ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pulmotil G100 Premix for medicated feeding stuff

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Tilmicosin (as phosphate) 100 g/kg

Excipients:

Qualitative composition of excipients and other constituents
Ground corn cobs
Soya-bean oil (as stated in the Ph. Eur.)
Soya-bean mill run

A yellowish tan to reddish tan free flowing granular material.

3. CLINICAL INFORMATION

3.1 Target species

Pigs and rabbits.

3.2 Indications for use for each target species

Pigs: Treatment and metaphylaxis of respiratory disease caused by *Actinobacillus pleuropneumoniae*, *Mycoplasma hyopneumoniae*, *Pasteurella multocida.*

Rabbits: Treatment and metaphylaxis of respiratory disease caused by *Pasteurella multocida* and *Bordetella bronchiseptica*, susceptible to tilmicosin.

The presence of the disease in the group or flock must be established before the product is used.

3.3 Contraindications

Horses or other Equidae, must not be allowed access to feeds containing tilmicosin.
Horses fed with tilmicosin medicated feeds may present signs of toxicity with lethargy, anorexia, reduction of feed consumption, loose stools, colic, distension of the abdomen and death.

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

3.4 Special warnings

Under practical conditions, the management of respiratory disease outbreaks recognises that acutely ill animals are inappetant and require parenteral therapy.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to tilmicosin and may decrease the effectiveness of treatment with tilmicosin related substances.

Use of the product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

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

Tilmicosin may induce irritation. Macrolides, such as tilmicosin, may also cause hypersensitivity (allergy) following injection, inhalation, ingestion or contact with skin or eye. Hypersensitivity to tilmicosin may lead to cross reactions to other macrolides and vice versa. Allergic reactions to these substances may occasionally be serious and therefore direct contact should be avoided.

Personal protective equipment consisting of overalls, safety glasses, impervious gloves and either a disposable half mask respirator conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 with a filter to EN143 should be worn when handling the veterinary medicinal product.

Do not eat, drink or smoke when handling this veterinary medicinal product. Wash hands after use.

In case of accidental ingestion, wash out mouth immediately with water and seek medical advice immediately and show the label to the physician.

In case of accidental spillage onto skin, wash thoroughly with soap and water and seek medical advice immediately and show the label to the physician.

In case of accidental eye contact, flush the eyes with plenty of clean, running water and seek medical advice immediately and show the label to the physician.

People with known hypersensitivity to tilmicosin should avoid contact with the veterinary medicinal product.

If you develop symptoms following exposure, such as skin rash, seek medical advice and show the label to the physician. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

Special precautions for the protection of the environment:
The primary route of environmental exposure is from manure applied to agricultural land as fertilizer. Tilmicosin degrades/declines slowly in the soil. Therefore, to protect soil and ground water, pig manure should not be spread onto grass land and when spread onto arable land should be plough to a depth of 30 cm. Environmental assessments have demonstrated that the use of the veterinary medicinal product as indicated is not expected to have any impact on the environment.

3.6 Adverse events

Pigs and rabbits:

Very rare	Reduced food intake[1]

(<1 animal / 10,000 animals treated, including isolated reports):	

[1] Transient including feed refusal.

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 the national competent authority via the national reporting system. See the label for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy or lactation.

Fertility:
The safety of the veterinary medicinal product has not been established in boars used for breeding purposes.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

In-feed use.

The intake of medicated feed depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of tilmicosin may need to be adjusted accordingly.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{mg veterinary medicinal product/ kg body weight day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily feed intake (kg/animal)} \times \text{veterinary medicinal product strength (g/kg)}} = \text{kg veterinary medicinal product per tonne of feed}$$

Pigs
Administer in the feed at a dose of 8 to 16 mg/kg body weight/day of tilmicosin (equivalent to 200 to 400 ppm in the feed) for a period of 15 to 21 days.

Indication	Dose rate	Duration of treatment	Inclusion rate in feed
Treatment and metaphylaxis of respiratory disease	8-16 mg/kg bodyweight /day	15-21 days	2-4 kg veterinary medicinal product/tonne

Rabbits

Administer in the feed at 12.5 mg/kg body weight/day of tilmicosin (equivalent to 200 ppm in the feed) for 7 days.

Indication	Dose rate	Duration of treatment	Inclusion rate in feed
Treatment and metaphylaxis of respiratory disease	12.5 mg/kg bodyweight /day	7 days	2 kg veterinary medicinal product/tonne

To ensure thorough dispersion of the veterinary medicinal product, it should first be mixed with a suitable quantity of feed ingredients (20-50 kg) before incorporation into the finished feed.
This veterinary medicinal product can be incorporated into pelleted feed, preconditioned for the minimum time-period at a temperature not exceeding 75°C.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No symptoms of overdose have been seen in pigs fed a ration containing levels of tilmicosin up to 80 mg/kg bodyweight (equivalent to 2000 ppm in the feed or ten times the recommended dose) for 15 days.

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

This veterinary medicinal product is intended to be used for the preparation of medicated feed.
Do not use for prophylaxis.

3.12 Withdrawal periods

Pigs:
Meat and offal: 21 days.

Rabbits:
Meat and offal: 4 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code : QJ01FA91.

4.2 Pharmacodynamics

Tilmicosin is a semi-synthetic antibiotic of the macrolide group and is believed to affect protein synthesis. It has bacteriostatic action but at high concentrations it may be bactericidal. This antibacterial activity is predominantly against Gram-positive microorganism with activity against certain gram-negative ones and *Mycoplasma* of a bovine, porcine, ovine and avian origin. In particular its activity has been demonstrated against the following micro-organism:
Pigs: *Mycoplasma hyopneumoniae, Pasteurella multocida, Actinobacillus pleuropneumoniae.*
Rabbits: *Pasteurella multocida, Staphylococcus aureus* and *Bordetella bronchoseptica*

Scientific evidence suggests that macrolides act synergistically with the host immune system. Macrolides appear to enhance phagocyte killing of bacteria. Tilmicosin has been shown to inhibit *in vitro* the replication of the Porcine Reproductive and Respiratory Syndrome virus in alveolar macrophages in a dose dependent fashion.

Cross resistance between tilmicosin and other macrolides and lincomycin has been observed.

4.3 Pharmacokinetics

Pigs:
Absorption: When administered to pigs via the oral route at a dose of 400 mg tilmicosin/kg feed (equivalent to approximately 21.3 mg tilmicosin/kg bodyweight/day), tilmicosin moves rapidly out of the serum into areas of low pH. The highest concentration in the serum (0.23 + 0.08 μg/ml) was recorded on day 10 of medication, but concentrations above the limit of quantification (0.10 μg/ml) were not found in 3 out of 20 animals examined. Lung concentrations increased rapidly between days 2 and 4 but no significant changes were obtained following four days of dosing. The maximum concentration in lung tissue (2.59 + 1.01 μg/ml) was recorded on day 10 of medication. When administered at a dose of 200 mg tilmicosin/kg feed (equivalent to approximately 11.0 mg/kg/day), plasma concentrations above the limit of quantification (0.10 μg/ml) were found in 3 out of 20 animals examined. Quantifiable levels of tilmicosin were found in lung tissue with the maximum concentration (1.43 ± 1.13 μg/ml) being recorded on day 10 of medication.

Distribution: Following oral administration, tilmicosin is distributed throughout the body with especially high levels found in the lung and in lung tissue macrophages. It is also distributed in the liver and kidney tissues.

Rabbits:
Absorption: When administered orally to rabbits at a dose of 12 mg tilmicosin/kg b.w. as a single dose there is a quick absorption. Maximum concentrations were reached in 30 minutes, being the Cmax obtained of 0.35 μg/ml. Tilmicosin plasma concentrations decreased to 0.1 μg/ml within 2 hours and to 0.02 μg/ml after 8 hours. The elimination half-life was 22 hours.

Distribution: Following oral administration, tilmicosin is distributed throughout the body with especially high levels found in lungs. After 5 days of treatment with medicated feed at a dosage of 200 ppm of the veterinary product, tilmicosin concentrations in lung tissues were of 192 ± 103 μg/g.

Applicable to both species:
Biotransformation: Several metabolites are formed, the predominant one being identified as T1. However the bulk of tilmicosin is excreted unchanged.

Elimination: Following oral administration, tilmicosin is excreted mainly via the bile into the faeces, but a small proportion is excreted via the urine.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not to be incorporated into feeds containing bentonite.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 3 months.
Shelf life after incorporation into meal or pelleted feed: 3 months.

5.3 Special precautions for storage

Store in a dry place.
Do not store above 25 °C.
Protect from direct sunlight.

5.4 Nature and composition of immediate packaging

10 kg polyethylene/polyamide/polyethylene (inner layer) bag.
2 kg, 5 kg or 10 kg paper/polyethylene/aluminium/polyethylene/paper bag.

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

{Name}

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{MM/YYYY}

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 IMMEDIATE PACKAGE - COMBINED LABEL AND PACKAGE LEAFLET

BAG

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pulmotil G100 Premix for medicated feeding stuff

2. COMPOSITION

Tilmicosin (as phosphate) 100 g/kg
A yellowish tan to reddish tan free flowing granular material.

3. PACKAGE SIZE

2 kg
5 kg
10 kg

4. TARGET SPECIES

Pigs and rabbits.

5. INDICATIONS FOR USE

Indications for use
Pigs: Treatment and metaphylaxis of respiratory disease caused by *Actinobacillus pleuropneumoniae, Mycoplasma hyopneumoniae, Pasteurella multocida*.

Rabbits: Treatment and metaphylaxis of respiratory disease caused by *Pasteurella multocida* and *Bordetella bronchiseptica,* susceptible to tilmicosin.

The presence of the disease in the group or flock must be established before the product is used.

6. CONTRAINDICATIONS

Contraindications

Horses or other Equidae, must not be allowed access to feeds containing tilmicosin.
Horses fed with tilmicosin medicated feeds may present signs of toxicity with lethargy, anorexia, reduction of feed consumption, loose stools, colic, distension of the abdomen and death.

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

7. SPECIAL WARNINGS

Special warnings

Special warnings:

Under practical conditions, the management of respiratory disease outbreaks recognises that acutely ill animals are inappetant and require parenteral therapy.

Special precautions for safe use in the target species:

Inappropriate use of the veterinary medicinal product may increase the prevalence of bacteria resistant to tilmicosin and may decrease the effectiveness of treatment with tilmicosin related substances.
Use of the product should be based on identification and susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge susceptibility of the target pathogens at farm level, or at local/regional level.

Use of the product should be in accordance with official, national and regional antimicrobial policies.

An antibiotic with a lower risk of antimicrobial resistance selection (lower AMEG category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

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

Tilmicosin may induce irritation. Macrolides, such as tilmicosin, may also cause hypersensitivity (allergy) following injection, inhalation, ingestion or contact with skin or eye. Hypersensitivity to tilmicosin may lead to cross reactions to other macrolides and vice versa. Allergic reactions to these substances may occasionally be serious and therefore direct contact should be avoided.
Personal protective equipment consisting of overalls, safety glasses, impervious gloves and either a disposable half mask respirator conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 with a filter to EN143 should be worn when handling the veterinary medicinal product.
Do not eat, drink or smoke when handling this veterinary medicinal product. Wash hands after use.
In case of accidental ingestion, wash out mouth immediately with water and seek medical advice immediately and show the label to the physician.
In case of accidental spillage onto skin, wash thoroughly with soap and water and seek medical advice immediately and show the label to the physician.
In case of accidental eye contact, flush the eyes with plenty of clean, running water and seek medical advice immediately and show the label to the physician.
People with known hypersensitivity to tilmicosin should avoid contact with the veterinary medicinal product.
If you develop symptoms after exposure, such as skin rash, seek medical advice and show the label to the physician. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.

Special precautions for the protection of the environment:
The primary route of environmental exposure is from manure applied to agricultural land as fertilizer. Tilmicosin degrades/declines slowly in the soil. Therefore, to protect soil and ground water, pig manure should not be spread onto grass land and when spread onto arable land should be plough to a depth of 30 cm. Environmental assessments have demonstrated that the use of the veterinary medicinal product as indicated is not expected to have any impact on the environment.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy or lactation.

Fertility:

The safety of the veterinary medicinal product has not been established in boars used for breeding purposes.

Interactions with other medicinal products and other forms of interaction:
None known.

Overdose:
No symptoms of overdose have been seen in pigs fed a ration containing levels of tilmicosin up to 10 times the recommended dose for 15 days.

Special restrictions for use and special conditions for use:
This veterinary medicinal product is intended to be used for the preparation of medicated feed.
Do not use for prophylaxis.

Major incompatibilities:

Not to be incorporated into feeds containing bentonite.

8. ADVERSE EVENTS

Adverse events

Pigs and rabbits:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Reduced food intake[1]

[1] Transient including food refusal.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, 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 using the contact details on this label, or via your national reporting system {national system details}.

9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration

In-feed use.

The uptake of medicated feed depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of tilmicosin may need to be adjusted accordingly.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{mg veterinary medicinal product/ kg body weight day} \times \text{average body weight (kg) of animals to be treated}}{\text{average daily feed intake (kg/animal)} \times \text{veterinary medicinal product strength (g/kg)}} = \text{kg veterinary medicinal product per tonne of feed}$$

Pigs
Administer in the feed at a dose of 8 to 16 mg/kg body weight/day of tilmicosin activity (equivalent to 200 to 400 ppm in the feed) for a period of 15 to 21 days.

Indication	Dose rate	Duration of treatment	Inclusion rate in feed
Treatment and metaphylaxis of respiratory disease	8-16 mg/kg bodyweight /day	15 to 21 days	2-4 kg veterinary medicinal product/tonne

Rabbits
Administer in the feed at 12.5 mg/kg body weight/day of tilmicosin (equivalent to 200 ppm in the feed) for 7 days.

Indication	Dose rate	Duration of treatment	Inclusion rate in feed
Treatment and metaphylaxis of respiratory disease	12.5 mg/kg bodyweight /day	7 days	2 kg veterinary medicinal product/tonne

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration

To ensure thorough dispersion of the veterinary medicinal product, it should first be mixed with a suitable quantity of feed ingredients (20 to 50 kg) before incorporation into the finished feed.
This veterinary medicinal product can be incorporated into pelleted feed, preconditioned for the minimum time‑period at a temperature not exceeding 75 °C.

11. WITHDRAWAL PERIODS

Withdrawal periods

Pigs:
Meat and offal: 21 days.
Rabbits:
Meat and offal: 4 days.

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions

Keep out of the sight and reach of children.

Store in a dry place.
Do not store above 25°C.
Protect from direct sunlight.

Shelf life after first opening the immediate packaging: 3 months.
Shelf life after incorporation into meal or pelleted feed: 3 months.

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.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

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.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

Pack sizes

10 kg polyethylene/polyamide/polyethylene (inner layer) bag.
2 kg, 5 kg or 10 kg paper/polyethylene/aluminium/polyethylene/paper bag.

Not all pack sizes may be marketed.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database.

17. CONTACT DETAILS

Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Manufacturer responsible for batch release:
Elanco France S.A.S, 26 rue de la Chapelle, 68330 Huningue, France

18. OTHER INFORMATION

19. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

21. BATCH NUMBER

Lot {number}