

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

AMPHEN 200 mg/ml suspension for use in drinking water for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains:

Active substance:

Florfenicol 200.0 mg

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Hypromellose	
Docusate sodium	
Sodium benzoate	3.0 mg
Hydrochloric acid concentrated (for pH adjustment)	
Simethicone emulsion	
Water, purified	

White to almost white suspension for use in drinking water.

3. CLINICAL INFORMATION

3.1 Target species

Pigs.

3.2 Indications for use for each target species

Treatment and metaphylaxis at the group level of swine respiratory diseases associated with *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*. The presence of the disease in the group must be established before the product is used.

3.3 Contraindications

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

See also section 3.7 for further information.

3.4 Special warnings

Do not use the product with chlorinated water.

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

3.5 Special precautions for use

Special precautions for safe use in the target species:

In addition to medication, it is important to ensure proper husbandry conditions, including good hygiene, proper ventilation and avoiding crowded conditions.

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 AMEG¹ - category) should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.

Not for use for prophylaxis.

The duration of treatment should not exceed 5 days.

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

This veterinary medicinal product may cause hypersensitivity reactions. People with known hypersensitivity to florfenicol or sodium benzoate should avoid contact with the veterinary medicinal product.

This veterinary medicinal product may be slightly irritating to the skin and eyes. Avoid skin or eye contact, including hand-to-eye-contact.

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 product. Do not eat, drink or smoke while handling this product.

Personal protective equipment consisting of gloves, clothing and safety glasses should be worn when handling and mixing the veterinary medicinal product.

In case of accidental spillage onto eyes, wash them immediately with water. In case of accidental spillage onto skin, wash immediately the affected area and take the contaminated clothes off.

Wash hands after use.

¹ Antimicrobial Advice Ad Hoc Expert Group

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.

Special precautions for the protection of the environment:

The use of the veterinary medicinal product poses a risk to terrestrial organisms (plants) and to aquatic organisms (cyanobacteria), including groundwater organisms.

In order to prevent any adverse effects on terrestrial plants and algae and to prevent possible contamination of groundwater, manure from treated pigs must not be spread onto land without dilution with manure from untreated pigs. Manure from treated pigs must be diluted with at least 5 times the weight of manure from untreated pigs before it can be spread onto arable land or before the manure is traded.

3.6 Adverse events

Pigs:

Very common (>1 animal / 10 animals treated)	Diarrhoea Erythema ¹ Oedema ¹
Undetermined frequency (cannot be estimated from the available data)	Decreased drinking Constipation Abnormal stool colouration ² Rectal prolapse ³

¹perianal or rectal

²dark brown

³retroceding without treatment

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

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

Pregnancy and lactation:

The use in sows is not recommended during pregnancy and lactation. Laboratory studies in rats and mice have not revealed any evidence of potential embryotoxic or foetotoxic effect of florfenicol.

Fertility:

Do not administer to boars intended for breeding.

3.8 Interaction with other medicinal products and other forms of interaction

See section 3.4 for further information.

3.9 Administration routes and dosage

In drinking water use.

The recommended dose is 10 mg florfenicol per kg bodyweight per day (equivalent to 5 mL of the product/100 kg bw) for 5 consecutive days.

To ensure a correct dosage body weight should be determined as accurately as possible. In order to avoid under- and over-dosing, treated animals should be divided into groups of similar bodyweight and the dose should be calculated for each group individually.

Medicated water intake depends on many factors including the clinical condition of the animal as well as local conditions such as ambient temperature and humidity. All animals to be treated should have sufficient access to the water supply system to ensure adequate consumption of the medicated drinking water. In order to ensure consumption of the medicated water, animals should not have access to other water supplies whilst being treated. If, however, it is not possible to obtain a sufficient intake of medicated water, the animals should be treated parenterally.

The appropriate quantity of medicated water should be prepared based on the daily water consumption. In order to obtain the correct dosage, the water uptake has to be monitored and the concentration of florfenicol has to be adjusted accordingly.

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

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

If a weighing scale is used the required volume can be converted in grams as follows:

quantity in g of product required per day = number of ml of product required per day x 1.075.

Accuracy of the dosing device should be thoroughly checked.

Shake the bottle vigorously for 60 seconds before use. The product should be added to the water. Prepare the solution with fresh potable water.

For water tanks:

The maximal solubility is reached at concentrations of 2 mL/L (0.4 g of florfenicol/L), 2.5 mL/L (0.5 g of florfenicol/L) and 3 mL/L (0.6 g of florfenicol/L) at respectively 4°C, 10°C and 20°C. Solutions should be checked visually for complete dissolution.

To treat pigs drinking 10% of their bodyweight, at the dose of 10 mg/kg, add the veterinary medicinal product to the drinking water in the tank.

Use 1L of product for every 2000 L of water. This corresponds to a concentration of 0.10 g florfenicol /L in the drinking water.

Mix thoroughly, to achieve full dissolution the solution should be stirred vigorously using a manual whisk for 10 minutes. When using a magnetic stirrer at 100 rpm, the mixing time is of 5 min.

For dosing pumps:

The veterinary medicinal product can only be used at the concentration of 50 mL/L i.e. 10 g of florfenicol per litre of water of stock solution.

To treat pigs drinking 10% of their bodyweight, at the dose of 10 mg/kg, add the veterinary medicinal product to the water in the reservoir of the dosing pump.

Add 1L of product to 20 L of unmedicated water. This corresponds to a concentration of 10 g/L in the stock solution.

Mix thoroughly using a manual whisk for 10 minutes until a homogeneous white milky suspension is obtained.

Set the dosing pump on 1 % and turn on the dosing pump.

Medicated drinking water should be replaced every 24 hours.

After the end of the medication period the water supply system should be cleaned appropriately to avoid intake of sub-therapeutic amounts of the active substance.

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

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

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

Meat and offal: 20 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATC Vet code:

QJ01BA90

4.2 Pharmacodynamics

Florfenicol, a broad-spectrum synthetic antibiotic belonging to the phenicol group, acts by inhibiting protein synthesis at the ribosomal level, resulting in a bacteriostatic effect. *In vitro* studies have shown that florfenicol is active against the bacterial pathogens most commonly isolated in respiratory diseases in pigs, including *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*.

Furthermore, florfenicol exhibits bactericidal activity *in vitro*, particularly when maintained at concentrations exceeding the Minimal Inhibitory Concentration (MIC), for a duration of up to 12 hours.

Activity of florfenicol against 149 isolates of <i>P. multocida</i> cultured from swine with respiratory disease from Belgium, Denmark, France, Germany, The Netherlands, Poland, Spain and The United Kingdom. ¹											
Number of isolates with MIC (µg/ml)						Susceptible		Resistant		MIC (µg/ml)	
Florfenicol	0.12	0.25	0.5	1	32	[n]	[%]	[n]	[%]	MIC ₅₀	MIC ₉₀
		1	13	131	1	3	146	98.0	3	2.0	0.5

¹ Isolated between 2018-2020

Activity of florfenicol against 151 isolates of <i>A. pleuropneumoniae</i> cultured from swine with respiratory disease from Belgium, Denmark, France, Germany, The Netherlands, Poland, Spain, Switzerland and The United Kingdom. ¹														
Number of isolates with MIC (µg/ml)							Susceptible		Intermediate		Resistant		MIC (µg/ml)	
Florfenicol	0.25	0.5	1	4	8	32	[n]	[%]	[n]	[%]	[n]	[%]	MIC ₅₀	MIC ₉₀
		11	135	2	1	1	1	148	98.0	1	0.7	2	1.3	0.5

¹ Isolated between 2018-2020

Organism	Minimum inhibitory concentration breakpoints of florfenicol (µg/ml) ^{2,3}		
	Susceptible	Intermediate	Resistant
<i>Actinobacillus pleuropneumoniae</i>	≤2	4	≥8
<i>Pasteurella multocida</i>	≤2	4	≥8

² Clinical and Laboratory Standards Institute (CLSI). 2018. Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals: 4th ed. CLSI supplement VET08. Clinical and Laboratory Standards Institute

³ CLSI. 2017. Methods for Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria Isolated From Animals. 1st ed. CLSI supplement VET06. Clinical and Laboratory Standards Institute

Resistance to florfenicol is found in the floR gene, strongly associated with the floR efflux pump, which is usually plasmid-mediated and transferred horizontally into other Pasteurellaceae species. At least the following plasmids have been found to be the carrier of the floR genes on *Pasteurellaceae* species: pFA11, pMAF5, pMAF6, pM3446F, p518, pCCK381, pCCK1900.

Resistance to florfenicol has also been detected in *Salmonella typhimurium* and other foodborne pathogens.

There is cross-resistance between substances of the phenicol class. Additionally, other resistance genes have been identified that can be located on plasmids or

transposons, such as the *cf* gene, which confers cross-resistance between pleuromutilins, oxazolidinones, phenicols, streptogramin A, and lincosamides.

4.3 Pharmacokinetics

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 florfenicol at a concentration of 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.

Environmental properties

Florfenicol is toxic for terrestrial plants, cyanobacteria and groundwater organisms.

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.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 8 months.

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

Shelf life after dilution according to directions: 24 hours.

5.3 Special precautions for storage

Do not store above 25°C.

Do not freeze.

Protect from frost.

5.4 Nature and composition of immediate packaging

White rectangular HDPE bottle of 1 litre closed with a white PP tamper-evident screw cap with a LDPE-lined multiple-layer insert.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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 aquatic organisms (cyanobacteria), including groundwater 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 for the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Huvepharma NV

7. MARKETING AUTHORISATION NUMBER

Vm 30282/3006

8. DATE OF FIRST AUTHORISATION

07 June 2024

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

June 2024

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) (<https://medicines.health.europa.eu/veterinary>).

Approved: 07 June 2024

Gavin Hall