[Version 8.1,01/2017]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alphafluben 50 mg/g Premix for Medicated Feeding Stuff for pigs and chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:
Active substance:
Flubendazole 50 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff
White or beige-white powder without mechanical impurities, clots or clusters.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs (pigs for fattening), chickens (broilers)

4.2 Indications for use, specifying the target species

For the treatment of infestations caused by mature and immature stages of the following nematodes:
Pigs: *Metastrongylus apri, Ascaris suum*, *Hyostrongylus rubidus* (red stomach worm), *Oesophagostomum dentatum*, *Trichuris suis* and *Strongyloides ransomi* (only adult form).
Chickens: *Ascaridia galli, Heterakis gallinarum, Capillaria spp*.

4.3 Contraindications

Do not use in pigeons and parrots.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

In the event of an infection occurring in clinical symptoms, all the animals in contact with each other must be treated and appropriate zoohygiene measures should be applied.
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, misadministration of the product, or lack of calibration of the dosing device (if any).

Suspected clinical cases of resistance to anthelmintics should be further investigated using appropriate tests (e.g. Faecal Egg Count Reduction Test). Where the results of the test(s) strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to a different pharmacological class and having a different mode of action should be used.

Resistance to benzimidazoles (which includes flubendazole) could be developed because of the too frequent and repeated use of anthelmintics from the same class, over an extended period of time. Therefore the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics**.**

4.5 Special precautions for use

Special precautions for use in animals

Not applicable.

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

Accidental ingestion by humans should be avoided. May cause sensitisation by skin contact. May cause skin and eye irritation. Avoid direct skin contact. People with known hypersensitivity to flubendazole should avoid contact with the veterinary medicinal product. Personal protective equipment consisting of overalls and impervious gloves should be worn when handling the veterinary medicinal product.
Wash affected parts if skin contact occurs. If accidental eye contact occurs, immediately rinse thoroughly with water. If the operation involves potential exposure to dust, wear either a disposable filter on a half mask respirator, conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 fitted with a filter to EN 143.
If allergic symptoms occur after the administration of the product, such as skin rash, seek medical advice immediately and show the package leaflet. Swelling of the face, lips, eyelids, difficult breathing is already a serious symptom that requires immediate medical attention. Do not eat, drink or smoke while using. Wash hands with soap and water after application.

4.6 Adverse reactions (frequency and seriousness)

None known in therapeutic dose.

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy.
Can be used during lay.
Flubendazole doesn’t influence the egg hatchability.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Method of administration
Oral use. In feed use only.

To ensure administration of a correct dose, body weight should be determined as accurately as possible; accuracy of the dosing device should be checked.

Pigs:
Breeding stock: The standard recommended total dosage is 1 mg flubendazole per kg bodyweight and day, equals 1 gram Alphafluben 50 mg/g premix for medicated feeding stuff for every 50 kg body weight and day, for 10 consecutive days.

Weaners and fattening pigs: The standard recommended total dosage is 1 mg flubendazole per kg bodyweight and day, equals 1 gram Alphafluben 50 mg/g premix for medicated feeding stuff for every 50 kg body weight and day, for 5 consecutive days. In the event of a heavy *Trichuris* infestation duration of the treatment is for 10 consecutive days.

When preparing a medicated feed, account must be taken of the daily feed consumption that depends on the clinical condition and, as well as body weight of the animals to be treated. Therefore, exact amount of the product to be added to the feed should be calculated according to the following formula to ensure the above dosage:

$$\frac{\text{20 mg of the veterinary medicinal product per kg body weight and day} \times \text{Average pig body weight (kg)}}{\text{Average daily feed intake (kg/animal)}} = \text{mg the veterinary medicinal product per kg of feed}$$

Chickens:
The standard recommended total dosage is 1.43 mg flubendazole per kg bodyweight and day, equals 28,6 mg Alphafluben 50 mg/g premix for medicated feeding stuff for every kg body weight and day, for 7 consecutive days.

When preparing a medicated feed, account must be taken of the daily feed consumption that depends on the clinical condition and, as well as body weight of the animals to be treated. Therefore, exact amount of the product to be added to the feed should be calculated according to the following formula to ensure the above dosage:

$$\frac{\text{28,6 mg of the veterinary medicinal product per kg body weight and day} \times \text{Average bird body weight (kg)}}{\text{Average daily feed intake (kg/animal)}} = \text{mg the veterinary medicinal product per kg of feed}$$

This veterinary medicinal product should not be mixed with drinking water or liquid feed.
Do not spray on pellets or grain.

If animals are to be treated collectively rather than individually, pigs and chickens should be grouped according to their bodyweight and dosed accordingly, in order to avoid under- or overdosing.
No special control of diet is necessary before or after treatment.
It may not be used for a dose different from the prescribed dose and for a longer period of time.

The veterinary medicinal product can be incorporated in pelleted feed preconditioned with steam at a temperature not exceeding 85ºC.

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

In pigs 5 mg flubendazole/kg body weight or higher concentration can cause mild diarrhoea (loose faeces).
In chickens flubendazole has a low acute oral toxicity and is well tolerated in the target species.

4.11 Withdrawal period(s)

Pigs: Meat and offal: 5 days.
Chickens: Meat and offal: 3 days.
Eggs: zero days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Benzimidazoles and related substances; Flubendazole.
ATC vet code: QP52AC12

5.1 Pharmacodynamic properties

Flubendazole is a synthetic anthelmintic belonging to the halogenated group of the benzimidazole carbamates which acts by inhibiting the microtubular assembly in absorptive cells of nematodes. Benzimidazoles progressively deplete energy reserves and inhibit excretion of waste products and protective factors from parasite cells. Inhibition of cellular transport and energy metabolism are consequences of the depolymerization of microtubules.

Flubendazole acts by binding to tubulin, the dimeric subunit protein of the microtubules. It inhibits microtubular assembly in absorptive cells: i.e. of intestinal cells of nematodes. This is shown by disappearance of cytoplasmic microtubules, accumulation of secretory granules in the cytoplasm due to a block in their transport, leading to an impaired coating of the cellular membrane and a decreased digestion and absorption of nutrients. Irreversible lytic degeneration of the cell, due to the accumulation of secretory substances (hydrolytic and proteolytic enzymes), results in the death of the parasite.

These changes are relatively fast and are primarily seen in those organelles directly involved in the secretory and absorptive functions of the cells.

In contrast the changes are not seen in cells of host animals.

5.2 Pharmacokinetic particulars

Flubendazole absorbs very poorly 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.
In pigs the highest tissue levels of poorly absorbed quantities are measured in liver and kidneys. The half-life of Flubendazole in tissues is 1 to 2 days. In chickens the half-life of Flubendazole in plasma and tissues is 1 to 4 days.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Titanium dioxide (E171)
Sodium laurilsulfate

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: 4 years.
Shelf life after first opening the immediate packaging: 42 days.
Shelf life after incorporation into pelleted feed: 3 months.

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Do not refrigerate or freeze.
Keep the opened bag tightly closed.

6.5 Nature and composition of immediate packaging

Three-layered paper bag with HDPE inner layer.
Package size: 12 kg premix for medicated feeding stuff.

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.
H-1194 Budapest, Hofherr A. u. 42.
Telephone number: +36/22-516-546
Fax number (optional): +36/22-516-546
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

Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.

LABELLING AND PACKAGE LEAFLET

COMBINED LABEL AND PACKAGE LEAFLET:
Alphafluben 50 mg/g Premix for Medicated Feeding Stuff for pigs and chickens

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

Marketing authorisation holder and manufacturer responsible for batch release: ALPHAVET Zrt., H-1194 Budapest, Hofherr A. u. 42., Hungary.

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Alphafluben 50 mg/g Premix for Medicated Feeding Stuff for pigs and chickens

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

Each gram contains:
Active substance:
Flubendazole 50 mg

White or beige-white powder without mechanical impurities, clots or clusters.

4. PHARMACEUTICAL FORM

Premix for Medicated Feeding Stuff

5. PACKAGE SIZE

12 kg

6. INDICATION(S)

For the treatment of infestations caused by mature and immature stages of the following nematodes:
Pigs: *Metastrongylus apri, Ascaris suum*, *Hyostrongylus rubidus* (red stomach worm), *Oesophagostomum dentatum*, *Trichuris suis* and *Strongyloides ransomi* (only adult form).
Chickens: *Ascaridia galli, Heterakis gallinarum, Capillaria spp*.

7. CONTRAINDICATIONS

Do not use in pigeons and parrots.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

8. ADVERSE REACTIONS

None known in therapeutic dose.
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. For details regarding the national system please contact NCA.

9. TARGET SPECIES

Pigs (pigs for fattening), chickens (broilers)

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

Method of administration
Oral use. In feed use only.
To ensure administration of a correct dose, body weight should be determined as accurately as possible; accuracy of the dosing device should be checked.

Pigs:
Breeding stock: The standard recommended total dosage is 1 mg flubendazole per kg bodyweight and day, equals 1 gram Alphafluben 50 mg/g premix for medicated feeding stuff for every 50 kg body weight and day, for 10 consecutive days.

Weaners and fattening pigs: The standard recommended total dosage is 1 mg flubendazole per kg bodyweight and day, equals 1 gram Alphafluben 50 mg/g premix for medicated feeding stuff for every 50 kg body weight and day, for 5 consecutive days. In the event of a heavy *Trichuris* infestation duration of the treatment is for 10 consecutive days.

When preparing a medicated feed, account must be taken of the daily feed consumption that depends on the clinical condition and, as well as body weight of the animals to be treated. Therefore, exact amount of the product to be added to the feed should be calculated according to the following formula to ensure the above dosage:

$$\frac{\text{20 mg of the veterinary medicinal product per kg body weight and day} \times \text{Average pig body weight (kg)}}{\text{Average daily feed intake (kg/animal)}} = \text{mg the veterinary medicinal product per kg of feed}$$

Chickens:
The standard recommended total dosage is 1.43 mg flubendazole per kg bodyweight and day, equals 28,6 mg Alphafluben 50 mg/g premix for medicated feeding stuff for every kg body weight and day, for 7 consecutive days.

When preparing a medicated feed, account must be taken of the daily feed consumption that depends on the clinical condition and, as well as body weight of the animals to be treated. Therefore, exact amount of the product to be added to the feed should be calculated according to the following formula to ensure the above dosage:

28,6 mg of the veterinary medicinal product per kg body weight and day x Average bird body weight (kg) = mg the veterinary medicinal product per kg of feed

Average daily feed intake (kg/animal)

This veterinary medicinal product should not be mixed with drinking water or liquid feed.
Do not spray on pellets or grain.
If animals are to be treated collectively rather than individually, pigs and chickens should be grouped according to their bodyweight and dosed accordingly, in order to avoid under- or overdosing.
No special control of diet is necessary before or after treatment.
It may not be used for a dose different from the prescribed dose and for a longer period of time.

11. ADVICE ON CORRECT ADMINISTRATION

Do not use veterinary medicinal product if you notice any visible signs of deterioration.
The veterinary medicinal product can be incorporated in pelleted feed preconditioned with steam at a temperature not exceeding 85ºC.

12. WITHDRAWAL PERIOD(S)

Pigs: Meat and offal: 5 days.
Chickens: Meat and offal: 3 days.
Eggs: zero days.

13. 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 refrigerate or freeze.
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.
Keep the opened bag tightly closed.

14. SPECIAL WARNING(S)

Special warnings for each target species:
In the event of an infection occurring in clinical symptoms, all the animals in contact with each other must be treated and appropriate zoohygiene measures should be applied.
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, misadministration of the product, or lack of calibration of the dosing device (if any).

Suspected clinical cases of resistance to anthelmintics should be further investigated using appropriate tests (e.g. Faecal Egg Count Reduction Test). Where the results of the test(s)

strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to a different pharmacological class and having a different mode of action should be used.

Resistance to benzimidazoles (which includes flubendazole) could be developed because of the too frequent and repeated use of anthelmintics from the same class, over an extended period of time. Therefore the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

Special precautions for use in animals:
Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Accidental ingestion by humans should be avoided. May cause sensitisation by skin contact. May cause skin and eye irritation. Avoid direct skin contact. People with known hypersensitivity to flubendazole should avoid contact with the veterinary medicinal product.
Personal protective equipment consisting of overalls and impervious gloves should be worn when handling the veterinary medicinal product.. Wash affected parts if skin contact occurs. If accidental eye contact occurs, immediately rinse thoroughly with water. If the operation involves potential exposure to dust, wear either a disposable filter on a half mask respirator, conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 fitted with a filter to EN 143.
If allergic symptoms occur after the administration of the product, such as skin rash, seek medical advice immediately and show the package leaflet. Swelling on the face, lips, eyelids, difficult breathing is already a serious symptom that requires immediate medical attention. Do not eat, drink or smoke when handling the product. Wash hands thoroughly with soap and water after use of the product or medicated feeding stuff.

Pregnancy:
Can be used during pregnancy.

Lay:
Can be used during lay.
Flubendazole doesn’t influence the egg hatchability.

Interaction with other medicinal products and other forms of interaction:
No data available.

Overdose (symptoms, emergency procedures, antidotes):
In pigs 5 mg flubendazole/kg body weight or higher concentration can cause mild diarrhoea (loose faeces). In chickens flubendazole has a low acute oral toxicity and is well tolerated in the target species.

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

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

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

16. DATE ON WHICH THE LABEL WAS LAST APPROVED

{DD month YYYY}.

17. OTHER INFORMATION

Container: Three-layered paper bag with HDPE inner layer.
Package size: 12 kg premix for medicated feeding stuff.
Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.

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

18. 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.

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

Keep out of the sight and reach of children.

20. EXPIRY DATE

EXP {month/year}
Shelf life after first opening the container: 42 days.
Shelf life after incorporation into pelleted feed: 3 months.

21. MARKETING AUTHORIZATION NUMBER(S)

Marketing authorization number {number}

22. MANUFACTURER'S BATCH NUMBER

Batch {number}