[Version 8.1,01/2017]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metrovis 100 mg tablets for dogs and cats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains:

Active substance:
Metronidazole 100 mg.

Excipient(s):
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
Beige coloured, round tablets with a cross-shaped break line on one side.
Tablets can be divided into 2 or 4 equal parts.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs and cats.

4.2 Indications for use, specifying the target species

Treatment of gastrointestinal tract 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.

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.
In very rare cases, neurological signs may occur especially after prolonged treatment with metronidazole.

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.
Impervious gloves should be worn during administration of the product to avoid skin contact with the product.

To avoid accidental ingestion, particularly by a child, unused tablets and part-tablets should be returned to the open blister space, 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. Wash hands thoroughly after handling the tablets.

Metronidazole may cause hypersensitivity reactions. In case of known hypersensitivity to metronidazole, avoid contact with the veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

The following adverse reactions may occur after administration of metronidazole: vomiting, hepatotoxicity, neutropenia and neurological signs.

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

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

Lactation:
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.

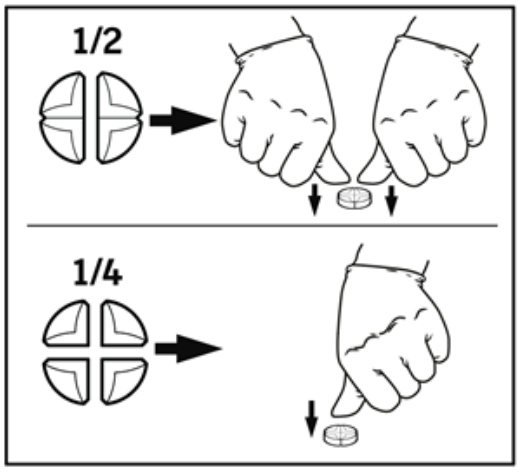
4.9 Amounts to be administered and administration route

For oral use.
The recommended dose is 50 mg metronidazole per kg bodyweight per day, for 5-7 days. The daily dose may be split into two administrations per day (i.e. 25 mg/kg bodyweight twice daily).

To ensure administration of the correct dosage, bodyweight should be determined as accurately as possible. The following table is intended as a guide to dispensing the product at the recommended dose rate of either 50 mg per kg bodyweight, administered once daily or, preferably, administered twice daily in 25 mg per kg bodyweight.

	Number of tablets		
	Twice daily		**Once daily**
Bodyweight (kg)	Morning	Evening	
0.5 kg	¼	-	¼
1 kg	¼	¼	½
2 kg	½	½	1
3 kg	¾	¾	1 ½
4 kg	1	1	2
5 kg	1 ¼	1 ¼	2 ½
6 kg	1 ½	1 ½	3
7 kg	1 ¾	1 ¾	3 ½
8 kg	2	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.



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 neurologic 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: Antiprotozoals against protozoal disease, (nitro-) imidazole derivatives
ATC code: QP51AA01

5.1 Pharmacodynamic properties

After metronidazole has penetrated the bacteria, the molecule is reduced by the susceptible 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 susceptible bacteria in concentrations equal to or slightly higher than the minimum inhibiting concentration (MIC).

5.2 Pharmacokinetic particulars

Metronidazole is immediately and well absorbed after oral administration. The bioavailability of metronidazole is almost 100%.
In dogs, a C_{max} of 79.5 µg/ml is observed following 1 hour after a single oral dose of 62 mg/kg bw. The terminal half-life in the plasma is about 5.3 hours (3.5 to 7.3 hours).
In cats, a C_{max} of 93.6 µg/ml is observed following 1.5 hours after a single oral dose of 83 mg/kg bw. The terminal half-life in the plasma is about 6.7 hours (5.2 to 8.3 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline
Sodium starch glycolate, type A
Hydroxypropylcellulose
Yeast (dried)
Beef Flavour
Magnesium stearate

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

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

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Aluminium - PVC/PE/PVDC blister
Cardboard box of 1, 2, 5, 10, 25 or 50 blisters of 10 tablets
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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Livisto Int'l S.L.
Av. Universitat Autònoma 29
08290 Cerdanyola del Vallès
Barcelona, Spain

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE CARDBOARD BOX OF 1, 2, 5, 10, 25 OR 50 BLISTERS OF 10 TABLETS

{CARDBOARD BOX}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metrovis 100 mg tablets for dogs and cats
Metronidazole

2. STATEMENT OF ACTIVE SUBSTANCES

Metronidazole 100 mg.

3. PHARMACEUTICAL FORM

Tablet.

4. PACKAGE SIZE

10 tablets
20 tablets
50 tablets
100 tablets
250 tablets
500 tablets

5. TARGET SPECIES

Dogs and cats.

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
Metronidazole may cause severe adverse reactions and has been associated with carcinogenicity.
Avoid skin contact and accidental ingestion. Wear gloves. Store the product in a safe place. See package leaflet for full user warnings.

10. EXPIRY DATE

<EXP {month/year}>
Shelf life of divided tablets: 3 days

11. SPECIAL STORAGE CONDITIONS

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Livisto Int'l S.L.
Av. Universitat Autònoma 29
08290 Cerdanyola del Vallès
Barcelona, Spain

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

<Batch><Lot> {number}

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

{ALUMINIUM - PVC/PE/PVDC BLISTER CONTAINING 10 TABLETS}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metrovis 100 mg tablets
Metronidazole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Livisto Int'l S.L.

3. EXPIRY DATE

<EXP {month/year}>

4. BATCH NUMBER

<Batch><Lot> {number}

5. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

{Metrovis 100 mg tablets for dogs and cats}

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Livisto Int'l S.L.
Av. Universitat Autònoma 29
08290 Cerdanyola del Vallès
Barcelona, Spain

Manufacturer responsible for batch release:
aniMedica GmbH
Im Südfeld 9
48308 Senden-Bösensell
Germany

OR

aniMedica Herstellungs GmbH
Im Südfeld 9
48308 Senden-Bösensell
Germany

OR

Industrial Veterinaria S.A.
Esmeralda 19, Esplugues de Llobregat
08950 Barcelona
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Metrovis 100 mg tablets for dogs and cats
Metronidazole

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

1 tablet contains:
Active substance:
Metronidazole 100 mg
Beige coloured, round tablets with a cross-shaped break line on one side.
Tablets can be divided into 2 or 4 equal parts.

4. INDICATION(S)

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

6. ADVERSE REACTIONS

The following adverse reactions may occur after administration of metronidazole: vomiting, hepatotoxicity, neutropenia and neurological signs.

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).

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 inform your veterinary surgeon. Alternatively you can report via your national reporting system {national system details}.

7. TARGET SPECIES

Dogs and cats.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

For oral use.
The recommended dose is 50 mg metronidazole per kg bodyweight per day, for 5-7 days. The daily dose may be split into two administrations per day (i.e. 25 mg/kg bodyweight twice daily).

To ensure administration of the correct dosage, bodyweight should be determined as accurately as possible. The following table is intended as a guide to dispensing the product at the recommended dose rate of either 50 mg per kg bodyweight, administered once daily or, preferably, administered twice daily in 25 mg per kg bodyweight.

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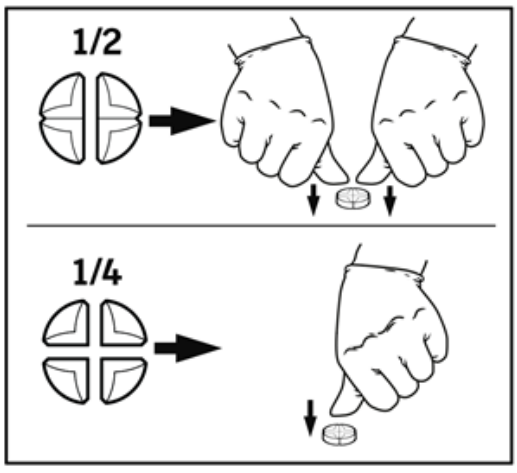
4 kg	1	1	2
5 kg	1 ¼	1 ¼	2 ½
6 kg	1 ½	1 ½	3
7 kg	1 ¾	1 ¾	3 ½
8 kg	2	2	4

9. ADVICE ON CORRECT ADMINISTRATION

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.



10. WITHDRAWAL PERIOD(S)

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.
Do not use this veterinary medicinal product after the expiry date which is stated on the carton.
Shelf life of divided tablets: 3 days

12. SPECIAL WARNING(S)

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.
In very rare cases, neurological signs may occur especially after prolonged treatment with metronidazole.

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Metronidazole may be harmful for the unborn child.
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Metronidazole may cause hypersensitivity reactions. In case of known hypersensitivity to metronidazole, avoid contact with the veterinary medicinal product.

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

Lactation:
Metronidazole is excreted in milk and use during lactation is therefore not recommended.

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 (symptoms, emergency procedures, antidotes):
Adverse events are more likely to occur at doses and treatment durations in excess of the recommended treatment regimen. If neurologic signs occur, treatment should be discontinued, and the patient should be treated symptomatically.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Cardboard box of 1, 2, 5, 10, 25 or 50 blisters of 10 tablets.
Not all pack sizes may be marketed.