oral use. Before starting treatment, an evaluation of all alternative treatment options should be made.

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 veterinary medicinal product should be administered in accordance with the following table:

Body weight (kg)	Dose (ml)
2	0.14
3	0.21
4	0.28
5	0.35
6	0.42
7	0.49
8	0.56
9	0.63
10	0.70

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 severity of lesions – excoriations, miliary dermatitis, eosinophilic plaques and/or self-induced alopecia). This will generally be the case within 4 to 8 weeks.

Once the symptoms of allergic dermatitis are satisfactorily controlled, the product can then be given every other day. In some cases where the symptoms of allergic dermatitis are controlled with every-other-day dosing, your veterinary surgeon may decide to give the medicinal product every 3 to 4 days. The lowest effective frequency of dosing should be used to maintain remission of clinical signs.

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.

Dose adjustment should only be carried out in consultation with the veterinary surgeon. The veterinary surgeon will perform a clinical assessment at regular intervals,

and will adjust the frequency of administration up or down according to the clinical response obtained and review alternative treatment options.

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 syringe directly into the cat's mouth and delivering the entire dose. If the cat only partially consumes the product mixed with food, administration of the medicinal product with the syringe should be resumed only the next day.

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

Dogs:

The mean recommended daily dose of ciclosporin is 5 mg/kg body weight (0.05 ml of oral solution per kg). The veterinary medicinal product should be administered in accordance with the following table:

Body weight (kg)	Dose (ml)	Body weight (kg)	Dose (ml)	Body weight (kg)	Dose (ml)
		21	1.05	41	2.05
2	0.10	22	1.10	42	2.10
3	0.15	23	1.15	43	2.15
4	0.20	24	1.20	44	2.20
5	0.25	25	1.25	45	2.25
6	0.30	26	1.30	46	2.30
7	0.35	27	1.35	47	2.35
8	0.40	28	1.40	48	2.40
9	0.45	29	1.45	49	2.45
10	0.50	30	1.50	50	2.50
11	0.55	31	1.55	51	2.55
12	0.60	32	1.60	52	2.60
13	0.65	33	1.65	53	2.65
14	0.70	34	1.70	54	2.70
15	0.75	35	1.75	55	2.75
16	0.80	36	1.80	56	2.80
17	0.85	37	1.85	57	2.85
18	0.90	38	1.90	58	2.90
19	0.95	39	1.95	59	2.95
20	1.00	40	2.00	60	3.00

The veterinary medicinal product will initially be given daily until a satisfactory clinical improvement is seen. This improvement is generally achieved within 4 weeks. If no response is obtained within the first 8 weeks, the treatment should be stopped.

Once the clinical symptoms of atopic dermatitis are satisfactorily controlled, the veterinary medicinal product can then be given every other day as a maintenance dose. In some cases where the clinical symptoms are controlled with every-other-day dosing, your veterinary surgeon may decide to give the veterinary medicinal product every 3 to 4 days.
Adjunct treatment (e.g. medicated shampoos, fatty acids) may be considered before reducing the dosing interval.
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.

Dose adjustment should only be carried out in consultation with your veterinary surgeon. Your veterinary surgeon will perform a clinical assessment at regular intervals, adjust the frequency of administration up or down according to the clinical response obtained and review alternative treatment options.

The veterinary medicinal product should be given at least 2 hours before or after feeding. The product should be given by inserting the syringe directly into the dog's mouth and delivering the entire dose.

8. HOW TO USE THE MEDICINAL PRODUCT

Follow the instructions given by your veterinary surgeon. Take out the required volume of the medicinal product according to the body weight of the animal.

For the dosing process, carefully follow the handling/dispensing instructions as described below.

<table>
<tr>
<td>The Dispensing System

The dispensing system consists of:

1. A bottle (17 ml): with a rubber stopper and a child-resistant screw cap.

2. A plastic tube containing
• A plastic adapter with a tube and an oral dosing syringe

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<tr>
<td>Preparation of the dispensing system

To open the bottle, push and turn the child-resistant screw cap.</td>
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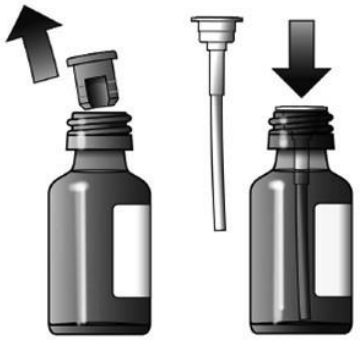
1. Remove and dispose of the rubber stopper.
2. Hold the open bottle upright on a table and push the plastic adapter firmly into the neck of the bottle as far as possible.
3. Close the bottle with the child-resistant screw cap.

The bottle is now ready for use.

Note: Always close the bottle with the child-resistant screw cap after use. The adapter must always remain in the bottle after first use.



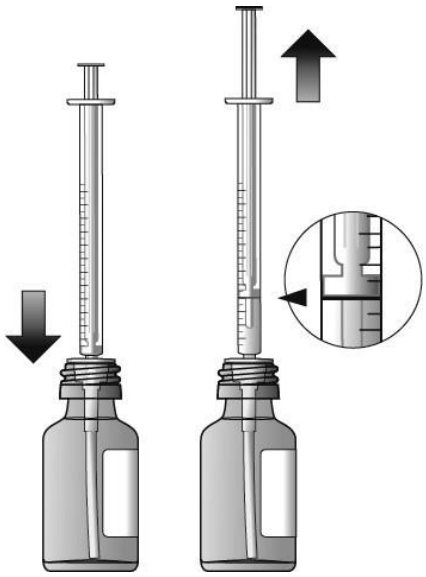
Preparing a Dose of Medicine

1. To open the bottle, push and turn the child-resistant screw cap.
2. Check that the plunger of the appropriate oral dosing syringe is pushed all the way down.
3. Keep the bottle upright and insert the syringe firmly into the plastic adapter.

4. Slowly pull the plunger up to fill the syringe with medicine.
5. Withdraw the prescribed dose of medicine.

6. Remove the syringe by gently twisting it out of the plastic adapter.
7. Push the entire dose out of the syringe, directly into the mouth of the cat or dog. Alternatively, for cats, the dose can be mixed into the cat's food.
8. Close the bottle with the child-resistant screw cap after use. Store the syringe in the plastic tube for future use.

Note: If the prescribed dose is more than the maximum volume marked on the syringe, you will need to repeat steps 2 to 7 to administer the remaining amount of the prescribed dose.
Do not clean the oral dosing syringe (e.g., with water) in between uses.



9. WITHDRAWAL PERIOD

Not applicable

10. WARNINGS

Special precautions for use in animals:
Clinical signs of atopic and allergic dermatitis, such as itching and skin inflammation, are not specific for this disease. Where possible, consult your veterinary surgeon so he/she can evaluate and eliminate other causes of dermatitis, such as ectoparasitic infestations or food allergy. It is recommended to treat flea infestations before and during treatment of atopic and allergic dermatitis.

Your veterinary surgeon will carry out a complete clinical examination prior to treatment. Any infections should be properly treated before initiation of treatment. Infections occurring during treatment are not necessarily a reason for discontinuing the medicine, unless the infection is severe.

While ciclosporin does not induce the development of tumours, it does inhibit T-lymphocytes. Ciclosporin could therefore lead to an increased incidence of clinically apparent malignancy due to the decrease in antitumor immune response. The potentially increased risk of tumour progression must be weighed against the clinical benefit. If lymphadenopathy (enlargement of the lymph glands) is observed in cats and dogs being treated with ciclosporin, it is recommended to carry out further clinical investigations and to stop treatment if necessary.

Ciclosporin may cause elevated blood sugar levels. The use of ciclosporin is not recommended in diabetic cats and dogs.

Particular attention must be paid to vaccination. Treatment with the medicinal product may result in a decreased immune response to vaccination. It is recommended not to vaccinate with inactivated vaccines during treatment or within a two-week interval before or after administration of the medicine.

Concomitant use of other immunosuppressive medicinal products is not recommended.
Carefully monitor creatinine levels in cases of 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 your cat to FeLV and FIV infections should be assessed before treatment.

Cats that are seronegative for Toxoplasma gondii (T. gondii) may be at risk of developing clinical toxoplasmosis if they become infected while under treatment with the medicinal product. In rare cases, this disease can be fatal. Potential exposure to toxoplasma of seronegative cats or of cats that may reasonably be suspected to be seronegative should therefore be minimised (e.g., keep your cat 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, consult your veterinary surgeon. Treatment with the medical preparation should be stopped and treatment of the disease initiated.

Clinical studies in cats have shown that decreased appetite and weight loss may occur during ciclosporin treatment. It is recommended to monitor the cat's body weight. Significant reduction in body weight may result in hepatic lipidosis (excessive accumulation of fat in the liver). 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 not been assessed in cats that are younger than 6 months or weigh less than 2.3 kg.

Use during pregnancy or lactation
The safety of the medicine has not been studied in male cats or dogs used for breeding or in pregnant or lactating queens and bitches. In the absence of such studies, it is recommended to use the medicine in breeding animals only upon a positive risk/benefit assessment by the veterinary surgeon. You should inform your veterinary surgeon if the animal is a breeding animal, so that a risk/benefit assessment can be made. The treatment of lactating queens and bitches 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 certain clinically justified cases, an adjustment of the dosage of the medicinal product may be required. The toxicity of some medicines may be increased by administration with ciclosporin. Consult your veterinary surgeon prior to administering other products during therapy with this medicinal product.

Overdose (symptoms, emergency procedures, antidotes):
The frequency and severity of adverse reactions are generally dose- and time-dependent. In case of signs of overdose, consult your veterinary surgeon immediately. There is no specific antidote and the animal should be treated symptomatically.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Accidental ingestion of this medicinal product may lead to nausea and/or vomiting. To avoid accidental ingestion, the medicinal product must be used and kept out of reach of children. Do not leave an 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 children, 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 veterinary medicinal product.
This veterinary medicinal product may cause irritation in case of eye contact. Avoid contact with eyes. In case of such contact, rinse thoroughly with clean water.
Wash hands and exposed skin after administering the veterinary medicinal product.

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

11. STORAGE INSTRUCTIONS

Avoid poisoning! This medicine, as well as all other medicines, must be stored in a closed place out of the sight and reach of children and/or infants, in order to prevent poisoning.

Store between 15°C and 30°C but not below 20°C for more than one month.
Storage in the refrigerator should be avoided.

Keep the bottle in the outer package.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month. After first broaching the bottle, the medicinal product may be used for up to 70 days.

The medicinal product contains oily components of natural origin, which can become solid at low temperatures. A jelly-like sediment may be formed below 20°C, which is however reversible at temperatures up to 30°C. Minor flakes or a slight sediment may still be observed, but this affects neither the administration nor the efficacy and safety of the medicinal product.

12. INSTRUCTIONS FOR THE DISPOSAL OF THE MEDICINAL PRODUCT / REMNANTS OF THE MEDICINAL PRODUCT AFTER USE

All remnants of a veterinary medicinal product or any waste produced by use of a veterinary medicinal product must be disposed of as toxic waste. Do not dispose of via wastewater.

13. OTHER INFORMATION

In addition to the active substance, the medicinal product also contains:

Polyoxyl 40 hydrogenated castor oil

Corn oil-mono-di-triglyceride

Propylene glycol

Ethanol anhydrous

α-Tocopherol

- What the medicine looks like and what the package contains:

  The medicine is a clear yellowish-brown liquid in a brown glass bottle with a child-resistant cap together with a syringe, plastic adaptor and tube used for dispensing the medicine.
- Registration holder: Euromar Ltd., P.O.B. 1064, Ramat HaSharon, 47110
- Manufacturer: Elanco France S.A.S, 26, Rue de la Chapelle , F-68330 Huningue, France
- The leaflet was approved in October 2021.
- Registration number of the medicine in the Ministry of Health National Drug Registry: 168-38-35713-00