[Version 9,03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BG, FR, HU, IT, PL, RO	Metronidavet 250 mg tablets for dogs and cats
AT, CZ, EL, ES, LT, PT	Protozoks 250 mg tablets for dogs and cats
NL, BE	Metroclos 250 mg tablets for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:

Metronidazole 250 mg

Excipients:

Qualitative composition of excipients and other constituents
Cellulose, microcrystalline
Sodium starch glycolate (type A)
Hydroxypropylcellulose
Silica colloidal, hydrated
Magnesium stearate
Yeast extract
Brown iron oxide (E172) (black, yellow and red)

Light brown with brown spots, round and convex flavoured tablet with a cross-shaped break line on one side. The tablets can be divided into two or four equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Dogs and cats

3.2 Indications for use for each target species

Treatment of gastrointestinal infections caused by *Giardia* spp. and *Clostridia* 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. *Clostridia* spp.) susceptible to metronidazole.

3.3 Contraindications

Do not use in animals with 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.
Especially after prolonged treatment with metronidazole, neurological signs could occur.
As tablets are flavoured, store tablets out of reach of the animals in order to avoid accidental ingestion.

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 has possible carcinogenic effects in humans. However, there is inadequate evidence in humans for the carcinogenicity of metronidazole.
Metronidazole may be harmful for the unborn child. Pregnant women should be careful when handling this veterinary medicinal product.
Personal protective equipment consisting of impervious gloves should be worn when handling the veterinary medicinal product.

To avoid accidental ingestion, particularly by a child, unused part-tablets should be returned to the open blister space and inserted back into the outer packaging and kept in a safe place out of the sight and reach of children. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Metronidazole may cause hypersensitivity reactions. People with known hypersensitivity to metronidazole should avoid contact with the veterinary medicinal product.

Wash hands thoroughly after handling the tablets.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs and cats:

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

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:
Laboratory studies in animals have shown inconsistent results with regard to teratogenic/embryotoxic effects of metronidazole. Therefore, the use of veterinary medicinal product is not recommended during pregnancy.

Lactation:
Metronidazole is excreted in milk and therefore, the use is 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

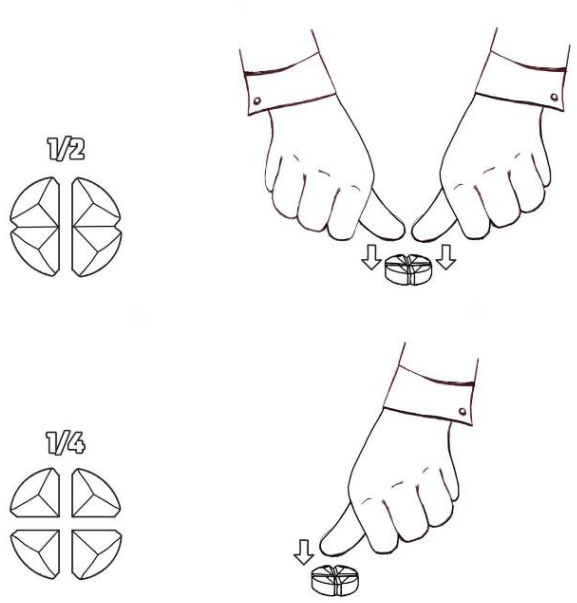
Oral use.

The recommended dose is 50 mg metronidazole per kg body weight per day for 5-7 days.
The daily dose should preferably be divided in two equal doses for twice daily administration (i.e. 25 mg/kg bodyweight twice daily).
To ensure a correct dosage, body weight should be determined as accurately as possible.

	Number of tablets of 250 mg	
Body weight (kg)	**Twice daily**	**Once daily**
1.25 kg	-	¼
2.5 kg	¼	½
5 kg	½	1
7.5 kg	¾	1½
10 kg	1	2
12.5 kg	1¼	2½
15 kg	1½	3
17.5 kg	1¾	3½
20 kg	2	4

Tablets can be divided into 2 or 4 equal parts to ensure accurate dosing.

Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.
Halves: press down with your thumbs on both sides of the tablet.
Quarters: press down with your thumb in the middle of the tablet.



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 inhibitory concentration (MIC).

4.3 Pharmacokinetics

Metronidazole is immediately and well absorbed after oral administration. After 1 hour a plasma concentration of 10 µg/ml was reached with a single dose of 50 mg. The bioavailability of metronidazole is almost 100% and the terminal half-life in the plasma is approximately 8-10 hours. Metronidazole penetrates well into the tissues and bodily fluids, such as saliva, milk, vaginal secretions and semen. Metronidazole is primarily metabolised in the liver. Within 24 hours after oral administration 35-65% of the administered dose (metronidazole and the metabolites thereof) is excreted in the urine.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months
Shelf life of divided tablets: 3 days

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Return any divided tablet to the blister.

5.4 Nature and composition of immediate packaging

PVC - Aluminium - oPA (oriented polyamide) / heat seal lacquer – Aluminium blister.

Package sizes:
Cardboard box with 20 tablets (2 blisters of 10 tablets).
Cardboard box with 100 tablets (10 blisters of 10 tablets).
Cardboard box with 250 tablets (25 blisters of 10 tablets).

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

Vet-Agro Multi-Trade Company Sp. z o.o.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

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

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).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metroclos 250 mg tablets (RMS)

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains:

Active substance:

Metronidazole 250 mg

3. PACKAGE SIZE

20 tablets
100 tablets
250 tablets

4. TARGET SPECIES

Dogs and cats

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Return any divided tablet to the blister.

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

{Logo name of the marketing authorisation holder}

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Blister

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metroclos (RMS)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Metronidazole 250 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

{Logo name of the marketing authorisation holder}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Metroclos 250 mg tablets for dogs and cats (RMS)

2. Composition

Each tablet contains:

Active substance:

Metronidazole 250 mg

Light brown with brown spots, round and convex flavoured tablet with a cross-shaped break line on one side. The tablets can be divided into two or four equal parts.

3. Target species

Dogs and cats

4. Indications for use

Treatment of gastrointestinal infections caused by *Giardia* spp. and *Clostridia* 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. *Clostridia* spp.) susceptible to metronidazole.

5. Contraindications

Do not use in animals with hepatic disorders.
Do not use in cases 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.
Especially after prolonged treatment with metronidazole, neurological signs could occur.
As tablets are flavoured, store tablets out of reach of the animals in order to avoid accidental ingestion.

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 has possible carcinogenic effects in humans. However, there is inadequate evidence in humans for the carcinogenicity of metronidazole.

Metronidazole may be harmful for the unborn child. Pregnant women should be careful when handling this veterinary medicinal product.
Personal protective equipment consisting of impervious gloves should be worn when handling the veterinary medicinal product.
To avoid accidental ingestion, particularly by a child, unused part-tablets should be returned to the open blister space and inserted back into the outer packaging and kept in a safe place out of the sight and reach of children. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Metronidazole may cause hypersensitivity reactions. People with known hypersensitivity to metronidazole should avoid contact with the veterinary medicinal product.
Wash hands thoroughly after handling the tablets.

Pregnancy:
Laboratory studies in animals have shown inconsistent results with regard to teratogenic/embryotoxic effects of metronidazole. Therefore, the use of veterinary medicinal product is not recommended during pregnancy.

Lactation:
Metronidazole is excreted in milk and therefore, the use is 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.

7. Adverse events

Dogs and cats:

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

Reporting adverse events is important. It allows continuous safety monitoring of a 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 body weight per day for 5-7 days.
The daily dose should preferably be divided in two equal doses for twice daily administration (i.e. 25 mg/kg bodyweight twice daily).

	Number of tablets of 250 mg	
Body weight (kg)	**Twice daily**	**Once daily**
1.25 kg	-	¼
2.5 kg	¼	½
5 kg	½	1
7.5 kg	¾	1½
10 kg	1	2
12.5 kg	1¼	2½
15 kg	1½	3
17.5 kg	1¾	3½
20 kg	2	4

9. Advice on correct administration

To ensure a correct dosage, body weight should be determined as accurately as possible.

Tablets can be divided into 2 or 4 equal parts to ensure accurate dosing.

Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.
Halves: press down with your thumbs on both sides of the tablet.
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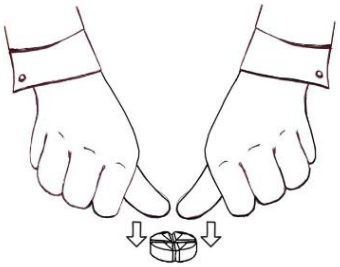

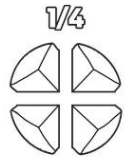

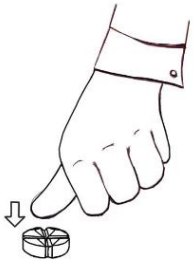

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.
Return any divided tablet to the blister.

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 months
Shelf life of divided tablets: 3 days

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

Package sizes:
Cardboard box with 20 tablets (2 blisters of 10 tablets).
Cardboard box with 100 tablets (10 blisters of 10 tablets).
Cardboard box with 250 tablets (25 blisters of 10 tablets).

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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:
Vet-Agro Multi-Trade Company Sp. z o.o.
Gliniana 32, 20-616 Lublin,
Poland

Manufacturer responsible for batch release:
Lelypharma B.V.
Zuiveringweg 42
8243 PZ Lelystad
The Netherlands

Contact details to report suspected adverse reactions:

<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