ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Slentrol 5 mg/ml oral solution for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains :

Active substance:

Dirlotapide 5 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.
A colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

As an aid in the management of overweight and obesity in adult dogs. To be used as part of an overall weight management programme which also includes appropriate dietary changes and exercise practice.

4.3 Contraindications

Do not use in dogs in the growth phase.
Do not use during pregnancy or lactation.
Do not use in dogs with impaired liver function.
Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in dogs in which overweight or obesity is caused by a concomitant systemic disease such as hypothyroidism or hyperadrenocorticism.
Do not use in cats due to the risk of development of hepatic lipidosis.

4.4 Special warnings

In clinical trials, treated dogs rapidly regained weight following cessation of treatment when diet was not restricted. In order to avoid this rebound weight gain, it is necessary to feed the dogs to maintenance energy requirements. Thus, during treatment or at the end of treatment at the latest, an appropriate feeding and exercise regimen should be implemented in order to ensure long term maintenance of the bodyweight.

4.5 Special precautions for use

Special precautions for use in animals

The liver function of dogs suspected of suffering from a liver disease or dysfunction should be evaluated before commencing treatment with the veterinary medicinal product.

Any clinical indication of liver disease or dysfunction during treatment should be investigated through the evaluation of liver function. Any indication of progressive liver damage or of dysfunction should result in discontinuation of treatment.

In the treatment phase, because food intake is reduced as when using a traditional non-medical calorie restriction method, care must be taken to ensure that protein, vitamins, essential fatty acids and minerals supplied by the consumed daily food ration meet minimal recommended requirements in order to ensure a complete and balanced nutritional supply.

If vomiting, diarrhoea or significantly reduced appetite or excessive weight loss occurs, treatment should be interrupted and the advice of a veterinarian should be sought. Resolution of adverse reactions will occur shortly after suspension of treatment. Dosing may be recommenced at the same or at a reduced dose volume (reduced by 25%), but if vomiting reoccurs, the veterinary medicinal product may need to be withdrawn.

Fertility studies have not been conducted in the target species. Use in dogs intended for breeding should be subject to a risk-benefit analysis (see section 4.7).

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

In case of contact with the skin, wash off any veterinary medicinal product immediately with soap and water.

Slentrol may cause eye-irritation.

Avoid contact with eyes. If accidental eye exposure occurs, flush the eyes immediately with clean water.

When the veterinary medicinal product is drawn into syringe, administer immediately.

Where the veterinary medicinal product has been administered on food, discard unconsumed food immediately to avoid unintentional ingestion by other animals or persons in the household. Ingestion can be harmful to children and pregnant women.
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

In clinical studies, vomiting, sometimes accompanied by signs of lethargy, anorexia or diarrhoea was observed during treatment with the veterinary medicinal product. These signs typically started during the first month of treatment (about 30% of dogs showed at least one vomiting event and up to 12% showed any of the other signs) and decreased continuously during the course of treatment. Some dogs (less than 10%) experienced repeated vomiting (i.e. more than once every 20 days on average).

Sporadic and mild ALT (alanine aminotransferase) elevations up to 4 times the upper reference range and not associated with histopathological liver lesions or noticeable changes in other liver parameters may be observed in some dogs during the course of treatment.

On rare occasions, reports of change of behaviour such as polyphagia, or very rarely reports of aggression associated with food and feeding have been observed in Slentrol-treated dogs. If these changes were observed, treatment should be stopped.

4.7 Use during pregnancy, lactation or lay

Do not use in dogs during pregnancy and lactation. MTP (Microsomal Trigylyceride transfer Protein) inhibitors as a class have the potential to disrupt yolk sac development and laboratory studies on rats and rabbits have shown evidence of embryolethality, teratogenicity, and developmental toxicity.

4.8 Interaction with other medicinal products and other forms of interaction

Interactions with other drug types have not been specifically investigated. Therefore, for dogs receiving treatments in addition to the veterinary medicinal product, drug interactions should be monitored closely.

4.9 Amounts to be administered and administration route

Dogs should undergo a physical examination by a veterinarian before commencing treatment, and a desired bodyweight or body condition score identified. To ensure correct dosing during the treatment period the owner should seek advice from the responsible veterinarian in connection to each monthly dose adjustment.

The recommended starting dose is 0.05 mg/kg initial bodyweight per day (0.01 ml/kg/day). After two weeks of therapy, the initial dose (number of ml administered) should be increased by 100% (doubled). Following these initial 4 weeks of therapy, dogs should be weighed monthly during treatment and dose adjustments are made monthly according to effect as described below.

The duration of treatment must not exceed 12 months and the dose must not exceed a maximum of 0.2 ml /kg current bodyweight (1 mg/kg dirlotapide).

Administer the veterinary medicinal product once daily directly into the mouth or on a small amount of food. Slentrol can be administered with or without food.

At the end of each month of therapy, the percentage of bodyweight loss should be determined. If the bodyweight loss since previous monthly weighing has been ≥3% bodyweight per month (equivalent to 0.1% bodyweight per day); the dose (number of ml administered) should be kept the same. If the bodyweight loss since previous monthly weighing has been <3% bodyweight per month, the dose should be increased without adjusting for the dog's current bodyweight. The first time a conditional increase is required, the dose should be increased by 100%, (doubled). In subsequent required conditional increases, the dose should be increased by 50% (increasing the dose volume to 1.5 times the volume administered in the previous month) up to a maximum dose of the veterinary medicinal product of 0.2 ml/kg current bodyweight. These adjustments should be continued until the weight targeted at the start of therapy is achieved.

Although not observed in clinical trials, in the case where bodyweight loss since previous monthly weighing has been ≥12% per month (equivalent to 0.4% bodyweight per day), the dose should be reduced by 25%.

According to clinical studies, a mean weight loss of about 18 to 20% after six months of weight loss therapy can be anticipated.

DOSE PROGRESSION TABLE DURING WEIGHT LOSS

Dose level	Trigger for increase	Volume to administer in ml
1 (start)	Not applicable	Dose 1 = Starting dose = Initial BW x 0.01 ml/kg

DOSE PROGRESSION TABLE DURING WEIGHT LOSS		
Dose level	Trigger for increase	Volume to administer in ml
2 (automatic day 14 increase)	Not applicable (systematic)	Dose 2 = Dose 1 x 2
3 (conditional)	First monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 3 = Dose 2 x 2
4 (conditional)	Second monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 4 = Dose 3 x 1.5
5 (conditional)	Third monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 5 = Dose 4 x 1.5
6 (conditional)	Fourth monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 6 = Dose 5 x 1.5

3% bodyweight loss per month = 0.7% per week = 0.1% per day
The lowest validated dose for the dosing device is 0.05 ml. This is the starting dose for a 5 kg dog.

4.10 Overdose (symptoms, emergency procedures, antidotes)

Overdose up to 10 times the maximum authorised dose of 1 mg/kg current bodyweight may produce vomiting or diarrhoea or increased ALT/AST (alanine aminotransferase/aspartate aminotransferase) levels. These signs will resolve spontaneously following treatment discontinuation,

4.11 Withdrawal period

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Peripherally acting antiobesity products, ATCvet code: QA08AB91

5.1 Pharmacodynamic properties

Dirlotapide is a potent selective inhibitor of the Microsomal Triglyceride transfer Protein (MTP). The MTP is pivotal for the absorption and distribution of fat. The inhibition of intestinal and hepatic MTP reduces plasma cholesterol and triglyceride concentration. The selective inhibition of intestinal MTP also reduces intestinal fat absorption.

Clinical and pharmacodynamic data strongly suggest that the efficacy of dirlotapide results from a primary local action in the gut after oral administration. This is consistent with *in vivo* data generated in mice which shows that dirlotapide has selectivity for intestinal MTP. The effect is mainly mediated indirectly due to reduced feed intake during therapy.

As a consequence of reducing intestinal fat absorption, dirlotapide reduces food intake in dogs in a dose-dependent manner. This food inhibitory effect of dirlotapide results from a primary local effect on the gastrointestinal tract following oral administration and is not a result of systemic exposure.

The efficacy of dirlotapide has been demonstrated with various types of diets, representing the whole range of fat contents available in commercial diets.

5.2 Pharmacokinetic properties

Systemic blood levels of dirlotapide are not well correlated with efficacy in the dog.

Dirlotapide exhibited rapid oral absorption with mean C_{max} values in the range of 8.5- 115 ng/ml, at 0.5 to 4 hours post-treatment (mean T_{max}: 1.0 to 2.1 hours). Mean oral bioavailability values were approximately 24% - 41% for fed dogs and 22% in fasted dogs. Systemic exposure was 1.5 times higher in fed dogs. AUC and C_{max} increased with increasing dose but not in a dose-proportional manner. In a 14-day repeated dose study, AUC increased 3-fold from Day 1to Day 14. In a 3-month study, exposures were 2 times higher at Day 29 but returned to Day 1 values at days 56 and 87. There is no gender effect on pharmacokinetic parameters.

In a radiolabeled metabolism study, the primary route of excretion was via the faeces with minimal excretion via urine (<1%). Additionally, dirlotapide was highly protein bound (>99%) in dog plasma.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Medium chain triglycerides

6.2 Incompatibilities

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

The veterinary medicinal product is not miscible with water. Oral dosing devices used for measuring the dose may be cleaned with water but must be dried before re-use.

6.3 Shelf life

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

Shelf life after first opening the immediate packaging: 3 months.

6.4 Special precautions for storage

Store in the original container in order to protect from light.

6.5 Nature and composition of immediate packaging

Polypropylene bottles of 20, 50 and 150 ml fitted with a low density polyethylene (LDPE) Press-In-bottle adapter and a child resistant closure.
Bottles of 20 ml are packed with two dosing devices of 1 ml.
Bottles of 50 ml are packed with two dosing devices of 3 ml.
Bottles of 150 ml are packed with two dosing devices of 10 ml.

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

Pfizer Limited
Ramsgate Road
Sandwich
Kent
CT13 9NJ
United Kingdom

8. MARKETING AUTHORISATION NUMBERS

EU/2/07/071/001-003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13.04.2007
Date of last renewal:

10. DATE OF REVISION OF THE TEXT

Detailed information on this product is available on the website of the European Medicines Agency (EMA) http://www.ema.europa.eu/

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND> MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Pfizer Service Company
Hoge Wei 10
1930 Zaventem
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY OR USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

Not applicable

D. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Pharmacovigilance system

The MAH must ensure that the system of pharmacovigilance, as described in Part I of the marketing authorisation application, is in place and functioning before and whilst the veterinary medicinal product is on the market.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

NATURE: 20 ml, 50 ml 150 ml bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Slentrol 5 mg/ml oral solution for dogs

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Dirlotapide 5 mg/ml

3. PHARMACEUTICAL FORM

Oral solution

4. PACKAGE SIZE

20 ml packed with 2 dosing devices of 1 ml
50 ml packed with 2 dosing devices of 3 ml
150 ml packed with 2 dosing devices of 10 ml

5. TARGET SPECIES

Dogs

6. INDICATION

As an aid in the management of overweight and obesity in adult dogs.

7. METHOD AND ROUTE OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Not applicable.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached, use within 3 months.

11. SPECIAL STORAGE CONDITIONS

Store in the original container in order to protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT 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

For animal treatment only - to be supplied only on veterinary prescription.

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

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent
CT13 9NJ
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/07/071/001 20ml
EU/2/07/071/002 50ml
EU/2/07/071/003 150ml

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

NATURE: 20 ml, 50 ml, 150 ml bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Slentrol 5 mg/ml oral solution for dogs
Dirlotapide

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

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

20ml
50ml
150ml

4. ROUTE OF ADMINISTRATION

Oral use.

5. WITHDRAWAL PERIOD

Not applicable

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once opened, use within 3 months

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Slentrol 5 mg/ml oral solution 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

Pfizer Limited
Ramsgate Road
Sandwich
Kent
CT13 9NJ
United Kingdom

Manufacturer for the batch release:

Pfizer Service Company
Hoge Wei 10
1930 Zaventem
Belgium

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Slentrol 5 mg/ml oral solution for dogs
Dirlotapide

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENT

Dirlotapide 5 mg/ml is a colourless to pale yellow solution.

4. INDICATION

As an aid in the management of overweight and obesity in adult dogs. Your veterinary surgeon will identify a target weight and explain how Slentrol should be used as part of an overall weight management programme which also includes appropriate dietary changes and exercise practice.

5. CONTRAINDICATIONS

Do not use in dogs in the growth phase.
Do not use during pregnancy or lactation.
Do not use in dogs with impaired liver function.
Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in dogs in which overweight or obesity is caused by a concomitant systemic disease such as hypothyroidism or hyperadrenocorticism.
Do not use in cats due to the risk of development of hepatic lipidosis.

6. ADVERSE REACTIONS

Some dogs may show one or more vomiting events, sometimes accompanied by signs of tiredness, disinterest in food or diarrhoea, which reoccur occasionally during the course of treatment. These signs typically started during the first month of treatment (about 30% of dogs showed at least one vomiting event and up to 12% showed any of the other signs) and decreased continuously during the course of treatment. Some dogs (less than 10%) experienced repeated vomiting (i.e. more than once every 20 days on average). If your dog suffers from repeated vomiting, diarrhoea or significantly reduced appetite and excessive weight loss, you should consult your veterinary surgeon who may advise you to stop therapy.

Sporadic and mild ALT (alanine aminotransferase) elevations up to 4 times the upper reference range and not associated with histopathological liver lesions or noticeable changes in other liver parameters may be observed in some dogs during the course of treatment.

On rare occasions, reports of change of behaviour such as polyphagia, or very rarely reports of aggression associated with food and feeding have been observed in Slentrol-treated dogs. If these changes were observed, treatment should be stopped.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Dogs

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

Advice for Dog Owner
The veterinarian will examine your dog at the beginning of treatment and recommend a starting dose. The veterinarian will advise you when dose adjustments become necessary.

Advice for Veterinarian
The recommended starting dose of Slentrol is 0.05 mg/kg (0.01ml/kg) by oral administration. After two weeks of therapy, the initial dose volume should be doubled. Following these initial 4 weeks of therapy, dose adjustments are made monthly according to effect as described in section 9.

9. ADVICE ON CORRECT ADMINISTRATION

Advice for Dog Owner
Withdraw the veterinary medicinal product from the bottle using the supplied dosing device and administer the veterinary medicinal product once daily directly into the mouth or on a small amount of food. The veterinary medicinal product can be administered with or without food. To ensure correct dosing during the treatment period the owner should seek advice from the responsible veterinarian in connection to each monthly dose adjustment.

Advice for Veterinarian
Dogs should undergo a physical examination before commencing treatment, and a desired bodyweight or a body condition score identified.

The recommended starting dose of the veterinary medicinal product is 0.05 mg/kg initial bodyweight per day (0.01 ml/kg/day). After two weeks of therapy, the initial dose (number of ml administered) should be increased by 100% (doubled). Following these initial 4 weeks of therapy, dogs should be weighed monthly during treatment with the veterinary medicinal product and dose adjustments are made monthly according to effect as described below.

At the end of each month of therapy, the percentage of bodyweight loss should be determined. If the bodyweight loss since previous monthly weighing has been ≥3% bodyweight per month (equivalent to 0.1% bodyweight per day); the dose (number of ml administered) should be kept the same. If the bodyweight loss since previous monthly weighing has been <3% bodyweight per month, the dose should be increased without adjusting for the dog's current bodyweight. The first time a conditional increase is required, the dose should be increased by 100%, (doubled). In subsequent required conditional increases, the dose should be increased by 50% (increasing the dose volume to 1.5 times the volume administered in the previous month) up to a maximum dose of the veterinary medicinal product of 0.2 ml/kg current bodyweight. These adjustments should be continued until the weight targeted at the start of therapy is achieved.

Although not observed in clinical trials, in the case where bodyweight loss since previous monthly weighing has been ≥12% per month (equivalent to 0.4% bodyweight per day), the dose should be reduced by 25%.

According to clinical studies, a mean weight loss of about 18 to 20% after six months of weight loss therapy can be anticipated.

The duration of treatment with the veterinary medicinal product must not exceed 12 months and the dose of the veterinary medicinal product must not exceed a maximum of 0.2 ml/kg current bodyweight (1 mg/kg dirlotapide).

DOSE PROGRESSION TABLE DURING WEIGHT LOSS

Dose level	Trigger for increase	Volume to administer in ml
1 (start)	Not applicable	Dose 1 = Starting dose = Initial BW x 0.01 ml/kg
2 (automatic day 14 increase)	Not applicable (systematic)	Dose 2 = Dose 1 x 2
3 (conditional)	First monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 3 = Dose 2 x 2
4 (conditional)	Second monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 4 = Dose 3 x 1.5
5 (conditional)	Third monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 5 = Dose 4 x 1.5
6 (conditional)	Fourth monthly weighing where bodyweight loss < 3% per month since previous weighing	Dose 6 = Dose 5 x 1.5

3% bodyweight loss per month = 0.7% per week = 0.1% per day
The lowest validated dose for the dosing device is 0.05 ml. This is the starting dose for a 5 kg dog.

10. WITHDRAWAL PERIOD

Not applicable

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Store in the original container in order to protect from light..
Do not use after the expiry date stated on the bottle
Shelf life after first opening the container: 3 months

12. SPECIAL WARNINGS

Advice for dog owner:

Slentrol must not be used during pregnancy and lactation.
Fertility studies have not been conducted in the target species – use in dogs intended for breeding should be subject to a risk-benefit analysis by your veterinarian.

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

The veterinary medicinal product is not miscible with water. Oral dosing devices used for measuring the dose may be cleaned with water but must be dried before re-use.

In clinical trials, treated animals rapidly regained weight following cessation of treatment when diet was not restricted. In order to avoid this rebound weight gain, it is necessary to feed the animals to maintenance energy requirements. Thus, during treatment or at the end of treatment at the latest, an appropriate feeding and exercise regimen should be implemented in order to ensure long term maintenance of the bodyweight.

Wash hands after use. In case of contact with the skin, wash off any veterinary medicinal product immediately with soap and water**.** Slentrol may cause eye-irritation. Avoid contact with eyes**.** If accidental eye exposure occurs, flush the eyes immediately with clean water.
When the veterinary medicinal product is drawn into syringe, administer immediately.
Where the veterinary medicinal product has been administered on food, discard unconsumed food immediately to avoid unintentional ingestion by other animals or persons in the household. Ingestion can be harmful to children and pregnant women.

In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Advice for Veterinarian:

The liver function of dogs suspected of suffering from a liver disease or dysfunction should be evaluated, before commencing treatment with the veterinary medicinal product. Dogs with evidence of liver dysfunction should not be treated with the veterinary medicinal product.

Any clinical suspicion of liver disease or dysfunction during treatment should be investigated through the evaluation of liver function. Because the veterinary medicinal product is contraindicated in cases of liver dysfunction, any indication of progressive liver damage or dysfunction should result in the discontinuation of the treatment. Sporadic and mild serum alanine aminotransferase (ALT) elevations up to 4 times the upper reference range are not a reason for discontinuing therapy in the absence of any indication of liver dysfunction.

Do not use in dogs during pregnancy and lactation. MTP inhibitors (microsomal trigylyceride transfer protein inhibitors) as a class have the potential to disrupt yolk sac development and laboratory studies

on rats and rabbits have shown evidence of embryolethality, teratogenicity, and developmental toxicity.

During treatment, because food intake is reduced as when using a traditional non-medical calorie restriction method, care must be taken to ensure that protein, vitamins, essential fatty acids and minerals supplied by the daily food ration meet minimal recommended requirements in order to ensure a complete and balanced nutritional supply.

In clinical trials, treated animals rapidly regained weight following cessation of treatment when diet was not restricted. In order to avoid this rebound weight gain, it is necessary to feed the animals to maintenance energy requirements. Thus, during treatment or at the end of treatment at the latest, an appropriate feeding and exercise regimen should be implemented in order to ensure long term maintenance of the bodyweight.

If vomiting, diarrhoea or significantly reduced appetite or excessive weight loss occurs, treatment should be interrupted. Resolution of adverse reactions will occur shortly after the suspension of treatment. In case of excessive weight loss greater than 12% per month, the dose volume of the veterinary medicinal product should be reduced (by 25%).

Overdose up to 10 times the maximum authorised dose of 1 mg/kg current bodyweight may produce vomiting or diarrhoea or increased ALT/AST (alanine aminotransferate/aspartate aminotransferate) levels. These signs will resolve spontaneously following treatment discontinuation.

Interactions with other drug types have not been specifically investigated. Therefore, for dogs receiving treatments in addition to the veterinary medicinal product, drug interactions should be monitored closely.

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

Detailed information on this product is available on the website of the European Medicines Agency (EMA) http://www.ema.europa.eu/

15. OTHER INFORMATION

Polypropylene bottles of 20, 50 and 150 ml fitted with a low density polyethylene (LDPE) Press-In-bottle adapter and a child resistant closure.
Bottles of 20 ml are packed with two dosing devices of 1 ml.
Bottles of 50 ml are packed with two dosing devices of 3 ml.
Bottles of 150 ml are packed with two dosing devices of 10 ml.

Not all pack sizes may be marketed.

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

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