ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cadorex 100 mg/ml solution for use in drinking water for pigs and chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Florfenicol 100 mg

Excipients:

Qualitative composition of excipients and other constituents
Polyethylene glycol 200

Clear, colourless to yellowish solution

3. CLINICAL INFORMATION

3.1 Target species

Pig, chicken

3.2 Indications for use for each target species

Pig:

Treatment and metaphylaxis of respiratory infections caused by florfenicol susceptible bacteria such as: Pleuropneumonia (*Actinobacillus pleuropneumoniae*), atrophic rhinitis (*Pasteurella multocida, Bordetella bronchiseptica*), *Glasserella parasuis* infections, enzootic bronchopneumonia (*Mycoplasma hyopneumoniae*) and *Streptococcus suis* infections.
The presence of the disease in the group must be established before the product is used.

Chicken:

Treatment of infections caused by florfenicol susceptible bacteria such as: *Staphylococcus* spp., *E. coli*, *Ornithobacterium rhinotracheale, Pasteurella* spp.; acute catarrh conditions of the upper respiratory tract and other diseases caused by pathogens susceptible to florfenicol.

3.3 Contraindications

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

3.4 Special warnings

The oral uptake of medication by animals may be altered as a consequence of illness. In case of insufficient water uptake, animals should be treated parenterally instead, using a suitable injectable product prescribed by the veterinarian.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use of the product should be based on identification and susceptibility testing of the target pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of 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:
This veterinary medicinal product may cause irritation to skin and eyes. Personal protective equipment consisting of appropriate clothes, gloves, goggles, and mask should be worn when handling the veterinary medicinal product.
In case of accidental contact with skin or eyes, rinse these areas with plenty of water, if symptoms persists seek medical advice immediately and show the package leaflet or the label to the physician.

This veterinary medicinal product may be harmful when ingested, including effects on male fertility. Avoid oral ingestion, including hand-to-mouth contact when preparing the veterinary medicinal product. Do not smoke, eat or drink while handling the veterinary medicinal product. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

People with known hypersensitivity to florfenicol or to the excipient should avoid contact with the veterinary medicinal product. If you develop symptoms following exposure, such as skin rush, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
Wash hands after use.

Special precautions for the protection of the environment:
Manure from treated animals may be harmful to cyanobacteria and terrestrial plants.

3.6 Adverse events

Pig:

Undetermined frequency (cannot be estimated from the available data):	Anal irritation (erythema), anal oedema Diarrhoea, Constipation, Unusual stool colour[1)] Decreased drinking

[1)] Faeces turn a dark brown colour.

Chicken: None known.

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 <its local representative> or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Laboratory studies in rats and mice have shown evidence of teratogenic and maternotoxic effects.

Pregnancy and lactation:
The safety of the veterinary medicinal product in sows has not been established during pregnancy and lactation. The use is not recommended during those periods of time.

Fertility:
Do not administer to boars intended for breeding.

Laying birds:
Do not use in birds in lay.

3.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with thiamphenicol.

3.9 Administration routes and dosage

For use in drinking water.

Pig:
The daily dose is 10 mg florfenicol per kg body weight (0,1 ml of the veterinary medicinal product per kg body weight). Treatment should be continued for 5 days.

Chicken:
The daily dose is 20 mg florfenicol per kg body weight (0,2 ml of the veterinary medicinal product per kg body weight).
Treatment should be continued for 3-5 days.

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:

$$\frac{\text{ml veterinary medicinal product / kg body weight/ day} \times \text{Average body weight (kg) of animals to be treated}}{\text{Average daily water intake (l/animal)}} = \text{ml veterinary medicinal product per litre of drinking water}$$

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

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

The appropriate quantity of medicated water or pre-diluted medicated water should be prepared based on the daily water consumption.

The product should first be diluted in water to obtain a stock solution to be diluted in the drinking water tank or introduced by means of a water dosing pump.
When using a proportioner, adjust flow rate setting of the dosing pump according to concentration of the stock solution and water intake of the animals to be treated.
Solution with concentration of the veterinary medicinal product equal or higher than 12 ml/liter may precipitate.

Medicated drinking water should be refreshed or replaced every 24 hours.

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

In case of overdosing, a decrease in bodyweight gain, food and water consumption, peri-anal erythema and oedema may be observed. Due to dehydration, some haematological and biochemical parameters can be modified.

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

Not applicable.

3.12 Withdrawal periods

Pig: Meat and offal: 20 days.

Chicken: Meat and offal: 8 days.
Not for use in birds producing or intended to produce eggs for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01BA90

4.2 Pharmacodynamics

Florfenicol is a bacteriostatic, synthetic broad-spectrum antibiotic. It is active against most Gram-positive and Gram-negative bacteria by inhibiting protein synthesis in the bacterial cell. In protoplasm, it binds to the 70S ribosomal subunit, where it inhibits activity of peptidyltransferase enzyme. As a result, the synthesis of ribosomal proteins is inhibited in susceptible bacteria.
Florfenicol is a derivative of thiamphenicol. The hydroxyl group in the florfenicol molecule is replaced with a fluorine atom. As a result, florfenicol is effective against acetyltransferase producing bacteria and chloramphenicol resistant ones.
Laboratory tests have shown that florfenicol is active against numerous pathogens, such as: *Staphylococcus* spp., *Streptococcus* spp., *Bordetella bronchiseptica*, *Actinobacillus pleuropneumoniae*, *Escherichia coli*, *Haemophilus* spp., *Pasteurella multocida*, *Ornithobacterium rhinotracheale*, *Mycoplasma hyopneumoniae*.

Epidemiological cut-off values (ECOFF) (EUCAST 2024): *Staphylococcus aureus* ≤8 µg/ml
Streptococcus suis ≤4 µg/ml
Bordetella bronchiseptica ≤8 µg/ml
Actinobacillus pleuropneumoniae ≤1 µg/ml
Escherichia coli ≤16 µg/ml
Pasteurella multocida ≤1 µg/ml
No ECOFF data are available for *Haemophilus (Glassarella) parasuis, Ornithobacterium rhinotracheale* and *Mycoplasma hyopneumoniae.*

One main resistance gene (floR) has been identified leading to resistance to florfenicol. Additional genes have also been identified, but play a minor role in resistance mechanism. The resistance genes are most often located on mobile genetic elements, such as plasmids or transposons.

4.3 Pharmacokinetics

Pigs:
The distribution coefficient in pigs after intravenous administration was 863 ml / kg, while the biological half-life was 2.2 h. After the first intramuscular administration of the drug, the maximum concentration of florfenicol in serum ranged from 3.8 to 13.6 µg / ml, and the biological half-life was 2.5 h. After the second intramuscular injection, the maximum concentration of florfenicol in the blood serum ranged from 3.7 to 3.8 µg / ml. After oral administration of florfenicol at a dose of 5 mg / kg body weight maximum plasma of 3 µg / ml concentration was observed after 1 h and the bioavailability was 88%. High florfenicol levels are found in the kidneys, liver, bladder, lungs and intestines. Around half of the administered dose is excreted unchanged from the body and the remaining part is excreted in the form of metabolites, mainly amines.

Chickens:
After a single oral administration of 30 mg florfenicol / kg bodyweight, the highest concentration of 3.20 µg / ml in serum is reached after 63.1 min. and the bioavailability is 55.3%. After intramuscular

administration of the same dose, the highest serum concentration of 3.28 µg / ml is achieved after 100.4 minutes. and the bioavailability is 96.6%. After oral and intramuscular administration of florfenicol at a dose of 30 mg / kg body weight for 5 days the highest concentration was observed in kidneys (4.1 and 4.7 µg / g), lungs (2.8 and 2.9 µg / g), muscles (2.0 and 2.4 µg / g), bile (1.6 and 2.75 µg / g) / g), intestines (approx. 2.0 µg / g), myocardium (1.7 and 2.1 µg / g), liver (1.5 and 1.8 µg / g) and spleen (1.3 and 1.5 µg / g).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.
Data and information are available which show that this veterinary medicinal product can be used simultaneously and/or dissolved in drinking water with active chlorine or hydrogen peroxide.
This veterinary medicinal product may be administered using drinking water containing active chlorine at a maximum concentration of 1 ppm and hydrogen peroxide at a maximum concentration of 35 ppm.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 24 months.
Shelf life after first opening the immediate packaging: 6 months.
Shelf life after dilution according to directions: 24 hours.

5.3 Special precautions for storage

Store below 30°C.

5.4 Nature and composition of immediate packaging

High density polyethylene (HDPE) containers with a sealing foil made of paper/Alu/PET/PE and HDPE) screw cap.

Pack sizes:
1 l bottle
5 l bottle

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.

The veterinary medicinal product should not enter water courses as florfenicol may be dangerous for fish and other aquatic organisms.

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

Industrial Veterinaria, S.A.

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).