SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Atopica 100 mg/ml Oral solution for Cats and Dogs
Atoplus (IT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance: Ciclosporin 100 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
all-*rac*-α-tocopherol (E-307)	1.05 mg
Ethanol, anhydrous (E-1510)	94.70 mg
Propylene glycol (E-1520)	94.70 mg
Corn oil-mono-di-triglycerides	
Macrogolglycerol hydroxystearate	

Clear, yellow to brownish liquid.

3. CLINICAL INFORMATION

3.1 Target species

Cats
Dogs (weighing more than 2 kg).

3.2 Indications for use for each target species

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

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
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 (see also sections 3.5 “Special precautions for use” and 3.8 “Interaction with other medicinal products and other forms of interaction”).
Do not use in cats infected with FeLV or FIV.

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

3.4 Special warnings

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

3.5 Special precautions for use

Special precautions for safe use in the target species:
Clinical signs of atopic or allergic dermatitis such as pruritus and skin inflammation are not specific for this disease and therefore 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 before treatment.

It is recommended to clear any infection including 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.

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 antitumor immune response. The potentially increased risk of tumour progression must be weighed against the clinical benefit. If lymphadenopathy is observed in cats and dogs being treated with ciclosporin, further clinical investigations are recommended and treatment discontinued if necessary.

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 cats and dogs.

Closely monitor creatinine levels with severe renal insufficiency.

Particular attention must be paid to vaccination. Treatment with the product may result in 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 product. For live vaccines see also section 3.3 “Contraindications”.

It is not recommended to use immunosuppressive agents concomitantly.

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.
This veterinary medicinal 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 administering the veterinary medicinal product..

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cats:

Very common (>1 animal / 10 animals treated):	Digestive tract disorders (such as Vomiting, Diarrhoea)[1].
Common (1 to 10 animals / 100 animals treated):	Lethargy[2], Anorexia[2], Weight loss[2]; Hypersalivation[2]; Lymphopenia[2].
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Leucopenia, Neutropenia, Thrombocytopenia; Diabetes mellitus.

[1]generally mild and transient and do not require the cessation of the treatment.
[2]generally resolve spontaneously after treatment is stopped or following a decrease in the dosing frequency.

Side effects may be severe in individual animals.

Dogs:

Uncommon (1 to 10 animals / 1 000 animals treated):	Digestive tract disorders (such as Hypersalivation, Vomiting, Mucous stool, Loose stool, Diarrhoea)[1].
Rare (1 to 10 animals / 10 000 animals treated):	Lethargy[2], Anorexia[2]; Hyperactivity[2]; Gingival hyperplasia[2,3]; Skin reactions (such as Verruciform lesions, Hair change)[2]; Pinnal reddening[2], Pinnal oedema[2]; Muscle weakness[2], Cramp[2].
Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Diabetes mellitus[4].

[1]generally mild and transient and do not require the cessation of the treatment
[2]generally resolve spontaneously after treatment is stopped
[3]mild to moderate
[4]mainly in West Highland White Terriers

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See 'Contact details' of the package leaflet.

3.7 Use during pregnancy, lactation or lay

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

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 embryolethal or teratogenic effects. In laboratory animals ciclosporin crosses the placenta barrier and is excreted via milk. Therefore, the treatment of lactating queens and bitches is not recommended.

3.8 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 3A4).
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 cats and dogs, which is considered to be clinically relevant. Ketoconazole at 5-10 mg/kg is

known to increase the blood concentrations 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 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.

In dogs, no toxicological interactions between ciclosporin and prednisolone (at anti-inflammatory doses) are expected.

Particular attention must be paid to vaccination (see section 3.3 "Contraindications" and 3.5 "Special precautions for use"). Concomitant use of immunosuppressive agents: see section 3.5 "Special precautions for use".

3.9 Administration routes and dosage

For oral use.
Before starting treatment, an evaluation of all alternative treatment options should be made.
To ensure a correct dosage, body weight should be determined as accurately as possible.

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:

Bodyweight (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 lesion severity - excoriations, miliary dermatitis, eosinophilic plaques and/or self-induced alopecia). This will generally be the case within 4-8 weeks.

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 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 syringe should be resumed only the next day.

The efficacy and tolerability of this 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:

Bodyweight (kg)	Dose (ml)	Bodyweight (kg)	Dose (ml)	Bodyweight (kg)	Dose (ml)
		21	1.05	41	2.05
		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

Bodyweight (kg)	Dose (ml)	Bodyweight (kg)	Dose (ml)	Bodyweight (kg)	Dose (ml)
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	0.9	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 will generally be the case within 4 weeks. If no response is obtained within the first 8 weeks, the treatment should be stopped.

Once the clinical signs of atopic dermatitis are satisfactorily controlled, the veterinary medicinal product 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.
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.

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.

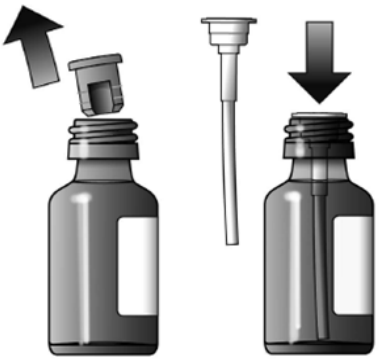
For the dosing process, carefully follow the handling/dispensing instructions as described below.

The Dispensing System

The dispensing system consists of:

1. Bottle (5 ml or 17 ml): with rubber stopper and a child-resistant screw cap.

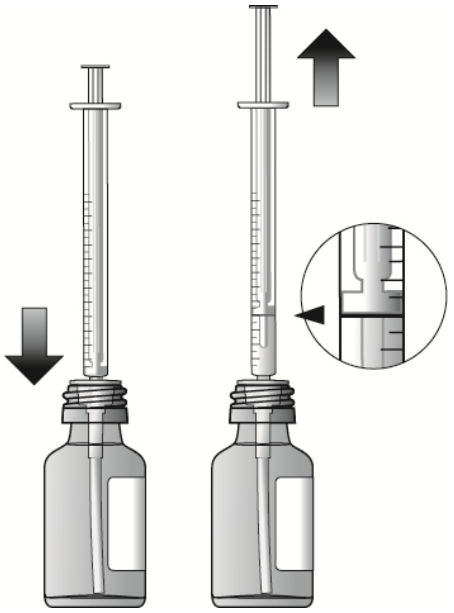
Bottle (50 ml): with rubber stopper and aluminum tear-off cap. A separate child-resistant screw cap is included in the carton.

2.A plastic tube containing • A plastic adapter with dip tube and an oral dosing syringe	
Prepare the Dispensing System Bottle (5 ml or 17 ml): Push and turn the child-resistant screw cap to open the bottle. Bottle (50 ml): Remove aluminum tear-off cap completely from the bottle.	
<u>All bottle sizes (5 ml, 17 ml and 50 ml):</u> 1.Remove and dispose 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 prepared for dispense. **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. Push and turn the child-resistant screw cap to open the bottle.
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 dosing 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, either directly into the mouth of the cat or dog. For cats, the dose can also 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 further 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 attempt to clean the oral dosing syringe (e.g. with water) in between uses.



3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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

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 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.

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: 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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QL04AD01.

4.2 Pharmacodynamics

Ciclosporin (also known as cyclosporin, cyclosporine, cyclosporine A, CsA) is a selective immunosuppressor. It is a cyclic polypeptide consisting of 11 amino acids, has a molecular weight of 1203 daltons and acts specifically and reversibly on T lymphocytes.

Ciclosporin exerts anti-inflammatory and antipruritic effects in the treatment of allergic and atopic dermatitis. Ciclosporin has been shown to preferentially inhibit the activation of T-lymphocytes on antigenic stimulation by impairing the production of IL-2 and other T-cell derived cytokines. Ciclosporin also has the capacity to inhibit the antigen-presenting function of the skin immune system. It likewise blocks the recruitment and activation of eosinophils, the production of cytokines by keratinocytes, the functions of Langerhans cells, the degranulation of mast cells and therefore the release of histamine and pro-inflammatory cytokines.
Ciclosporin does not depress haematopoiesis and has no effect on the function of phagocytic cells.

4.3 Pharmacokinetics

Cats:
Absorption:
The bioavailability of ciclosporin administered to cats fasted for 24 hours (either directly into the mouth or mixed with a small amount of food) or just after feeding was

29% and 23%, respectively. The peak plasma concentration is generally reached within 1 to 2 hours when given to fasted cats or mixed with food.
The absorption can be delayed by several hours when given after feeding. Despite differences in the pharmacokinetics of the drug given mixed with food or directly into the mouth of fed cats, it has been shown that the same clinical response is obtained.

Distribution
The volume of distribution at steady state is about 3.3 l/kg. Ciclosporin is widely distributed to all tissues, including the skin.

Metabolism
Ciclosporin is metabolised mainly in the liver by cytochrome P450 (CYP 3A 4), but also in the intestine. Metabolism takes place essentially in the form of hydroxylation and demethylation, leading to metabolites with little or no activity.

Elimination
Elimination is mainly via the faeces. A small proportion of the administered dose is excreted through urine as inactive metabolites.
A slight bioaccumulation related to the long half-life of the drug (approximately 24h) is observed with repeated dosing. The steady state is reached within 7 days, with a bioaccumulation factor in the range of 1.0 to 1.72 (typically 1-2).

In the cat, there are large inter-individual variations in plasma concentrations. At the recommended dosage, ciclosporin plasma concentrations are not predictive of the clinical response, therefore monitoring of blood levels is not recommended.

Dogs:
Absorption
The bioavailability of ciclosporin is about 35%. The peak plasma concentration is reached within 1 to 2 hours. The bioavailability is better and less subject to individual variations if ciclosporin is administered to fasted animals rather than at mealtimes.

Distribution
The volume of distribution is about 7.8 l/kg. Ciclosporin is widely distributed to all tissues. Following repeated daily administration to dogs ciclosporin concentration in the skin is several times higher than in blood.

Metabolism
Ciclosporin is metabolised mainly in the liver by cytochrome P450 (CYP 3A 4), but also in the intestine. Metabolism takes place essentially in the form of hydroxylation and demethylation, leading to metabolites with little or no activity.
Unchanged ciclosporin represents about 25% of circulating blood concentrations during the first 24 hours.

Elimination
Elimination is mainly via the faeces. Only 10% is excreted in the urine, mostly in the form of metabolites. No significant accumulation was observed in blood of dogs treated for one year.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging containing 5 ml or 17 ml oral solution: 70 days.
Shelf-life after first opening the immediate packaging containing 50 ml oral solution: 84 days.

5.3 Special precautions for storage

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

The product contains oily components from natural origin which can become solid at lower temperatures. A jelly-like formation may occur below 20°C which is however reversible at temperatures up to 30°C. Minor flakes or a slight sediment may still be observed. However, this does neither affect the dosing nor the efficacy and safety of the product.

5.4 Nature and composition of immediate packaging

Multi-dose type III amber glass bottle containing 5 ml or 17 ml oral solution closed with a rubber stopper and sealed with a polypropylene child-resistant screw cap. One bottle and a dispenser set (consisting of a PE dip tube and a 1 ml polypropylene syringe) packed in a cardboard box.

Multi-dose type III amber glass bottle containing 50 ml oral solution closed with a chlorobutyl rubber stopper and sealed with an aluminium tear-off cap. Each bottle is provided with two dispenser sets (consisting of a PE dip tube and a 1 ml or 4 ml polypropylene syringe) packed in a cardboard box. A polypropylene child-resistant screw cap is provided for closure of the bottle during the in-use period.

Pack sizes:
1 x 5 ml bottle and one dispenser set
1 x 17 ml bottle and one dispenser set
1 x 50 ml bottle and two dispenser sets.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

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

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann Strasse 4
Groden
27472 Cuxhaven
Germany

7. MARKETING AUTHORISATION NUMBER

Vm 52127/3061

8. DATE OF FIRST AUTHORISATION

16 September 2011

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

September 2025

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

Gavin Hall
Approved: 09 September 2025