[Version 8.2, 01/2021]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alphafluben 44 mg/ml oral gel for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Flubendazole: 44 mg

Excipients:
Methyl parahydroxybenzoate (E218) 1.8 mg
Propyl parahydroxybenzoate 0.2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral gel
White or almost white, odourless suspension gel

4. CLINICAL PARTICULARS

4.1 Target species

Dogs

4.2 Indications for use, specifying the target species

Anthelmintic for the treatment of dogs infected with roundworms, hookworms and tapeworms.
Roundworms: *Toxocara canis, Toxascaris leonina*
Hookworms: *Ancylostoma caninum*
Whipworms: *Trichuris vulpis*

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substance(s) or to any of the excipient(s).

4.4 Special warnings for each target species

Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:
- Too frequent and repeated use of anthelmintics from the same class, over an extended period of time
- Underdosing, which may be due to underestimation of body weight or misadministration of the product

The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infection based on its epidemiological features, for each individual animal

4.5 Special precautions for use

<u>Special precautions for use in animals</u>

Parasite resistance may develop to a particular class of anthelmintics after frequent and repeated administration of that anthelmintic class.

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

This veterinary medicinal product may cause allergic reactions. People with known hypersensitivity to flubendazole or to the excipients methyl parahydroxybenzoate and propyl parahydroxybenzoate should avoid contact with the veterinary medicinal product.

The product might be mildly irritant to eyes and skin. Direct contact of the product with the skin and eyes must be avoided. In the event of accidental skin or eye contact with the product, rinse the area immediately with plenty of clean water.

Additionally, pregnant women and women of child bearing potential should be careful to avoid accidental exposure.

This veterinary medicinal product may be harmful when ingested, particularly for children. Avoid accidental ingestion of the product. Do not leave a syringe in the sight or reach of children. In order to prevent children from getting access to used syringes, keep the syringe 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 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; wash hands when handling the product and cleaning the contaminated food bowl.

Wash hands thoroughly after use.

4.6 Adverse reactions (frequency and seriousness)

Transient vomiting has been observed in dogs very rarely.

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

Laboratory studies in rats have shown evidence of teratogenic and foetotoxic effects at high doses. Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

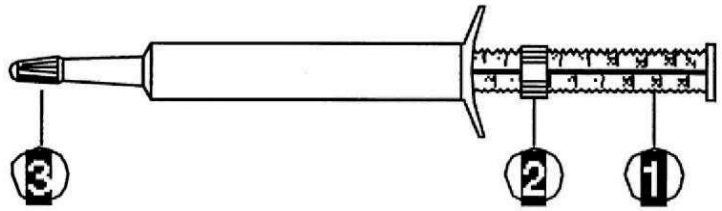
None known.

4.9 Amounts to be administered and administration route

Recommended dose
22 mg flubendazole per kg bodyweight, one 7.5 ml syringe contains 330 mg flubendazole.

Administration
1 ml gel/2 kg bodyweight, once a day for three consecutive days.
One syringe is for a dog of up to 15 kg.

Administration route
The gel can be administered as follows:
- the exact dosage should be administered directly onto the tongue of the dog,
- the exact dosage should be mixed into the feed of the dog (recommended in case of aggressive dogs that are difficult to treat).



Remove the safety cap (3). Turn the ring (2) counterclockwise until it is at the mark on the dosing piston (1), which corresponds to the body weight of the animal in kg. Give the animal the dose. At the next treatment, add the animal's body weight to the number that the ring (2) was previously set to; then turn the ring to this new mark and administer the appropriate dose.
Example: For a dog of 3 kg body weight the ring for the first treatment is set to the 3 kg mark, of 6 kg body weight for the second and of 9 kg body weight for the third treatment.

Recommended treatment
Dogs:
- Puppies: at 1-2 weeks of age
- Young dogs (under 12 months of age): every 2-3 months
- Breeding bitches: during oestrous cycle, 10 days before and 10 days after parturition
- Adult dogs: every 3-4 months considering the local regulations
- All dogs: prior to vaccination

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

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

This veterinary medicinal product has a wide therapeutic margin. Five time overdose does not cause adverse reactions.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anthelmintics, Benzimidazoles and related substances
ATC vet code: QP52AC12

5.1 Pharmacodynamic properties

Flubendazole is a synthetic anthelmintic belonging to the benzimidazole carbamates. Flubendazole acts by binding to tubulin of the parasites' microtubules and blocking polymerization of tubulin molecules. These changes are relatively fast and are primarily seen in those target cells directly involved but in contrast the changes are not seen in the host cells. Flubendazole blocks cellular functions, reducing absorption and digestion of nutrients in the intestinal tract of the parasite, with accumulation of protein-

digesting enzymes resulting in death of the parasite. Flubendazole also inhibits the egg production and oviposition of parasites.

5.2 Pharmacokinetic particulars

Flubendazole is poorly absorbed from the gastrointestinal tract. This is reflected by a high faecal excretion of unchanged parent drug. The very small fraction absorbed is extensively metabolised in the liver, involving hydrolysis and reduction. The biotransformation products are conjugated to glucuronides or sulphate conjugates and excreted in the bile and the urine in small quantities. The excretion in urine is relatively low and consists almost exclusively of metabolites, with only small amounts of unchanged compound.

The maximum plasma concentrations of unchanged substance after oral administration of 10 mg/kg of radiolabelled flubendazole in dogs were less than 10 ng/ml. The plasma half-life of flubendazole and its metabolites is 16 hours. After oral administration of the veterinary medicinal product at a dose of 22 mg/kg body weight, the maximum plasma concentrations were approximately 5 ng/ml.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol 85 percent (E422)
Carbomer
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate
Sodium Hydroxide *(for pH-adjustment*)
Purified water

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 90 days.

6.4. Special precautions for storage

Store below 25°C.
Do not refrigerate or freeze.

6.5 Nature and composition of immediate packaging

7.5 ml gel in a linear low density polyethylene (LLDPE) plastic oral syringe, with polystyrene plunger packaged in carton.

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

ALPHAVET Zrt., Hofherr
A. utca. 42.H-1194 Budapest
Hungary
Tel.: +36/22-534500
E-mail: alpha-vet@alpha-vet.hu

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}.

10. DATE OF REVISION OF THE TEXT

{DD month YYYY}

PROHIBITION OF SALE, SUPPLY AND/OR USE

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alphafluben 44 mg/ml oral gel for dogs
Flubendazole

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Active substance:
Flubendazole: 44 mg

3. PHARMACEUTICAL FORM

Oral gel

4. PACKAGE SIZE

7.5 ml

5. TARGET SPECIES

Dogs

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP: {month/year}
Once opened use within 90 days.
Once opened, use by……

11. SPECIAL STORAGE CONDITIONS

Store below 25°C.
Do not refrigerate or freeze.

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

Dispose of waste material in accordance with local requirements.

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

ALPHAVET Zrt. Hofherr A. utca
42.
H-1194, Budapest, Hungary
Tel.: +36/22-534500
E-mail: alpha-vet@alpha-vet.hu

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Label

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alphafluben 44 mg/ml oral gel for dogs
Flubendazole

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Flubendazole 44 mg/ml

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

7.5 ml

4. ROUTE(S) OF ADMINISTRATION

For oral use.

5. WITHDRAWAL PERIOD(S)

Not applicable.

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP: {month/year}
Once opened use within 90 days.
Once opened, use by……

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Alphafluben 44 mg/ml oral gel for dogs

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

Marketing authorisation holder:
ALPHAVET Zrt., Hofherr Albert utca 42., H-1194 Budapest, Hungary

Manufacturer responsible for batch release:
ALPHAVET Zrt., Bábolna, Köves János utca 13, H-2943 Bábolna, Hungary

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alphafluben 44 mg/ml oral gel for dogs
Flubendazole

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

Each ml contains:
Active substance:
Flubendazole: 44 mg

Excipients:
Methyl parahydroxybenzoate (E218) 1.8 mg
Propyl parahydroxybenzoate 0.2 mg

White or almost white, odourless suspension gel

4. INDICATION(S)

Anthelmintic for the treatment of dogs infected with roundworms, hookworms and tapeworms
Roundworms: *Toxocara canis, Toxascaris leonina*
Hookworms: *Ancylostoma caninum*
Whipworms: *Trichuris vulpis*

5. CONTRAINDICATIONS

Do not use in cases of hypersenitivity to the active substance(s), to the adjuvant(s) or to any of the excipient(s).

6. ADVERSE REACTIONS

Transient vomiting has been observed in dogs very rarely.

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

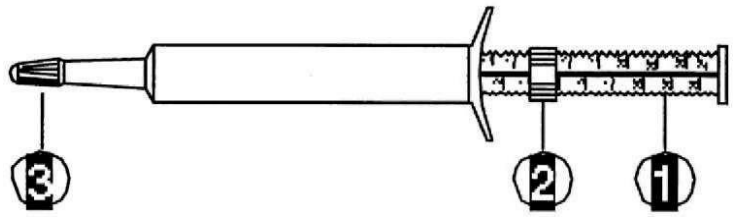
8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Recommended dose
22 mg flubendazole per kg bodyweight, one 7.5 ml syringe contains 330 mg flubendazole.

Administration
1 ml gel/2 kg bodyweight, once a day for three consecutive days.
One syringe is for a dog of up to 15 kg.

Administration route
The gel can be administered as follows:
- the exact dosage should be administered directly onto the tongue of the dog,
- the exact dosage should be mixed into the feed of the dog (recommended in case of aggressive dogs that are difficult to treat).

9. ADVICE ON CORRECT ADMINISTRATION



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Example: For a dog of 3 kg body weight the ring for the first treatment is set to the 3 kg mark, of 6 kg body weight for the second and of 9 kg body weight for the third treatment.

Recommended treatment
Dogs:
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- Breeding bitches: during oestrous cycle, 10 days before and 10 days after parturition
- Adult dogs: every 3-4 months considering the local regulations
- All dogs: prior to vaccination

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

10. WITHDRAWAL PERIOD(S)

Not applicable.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store below 25°C.
Do not refrigerate or freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Shelf life after first opening the container: 90 days.

12. SPECIAL WARNING(S)

Special warnings for each target species:

Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:

- Too frequent and repeated use of anthelmintics from the same class, over an extended period of time.

- Underdosing, which may be due to underestimation of body weight or misadministration of the product'

The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infection based on its epidemiological features, for each individual animal'

Special precautions for use in animals:

Parasite resistance may develop to a particular class of anthelmintics after frequent and repeated administration of that anthelmintic class.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product may cause allergic reactions. People with known hypersensitivity to flubendazole or to the excipients methyl parahydroxybenzoate and propyl parahydroxybenzoate should avoid contact with the veterinary medicinal product.

The product might be mildly irritant to eyes and skin. Direct contact of the product with the skin and eyes must be avoided. In the event of accidental skin or eye contact with the product, rinse the area immediately with plenty of clean water.

Additionally, pregnant women and women of child bearing potential should be careful to avoid accidental exposure.

This veterinary medicinal product may be harmful when ingested, particularly for children. Avoid accidental ingestion of the product. Do not leave a syringe in the sight or reach of children. In order to prevent children from getting access to used syringes, keep the syringe 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 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; wash hands when handling the product and cleaning the contaminated food bowl.
Wash hands thoroughly after use.

Pregnancy and lactation:
Laboratory studies in rats have shown evidence of teratogenic and foetotoxic effects at high doses.
Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

Overdose (symptoms, emergency procedures, antidotes):
This veterinary medicinal product has a wide therapeutic margin. Five time overdose does not cause adverse reactions.

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Package size:
7.5 ml gel in a linear low density polyethylene (LLDPE) plastic oral syringe, with polystyrene plunger packaged in carton.

When the container is opened for the first time, the discard date should be calculated using the in-use shelf life specified on this package leaflet and the date recorded in the available space on the carton.

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