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

For the treatment of swine respiratory disease associated with *Pasteurella multocida* susceptible to florfenicol.

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 piglets less than 6 weeks old.

4.4 Special warnings for each target species

If there is no significant improvement after 3 days of treatment, the diagnosis should be reviewed and if necessary the treatment should be changed.
In case of insufficient water intake, animals should be treated parenterally

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.

ii) Special precautions for the person administering the veterinary medicinal product to animals

People with known hypersensitivity to florfenicol or any of the excipients should avoid contact with the veterinary medicinal product.
Contact of the product or the medicated drinking water with skin and eyes should be avoided.
Personal protective equipment consisting of homologated protective gloves, coverall 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 contact with skin, wash immediately the affected area and take the contaminated clothes off.
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.
Do not smoke, eat or drink when handling the product or mixing the medicated drinking water.

4.6 Adverse reactions (frequency and seriousness)

Diarrhoea has been very commonly reported (up to 30% of animals) and inflammation of the perianal area (up to 5 % of animals) has been commonly reported in treated animals. These effects are transient and normally resolve within 5 days. Rectal prolapse has been uncommonly reported.

A slight reduction in food consumption may be observed during treatment.

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

The safety of the product during pregnancy and lactation has not been demonstrated. Use of the product during pregnancy and lactation is therefore not recommended.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amount(s) to be administered and administration route

Oral use in drinking water.
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 herd to be treated with the following formula:

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

* to be mixed with the estimated total water consumption of the herd 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 herd (**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	

FOR BULK TANK: To treat pigs drinking 10% of their bodyweight, at the dose of 10 mg/kg: add 5g product per 10L drinking water in the bulk tank and mix thoroughly until visually dissolved.
For pigs drinking 8% of their body weight, at a dose of 10mg/kg: add 6,25g product to every 10L drinking water in the tank and mix thoroughly until visually dissolved.

FOR PROPORTIONER: Convenient proportioner settings for the use of florfenicol in the drinking water is 20%

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 rapid dissolution, solutions should be prepared in accordance with the examples above. Otherwise, solutions should be visually inspected to ensure that dissolution is complete before the product is administered.
In order to ensure correct dosing and to prevent underdosing, the body weight of the herd 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. The maximum solubility of the product granules is 5g/L at 20°C and 2.0 g/L at 5°C. Any solutions for use in header tank must be limited to no more than 2.5 g/L. Dissolution may take up to 30 minutes and solutions should be checked visually for complete dissolution.

Medicated drinking water should be replaced every 24 hours.

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

After administration at 3 times the recommended dose a reduction in food and water consumption, together with a decrease in bodyweight has been observed. After administration at 3 times or more of the recommended dose, depression of some animals have been observed.

4.11 Withdrawal period(s)

Meat and offal: 20 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antimicrobials for systemic use, amphenicols

ATC Vet Code: QJ01BA90

5.1 Pharmacodynamic properties

Florfenicol is a synthetic, broad-spectrum antibiotic in the amphenicol group active against most Gram-positive and Gram-negative organisms isolated from domestic animals. Florfenicol acts by inhibiting protein synthesis at the ribosomal level and may be considered bacteriostatic.

However, bactericidal activity has been demonstrated in vitro against strains of *Pasteurella multocida* isolated from pigs and involved in respiratory disease.

Among clinical isolates of *P. multocida* collected from the respiratory tracts of swine between 2007-2012 in the EU, both MIC_{50} and MIC_{90} observed for florfenicol were 0.5

µg/ml. For *P. multocida* the following breakpoints have been determined for florfenicol in swine respiratory disease; susceptibe: ≤ 2 µg/ml, intermediate: 4 µg/ml and resistant: ≥ 8 µg/ml (CLSI M31-A3, 2008).
Acquired resistance to florfenicol is associated with several genes, including *floR* which encodes an efflux pump. Genes responsible for resistance are transferable by mobile genetic elements.

5.2 Pharmacokinetic properties

Following administration of florfenicol in drinking water for 5 consecutive days, the maximum plasma concentration of 3.92 µg/mL occurred at a median of 4 hours.
The mean plasma concentrations remained above 0.5 µg/mL for the 5 day administration period. The mean terminal half-life was 5.6 hours and mean AUC0-24 of 44.7 µg·h/mL. The major clearance mechanism is excretion in urine.

5.3 Environment properties

Florfenicol degrades in pig manure and in soil and as such will not persist in the environment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321)
Disodium Edetate
Macrogols (4000 and 400)
Maltodextrin
Polysorbate 80

6.2 Major Incompatibilities

In the absence of compatibility studied 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
Shelf life after dilution or reconstitution according to directions: 24 hours

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Store in the original package.

6.5 Nature and composition of immediate packaging

Polyester/aluminium/polythene bags containing 0.5 kg, 1 kg or 5 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, if appropriate

Any unused veterinary medicinal product or waste material 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 30282/4025

9. DATE OF FIRST AUTHORISATION

24 June 2013

10. DATE OF REVISION OF THE TEXT

July 2018

Approved 02 July 2018