SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AMPHEN 200 mg/g granules for use in drinking water for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

Active substance:

Florfenicol	200.0 mg

Excipient(s):

Butylhydroxytoluene (E321)	1.0 mg
Disodium Edetate	1.0 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Granules for use in drinking water.
White to cream waxy granules.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs

4.2 Indications for use, specifying the target species

Treatment and metaphylaxis of swine respiratory disease associated with *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol. The presence of the disease must be established in the group before metaphylactic treatment.

4.3 Contraindications

Do not administer to boars intended for breeding purposes.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in case of known resistance to florfenicol.

4.4 Special warnings for each target species

In case of insufficient water intake, animals should be treated parenterally. During treatment, unmedicated drinking water should only be administered after the daily amount of medicated drinking water has been ingested by pigs. The product is not intended to be used together with other antibiotics.

4.5 Special precautions for use

i) Special precautions for use in animals

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. It this not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
Official and local antimicrobial policies should be taken into account when the product is used.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to florfenicol and may decrease the effectiveness of treatment with amphenicols due to the potential for cross-resistance.
Treatment should not exceed 5 days. During treatment, increased serum calcium may also be observed.

Do not use the product with chlorinated water.

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

This product may cause hypersensitivity reactions. If you have known hypersensitivity to florfenicol, polysorbate 80 or polyethylene glycol, avoid skin contact with this product. Wear protective gloves and clothing when handling and mixing this product. If you develop symptoms following exposure such as skin rash, seek medical advice immediately and show the package leaflet or the label to the physician.

This product may be slightly irritating to the eyes and/or skin. Avoid contact with the skin and eyes, including hand-to-eye-contact. Wear safety glasses. In case of accidental spillage onto eyes, wash them immediately with water. In case of contact with the skin, wash immediately the affected area and take the contaminated clothes off.

This product may be harmful after ingestion. Do not smoke, eat or drink when handling the product or mixing the medicated drinking water.

iii) Special precautions for the environment

Manure from treated animals may be harmful to terrestrial plants.

4.6 Adverse reactions (frequency and seriousness)

A slight reduction of water consumption by the animals, inappetance, dark brown faeces and constipation may be observed during treatment.

Diarrhoea and/or peri-anal and rectal erythema/oedema have been observed very commonly in treated animals. These effects are transient.
Prolapse of the rectum, that resolves without treatment, has been observed very rarely in affected animals.

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 and lactation

Studies in laboratory animals have not produced any evidence of potential embryotoxic or foetotoxic effect of florfenicol.
The safety of the veterinary medicinal product in sows has not been established during pregnancy and lactation.
The use is not recommended during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amount(s) to be administered and administration route

In drinking water use.
10 mg florfenicol /kg bodyweight per day in drinking water for 5 consecutive days.

The daily amount of product to be mixed with drinking water can be calculated based on the Total Body Weight (TBW) of the group to be treated with the following formula:

$$\textbf{Amount of product (in grams) per day*} = \frac{\textbf{Total Body Weight of the group (TBW) in Kg}}{\textbf{20}}$$

* to be mixed with the estimated total water consumption of the group in 24 hr

The examples of medicated drinking water in the table below are calculated by applying the formula and by assuming that pigs drink 8% or 10% of their bodyweight.

	TBW of the group (**Kg**)	Product (**g**)	Estimated daily water consumption (**L**)	Product grams per 10 litres of water
Pigs drinking **8%** of their bodyweight	500 kg	25 g	40 L	6.25 g/10L
	1000 kg	50 g	80 L	
	5000 kg	250 g	400 L	
Pigs drinking **10%** of their bodyweight	500 kg	25 g	50 L	5 g/10L
	1000 kg	50 g	100 L	
	5000 Kg	250 g	500 L	

The maximum solubility of the product granules is 2.5g/L at 10°C and 20°C and 2.0 g/L at 5°C. Dissolution may take up to 30 minutes. During dissolution the solution should be stirred for at least 5 minutes at 50 RPM.Solutions should be checked visually for complete dissolution.

FOR BULK TANK:
Any solution for use in a header tank must be limited to not more than the maximum solubility

FOR PROPORTIONER:
For stock solutions and when using a proportioner, take care not to exceed the maximum solubility which can be achieved under the given conditions. Adjust flow rate settings of the dosing pump according to concentration of the stock solution and water intake of the animals to be treated.

To treat 5,000 kg of pigs, drinking 10% of their bodyweight, at the dose rate of 10 mg/kg:

1. Fill the proportioner with 100L drinking water (temperature not below 10°C).
2. Add 250g of product to the proportioner.
3. Mix thoroughly until visually dissolved
4. Set the proportioner to 20%.
5. Turn on the proportioner.

In order to ensure correct dosing and to prevent underdosing, the body weight of the group should be calculated as precisely as possible and water consumption should be monitored. The required quantity of granules should be measured by suitably calibrated weighing equipment.

The uptake of water depends on several factors including the age, the clinical state of the animals and the local conditions such as ambient temperature and humidity. The daily water consumption can be underestimated (e.g. reduced to 6% of bodyweight) in order to ensure total consumption of medicated water during the day (fresh drinking water can be made available following the consumption of the medicated water). If it is not possible to obtain sufficient uptake of medicated water animals should be treated parenterally.
Medicated drinking water should be replaced every 24 hours.

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

In case of overdosing, a decrease in weight gain, food and water consumption, peri-anal erythema and oedema and modification of some haematological and biochemical parameters indicative of dehydration may be observed.

4.11 Withdrawal period(s)

Meat and offal: 20 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, amphenicols

ATC Vet Code: QJ01BA90

5.1 Pharmacodynamic properties

Florfenicol is a broad-spectrum synthetic antibiotic in the phenicol group that is active against most Gram-positive and Gram-negative bacteria isolated from domestic animals. Florfenicol acts by inhibition of protein synthesis at the ribosomal level and is bacteriostatic. However, bactericidal activity has been demonstrated *in-vitro* against *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* when florfenicol is present at concentrations above the MIC for up to 12 hours.

In-vitro testing has shown that florfenicol is active against the bacterial pathogens most commonly isolated in respiratory diseases in pigs, including *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*.
The MIC_{50} and MIC_{90} values for *Actinobacillus pleuropneumoniae* were 0.5 µg/ml and 0.5µg/ml. The MIC_{50} and MIC_{90} values for *Pasteurella multocida* were 0.5 µg/ml and 1µg/ml. These strains were isolated from European countries during 2015-2016. Observed resistance was low based on the clinical breakpoints (CLSI): sensitive ≤ 2 µg/ml, intermediate 4 µg/ml and resistant ≥ 8 µg/ml.
Resistance to florfenicol mainly comes from the presence of specific (e.g. FloR) or multi-substance (e.g. AcrAB-TolC) efflux pumps. The genes corresponding to these mechanisms are coded on genetic elements such as plasmids, transposons or gene cassettes. Cross resistance with chloramphenicol is possible.

5.2 Pharmacokinetic properties

After administration to pigs by gavage at 15 mg/kg under experimental conditions, absorption of florfenicol was variable but peak serum concentrations of approximately 5 µg/mL were reached approximately 2 hours after dosing. The terminal half-life was between 2 and 3 hours. When pigs were given free access, for 5 days, to water medicated with 100 mg florfenicol per litre of water, serum concentrations of florfenicol exceeded 1 µg/mL for the entire 5 day treatment period except for a couple of short excursions below 1 µg/mL.
After absorption and distribution, florfenicol is extensively metabolised by pigs and rapidly eliminated, primarily in urine.

After parenteral dosing of florfenicol to pigs, it has been shown that lung concentrations are similar to serum concentrations.

5.3 Environmental properties

Manure from treated animals may be harmful to terrestrial plants.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321)
Disodium Edetate
Macrogol 4000
Macrogol 400
Maltodextrin
Polysorbate 80

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 of the immediate packaging: 3 months. The bag is opened and closed by unzipping respectively zipping.
Shelf life after dilution or reconstitution according to directions: 24 hours.

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Resealable block bottom zipped bags made of polyethylene /aluminium/polyethylene terephthalate laminate containing 0.5 kg and 1 kg of granules.
Not all pack sizes may be marketed.

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

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerp
Belgium

8. MARKETING AUTHORISATION NUMBER

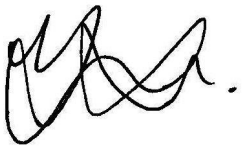
Vm 30282/4043

9. DATE OF FIRST AUTHORISATION

4 December 2019

10. DATE OF REVISION OF THE TEXT

March 2023



Approved: 15 March 2023