[Version 9, 11/2022]

ANNEX I

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:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Butylhydroxytoluene (E321)	0.2 mg
Aluminium stearate	
Stearic acid (E570)	
Poultry liver powder	
Triglycerides medium chain	

Oily suspension with brown visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each 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.

3.3 Contraindications

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

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Due to the likely variability (time, geographical) in the occurrence of metronidazole resistant bacteria, bacteriological sampling and susceptibility testing are recommended.
Whenever possible, the veterinary medicinal 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 veterinary medicinal product can cause skin sensitisation. In case of known hypersensitivity to metronidazole or other nitroimidazole derivatives or one of the components of the veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product.
Close the bottle immediately after use to avoid the child gaining access to the contents. Do not leave a syringe containing suspension 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 the physician.

Additional warnings when administering the veterinary medicinal 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 veterinary medicinal product and cleaning the contaminated food bowl.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Neurological signs*
Undetermined frequency (cannot be estimated from the available data)	Vomiting Hepatic toxicosis (liver toxicosis) Neutropenia

*Especially after prolonged treatment with metronidazole.

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 the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

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

3.8 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.

3.9 Administration routes and dosage

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.

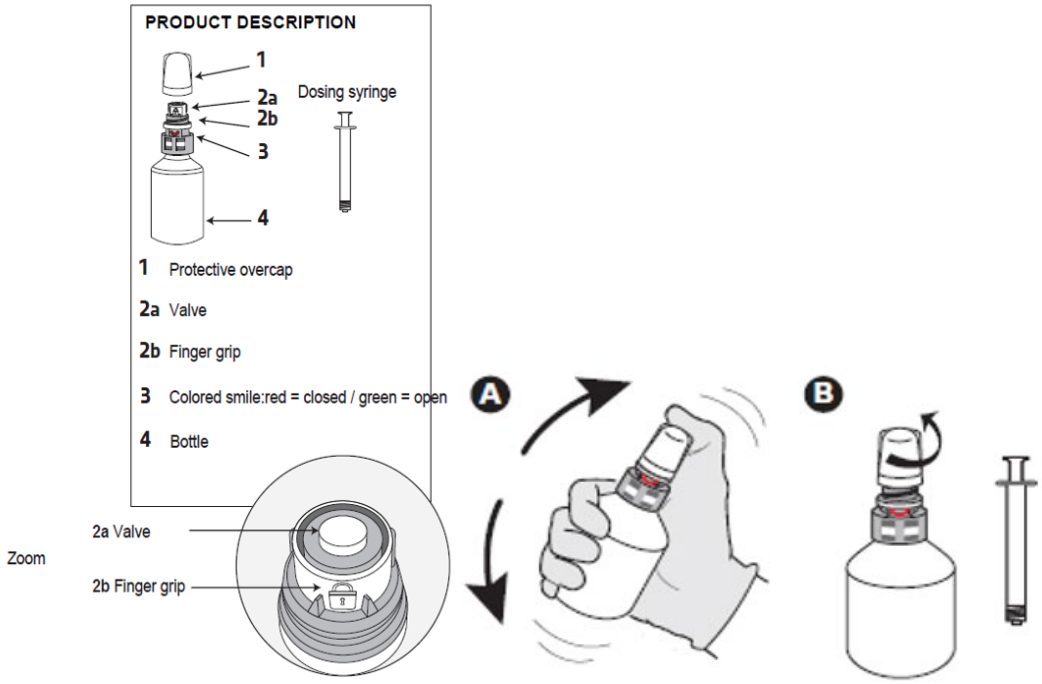
The following table is intended as a guide to dispensing the veterinary medicinal product at the volume corresponding to either 25 mg/kg for administration twice daily or 50 mg/kg for administration once daily.

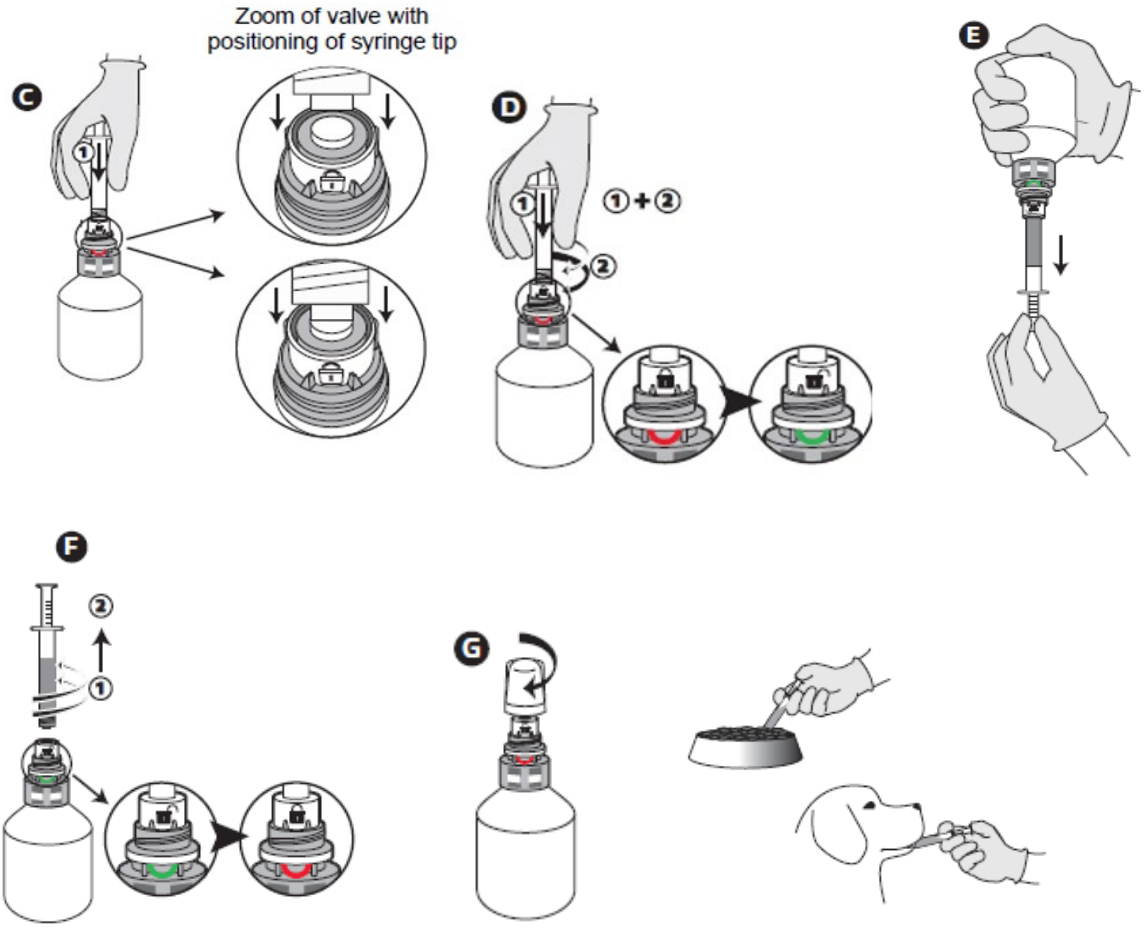
Examples of bodyweight (kg)	Volume to administer twice daily for 25mg/kg	Volume to administer once daily for 50mg/kg
1		0.4mL
2	0.4mL	0.8mL
3	0.6mL	1.2mL
4	0.8mL	1.6mL
5	1.0mL	2.0mL
10	2.0mL	4.0mL
15	3.0mL	6.0mL
20	4.0mL	8.0mL
25	5.0mL	10.0mL
30	6.0mL	12.0mL
35	7.0mL	14.0mL
40	8.0mL	16.0mL

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

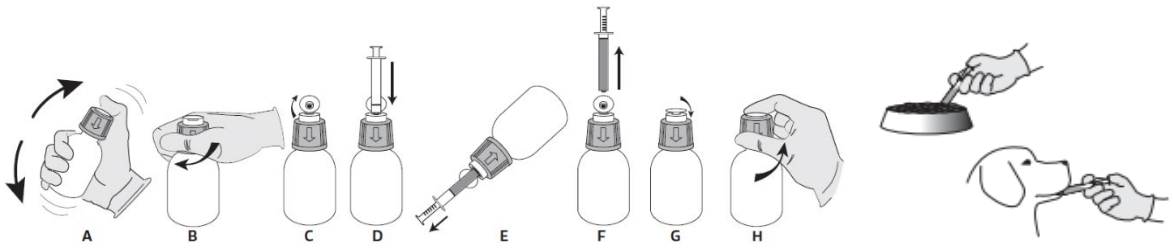
The oral suspension is delivered through the package described below:

[Snap cap packaging]
A - Shake the bottle vigorously before use.
B - Unscrew the protective overcap.
C - Firmly push the valve with the tip of the syringe
D - While pushing, turn the syringe to the right (clockwise) until
the green smile appears.
E - Turn the bottle upside down and withdraw the prescribed volume of the veterinary medicinal product, in the upside down position.
F - Once the correct volume of the veterinary medicinal 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.
G - Screw the protective overcap back on.
Administer the veterinary medicinal 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 veterinary medicinal product and/or administering the veterinary medicinal 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.





[**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 veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product and/or administering the veterinary medicinal 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.



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

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.

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: QP51AA01.

4.2 Pharmacodynamics

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.

4.3 Pharmacokinetics

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.

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:

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

5.3. Special precautions for storage

Store below 30° C.

5.4 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:
    - 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;
    - 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.

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

VIRBAC

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDECINAL 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*).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box containing a bottle of 30 ml or 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ERADIA 125 mg/ml oral suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Metronidazole 125 mg/mL

3. PACKAGE SIZE

30 ml.
100 ml.

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Once opened, use within 3 months.
Once opened, use within 6 months.

9. SPECIAL STORAGE PRECAUTIONS

Store below 30° C.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

VIRBAC

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Bottle of 30 ml or 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ERADIA

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

125 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

ERADIA 125 mg/ml oral suspension for dogs

2. Composition

Each ml contains

Active substance:
Metronidazole 125 mg

Excipients:
Butylhydroxytoluene (E321) 0.2 mg

Oily suspension with brown visible particles.

3. Target species

Dogs.

4. Indications for use

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.

5. 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.

6. Special warnings

Special precautions for safe use in the target species:
Due to the likely variability (time, geographical) in the occurrence of metronidazole resistant bacteria, bacteriological sampling and susceptibility testing are recommended.
Whenever possible, the veterinary medicinal 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 veterinary medicinal product can cause skin sensitisation. In case of known hypersensitivity to metronidazole or other nitroimidazole derivatives or one of the components of the veterinary medicinal product, avoid contact with the veterinary medicinal product.
Avoid contact with the skin or mucous membranes included hand-to-mouth contact.
To avoid such contact wear impervious gloves when handling the veterinary medicinal 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 veterinary medicinal product.
Close the bottle immediately after use to avoid the child gaining access to the contents. Do not leave a syringe containing suspension 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 the physician

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 veterinary medicinal product and cleaning the contaminated food bowl.

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

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.

Overdose:
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.

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

7. Adverse events

Dogs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports)

Neurological signs*
Undetermined frequency (cannot be estimated from the available data)
Vomiting Hepatic toxicosis (liver toxicosis) Neutropenia (low levels of neutrophilis)

*Especially after prolonged treatment with metronidazole.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes and method of administration

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 veterinary medicinal 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
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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

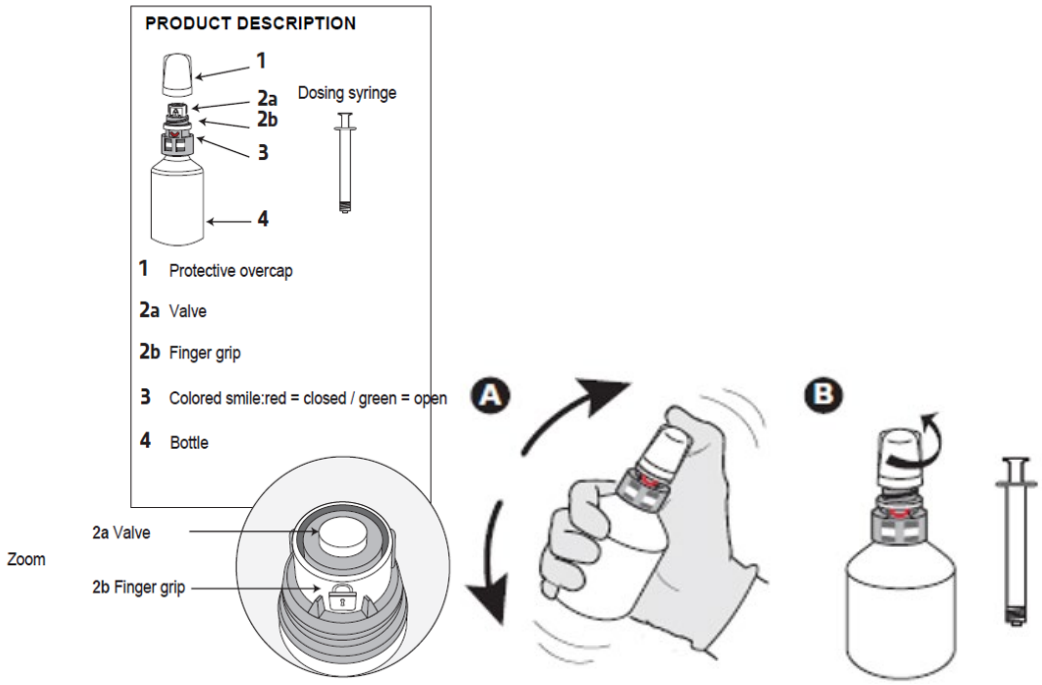
For doses requiring more than two filled syringes, the dosing should be twice daily in order to minimize counting and dosing errors.

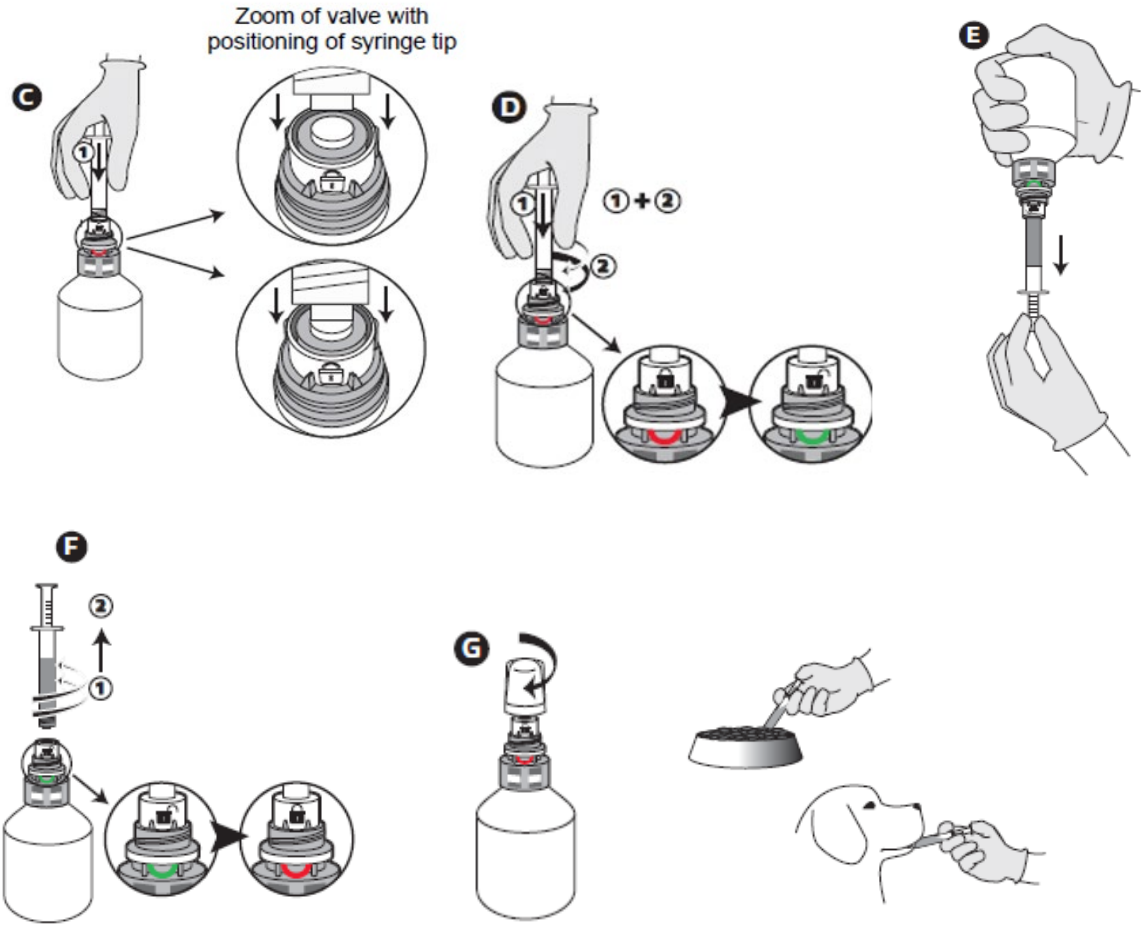
The oral suspension is delivered through the package described below

9. Advice on correct administration

[Snap cap packaging]

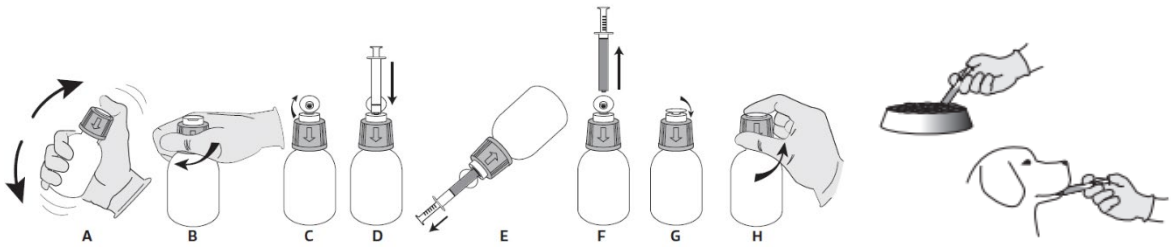
A - Shake the bottle vigorously before use.
B - Unscrew the protective overcap.
C - Firmly push the valve with the tip of the syringe
D - While pushing, turn the syringe to the right (clockwise) until
the green smile appears.
E - Turn the bottle upside down and withdraw the prescribed volume of the veterinary medicinal product, in the upside down position.
F - Once the correct volume of the veterinary medicinal 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.
G - Screw the protective overcap back on.
Administer the veterinary medicinal 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 veterinary medicinal product and/or administering the veterinary medicinal 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.





[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 veterinary medicinal 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 veterinary medicinal 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 veterinary medicinal product and/or administering the veterinary medicinal 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.



NOTE : The package leaflet on the market shall mention either the snap cap packaging or the screw cap packaging but not both.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Store below 30° C.
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.
Shelf life after first opening the immediate packaging:

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

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Bottle of 30 ml or 100 ml.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

VIRBAC
1ère avenue 2065m LID
06516 Carros
France

Manufacturer responsible for batch release:

VIRBAC
1ère avenue 2065m LID
06516 Carros
France

or:

DELPHARM Huningue
26 rue de Chapelle
68330 Huningue
France

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information