SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ERADIA 125 mg/mL oral suspension for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains

Active substance:
Metronidazole 125 mg

Excipients:
Butylhydroxytoluene (E321) 0.2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension.
Flavoured oily suspension with brown visible particles.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Treatment of infections of the gastrointestinal tract caused by *Giardia* spp. and *Clostridium* spp. (i.e. *C. perfringens* or *C. difficile*).
Treatment of infections of the urogenital tract, oral cavity, throat and skin caused by obligate anaerobic bacteria (e.g. *Clostridium* spp.) susceptible to metronidazole.

4.3 Contraindications

Do not use in case of hepatic disorders.
Do not use in case of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Due to the likely variability (time, geographical) in the occurrence of metronidazole resistant bacteria, bacteriological sampling and susceptibility testing are recommended.
Whenever possible, the product should only be used based on susceptibility testing. Official, national and regional antimicrobial policies should be taken into account when the veterinary medicinal product is used.

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

Metronidazole has confirmed mutagenic and genotoxic properties in laboratory animals as well as in humans. Metronidazole is a confirmed carcinogen in laboratory animals and thus may have carcinogenic effects in humans as well. However, there is inadequate evidence in humans for the carcinogenicity of metronidazole.

The product can cause skin sensitisation. In case of known hypersensitivity to metronidazole or other nitroimidazole derivatives or one of the components of the product, avoid contact with the veterinary medicinal product.
Avoid contact with the skin or mucous membranes including hand-to-mouth contact.
To avoid such contact wear impervious gloves when handling the product and/or for direct administration into the animal's mouth.
Do not allow treated dogs to lick persons immediately after intake of the medication.
Wash hands after use.
In case of skin contact, wash thoroughly the affected area.

Metronidazole may cause adverse (neurological) effects.
Avoid accidental ingestion.
Do not drink, eat or smoke when administering the product.
Close the bottle immediately after use to avoid the child gaining access to the contents. Do not leave a syringe containing solution in the sight or reach of children. In order to prevent children from getting access to used syringes, keep the syringes in the original packaging after use.
In case of accidental ingestion, seek-medical advice immediately and show the package leaflet or the label to physician.

Additional warnings when administering the product into the feed:
Avoid the access of children to the dog’s medicated food. In order to prevent children from getting access to the dog’s medicated food, pour it over a part of the feed and wait until the animal has completely consumed the medicated feed, then administer the rest of the feed. Give the treatment out of the sight and reach of children. Any uneaten medicated food must be removed immediately and the bowl washed thoroughly; wear gloves and wash hands when handling the product and cleaning the contaminated food bowl.

4.6 Adverse reactions (frequency and seriousness)

The following adverse reactions may occur after administration of metronidazole: vomiting, hepatotoxicity and neutropenia. In very rare cases, neurological signs may occur especially after prolonged treatment with metronidazole.

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).

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals have shown inconsistent results with regard to teratogenic/embryotoxic effects of metronidazole. Therefore, use of this product during pregnancy is not recommended. Metronidazole is excreted in milk and use during lactation is therefore not recommended.

4.8 Interaction with other medicinal products and other forms of interaction

Metronidazole may have an inhibitory effect on the degradation of other drugs in the liver, such as phenytoin, cyclosporine and warfarin.
Cimetidine may decrease the hepatic metabolism of metronidazole resulting in increased serum concentration of metronidazole.
Phenobarbital may increase hepatic metabolism of metronidazole resulting in decreased serum concentration of metronidazole.

4.9 Amounts to be administered and administration route

Oral use.

The recommended dose is 50 mg metronidazole per kg bodyweight per day (i.e. 0.4 mL per kg bodyweight), preferably given in two equally divided doses (i.e. 25 mg equivalent to 0.2 mL per kg bodyweight twice daily) for 5-7 days.

To ensure a correct dosage body weight should be determined as accurately as possible to avoid underdosing and overdosing.

The following table is intended as a guide to dispensing the product at the volume corresponding to either 25 mg/kg for administration twice daily or 50 mg/kg for administration once daily.

Examples of bodyweight (kg)	Volume to administer twice daily for 25mg/kg	Volume to administer once daily for 50mg/kg
1		0.4mL
2	0.4mL	0.8mL
3	0.6mL	1.2mL
4	0.8mL	1.6mL
5	1.0mL	2.0mL
10	2.0mL	4.0mL
15	3.0mL	6.0mL
20	4.0mL	8.0mL
25	5.0mL	10.0mL
30	6.0mL	12.0mL
35	7.0mL	14.0mL
40	8.0mL	16.0mL

For doses requiring more than two filled syringes, the dosing should be twice daily in order to minimize counting and dosing errors.

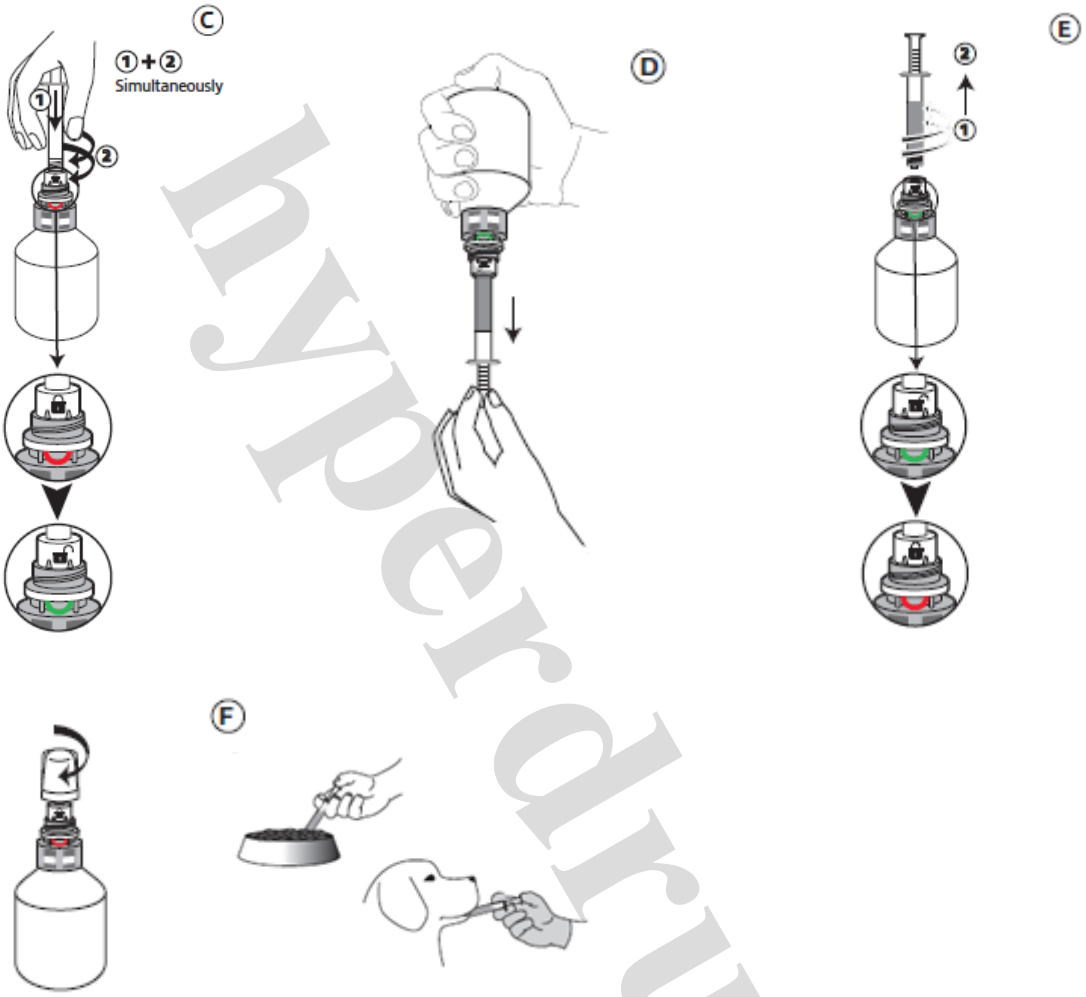
The oral suspension is delivered through the package described below:

[**Snap cap packaging]**
A - Shake the bottle vigorously before use.
B - Unscrew the protective overcap.
C - Insert the syringe into the upper white part of the cap (finger-grip) **by pushing firmly**, then, while pushing, turn the syringe to the right (clockwise) until the green smile appears.
D - Turn the bottle upside down and withdraw the prescribed volume of the product, in the upside down position.
E - Once the correct volume of the product has been drawn into the syringe, unscrew the syringe from the cap **without pushing** by turning it to the left (counterclockwise) until the red smile appears again, then continue to turn in order to unfasten the syringe.
The system can also be closed by turning the finger-grip manually.
F - Screw the protective overcap back on.
Administer the product by pouring it over a part of the feed or by direct administration into the animal's mouth. Wear impervious gloves when handling the product and/or administering the product into the animal's mouth.
When administered over the feed, wait until the animal has completely consumed the medicated feed, then administer the rest of the feed.

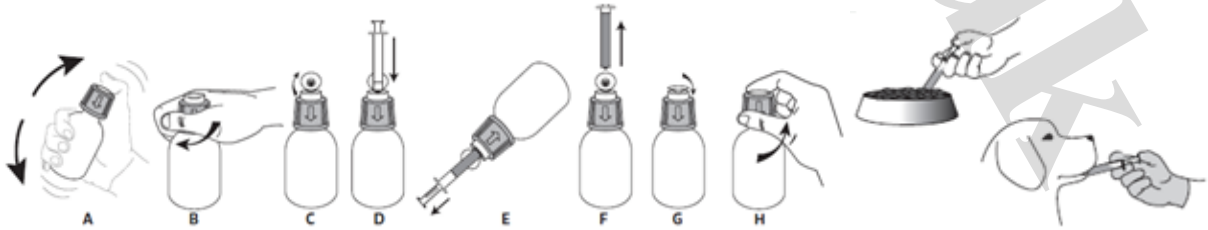
PRODUCT DESCRIPTION

1 Protective overcap
2 Delivery system = finger grip allowing the syringe to be screwed into place and the system to be opened by rotation

een = open



[Screw cap packaging]
A-Shake vigorously the bottle before use.
B-Push down strongly and turn right the colored part of the cap until it is locked.
C-Open the hindge flap.
D-Plug the syringe on the bottle in upright position.
E-Turn over the bottle and sample the prescribed volume of the product in upside down position.
F-Once filled, turn over the bottle. Unplug the syringe in upright position.
G-Close the hindge flap.
H-Turn left and pull up the colored part of the cap.
Administer the product by pouring it over a part of the feed or by direct administration into the animal's mouth. Wear impervious gloves when handling the product and/or administering the product into the animal's mouth.
When administered over the feed, wait until the animal has completely consumed the medicated feed, then administer the rest of the feed.



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

Adverse events are more likely to occur at doses and treatment durations in excess of the recommended treatment regimen. If neurological signs occur, treatment should be discontinued and the patient should be treated symptomatically.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Agent against protozoal disease, nitroimidazole derivative.
ATCvet code: QP51AA01.

5.1 Pharmacodynamic properties

After metronidazole has penetrated the bacteria the molecule is reduced by the sensitive bacteria (anaerobe). The metabolites that are created have a toxic effect on the bacteria through binding to the bacterial DNA. In general metronidazole is bactericidal for sensitive bacteria in concentrations equal to or a little higher than the minimum inhibiting concentration (MIC).

Minimum Inhibitory Concentrations (MICs) have been determined for metronidazole in European isolates of target bacteria, isolated from dogs with gastrointestinal disease in 2016.

Species	MIC range (µg/mL)	MIC50 (µg/mL)	MIC90 (µg/mL)
Clostridium spp. (*C. difficile* & *C.perfringens*)	0.5 – 2	1	1

The MICs of the collected pathogens showed mono-modal distribution profiles with good susceptibility towards metronidazole. Clinical breakpoints* for metronidazole are established for anaerobes: susceptible: ≤8 µg/ml; intermediate: 16 µg/ml; resistant: ≥32 µg/ml.

According to these breakpoints no clinical resistant strains of *Clostridium* spp. pathogens were observed.

*(CLSI, 2017. Performance Standards for Antimicrobial Susceptibility Testing - Twenty-Seventh Edition M100. Clinical and Laboratory Standards Institute (CLSI), Wayne, PA 19087-1898 USA)

Clinically metronidazole does not have any relevant effect on facultative anaerobe, obligate aerobe and microaerophilic bacteria.

Metronidazole is also active in protozoa. In *Giardia* spp. in particular, metronidazole primarily targets the trophozoites (active replication of the parasite) resulting in their death and by consequence leading to dramatic decrease in cyst shedding.

5.2 Pharmacokinetic particulars

After administration of the higher dose (50 mg/day/kg of bw), the absolute bioavailability is 98 % in fasted dog. The mean maximum concentration (Cmax) was 62.4 µg/mL +/- 9.7 (mean +/- SD) in plasma and occurs between 0.25 and 4 hours after dosing (Tmax). Food was shown to decrease the oral bioavailability which remains high in fed dogs with relative F of 81% (with F fasted = 100%). Metronidazole penetrates into the tissues and bodily fluids, such as saliva, milk, vaginal secretions and semen. Metronidazole is metabolised in the liver, by side chain oxidation and glucuronide synthesis. Both metabolites and unchanged drug are eliminated in the urine (mostly) and faeces. Elimination half-life is between 3 to 5 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321)
Aluminium stearate
Stearic acid (E570)
Poultry liver powder
Triglycerides medium chain

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging:

- 30 ml bottle: 3 months.
- 100 ml bottle: 6 months.

6.4 Special precautions for storage

Store below 30° C.

6.5 Nature and composition of immediate packaging

Opaque white polyethylene terephthalate bottle closed with a plastic dispenser cap.
Carton box containing a 30 ml or 100 ml bottle and a 3 ml graduated syringe.

- snap cap packaging:
    - 30 ml presentation: white opaque polyethylene terephthalate (PET) bottle equipped with a sampling polypropylene (PP) snap cap with silicon stopper and a 3 ml polypropylene (PP) syringe placed in a carton box;
    - 100 ml presentation: white opaque polyethylene terephthalate (PET) bottle equipped with a sampling polypropylene (PP) snap cap with

silicon stopper and a 3 ml polypropylene (PP) syringe placed in a carton box;

- screw cap packaging:
  - o 30 ml presentation: white opaque polyethylene terephthalate (PET) bottle equipped with a sampling polyethylene (PE) screw cap with PE seal and a 3 ml polypropylene (PP) oral syringe placed in a carton box;
  - o 100 ml presentation: white opaque polyethylene terephthalates (PET) bottle equipped with a sampling Polyethylene (PE) screw cap with PE seal and a 3 ml polypropylene (PP) oral syringe placed in a carton box.

Not all pack sizes may be marketed.

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

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

7. MARKETING AUTHORISATION HOLDER

Virbac
1ère avenue – 2065m – LID
06516 Carros
France

8. MARKETING AUTHORISATION NUMBER

Vm 05653/4210

9. DATE OF FIRST AUTHORISATION

10 April 2018

10. DATE OF REVISION OF THE TEXT

August 2019

Approved: 28 August 2019