1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Phenoxypen WSP, 325 mg/g powder for use in drinking water for pigs and chickens (AT, BE, BG, , EL, IT, LT, NL, PL, RO, SK)
Phenoxypen WSP 325 mg/g powder for use in drinking water for pigs and chickens (DE)
Phenoxypen WSP, 293 mg/g powder for use in drinking water for pigs and chickens (FR)
Phenoxypen 293 mg/g powder for use in drinking water for pigs and chickens (CZ)
Phenoxylin, 325 mg/g powder for use in drinking water for pigs and chickens (DK, ES)
Phenoxypen 325 mg/g powder for use in drinking water for pigs and chickens A.U.V. (HU)
Phenoxypen Water Soluble Powder, 325 mg/g powder for use in drinking water for pigs and chickens (IE, UK(NI))
Phenoxypen, 325 mg/g powder for use in drinking water for pigs and chickens (PT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substances:

Phenoxymethylpenicillin	293 mg
equivalent to potassium phenoxymethylpenicillin	325 mg

Excipients:

Qualitative composition of excipients and other constituents
Lactose monohydrate

White to off-white powder.

3. CLINICAL INFORMATION

3.1 Target species

Pigs and chickens.

3.2 Indications for use for each target species

Pigs: Treatment and metaphylaxis of infections caused by *Streptococcus suis*. The presence of the disease in the group must be established before the veterinary medicinal product is used.
Chickens: Prevention of mortality at a group level from necrotic enteritis in chickens caused by *Clostridium perfringens*.

3.3 Contraindications

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

3.4 Special warnings

Chickens: the administration of the veterinary medicinal product may lead to an increase in medicated water consumption.
Cross-resistance has been shown between phenoxymethylpenicillin and other beta-lactam antibiotics. Use of the veterinary medicinal product should be carefully considered when susceptibility testing has shown resistance to beta-lactam antibiotics because its effectiveness may be reduced.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Pigs with severe clinical symptoms, such as septicaemic shock, should be treated parenterally.

Use of the veterinary medicinal 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 of susceptibility of the target pathogens at farm level, or at local/regional level.
Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

The veterinary medicinal product should not be used to compensate for poor hygiene and management of the chicken houses.

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

Phenoxymethylpenicillin may cause hypersensitivity reactions after injection, inhalation, oral ingestion, skin or eye contact. Hypersensitivity to phenoxymethylpenicillin may lead to cross-sensitivity to other penicillins and cephalosporins, and vice versa. Allergic reactions caused by these substances can sometimes be serious.

People with known hypersensitivity to penicillins or cephalosporins should avoid contact with the veterinary medicinal product.

Handle this veterinary medicinal product with great care to avoid exposure, taking all recommended precautions. Personal protective equipment consisting of protective clothing, impervious gloves and either a disposable half mask respirator conforming to European Standard EN149 or a non-disposable respirator conforming to European Standard EN140 with a filter to EN 143 should be worn when mixing and handling the veterinary medicinal product.

Wash hands immediately after handling the veterinary medicinal product.

In case of accidental ingestion or serious symptoms of hypersensitivity reactions such as skin rash following exposure, swelling of the face, lips or eyes or difficulty with breathing, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Pigs and chickens:

Undetermined frequency (cannot be determined from the available data):	vomiting*[1], diarrhoea*[1], disorder of gastrointestinal flora*[1,2].

*[1] General for penicillins, not seen with the current veterinary medicinal product.
[2] Altered with selecting resistant bacteria

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 label or 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 and lactation. Use only according to the benefit-risk assessment by the responsible veterinarian.

Laboratory studies in animals and studies in humans have not produced any evidence of effects on reproductive function or foetotoxic effects.

3.8 Interaction with other medicinal products and other forms of interaction

Do not combine with bacteriostatic antibiotics.

3.9 Administration routes and dosage

In drinking water use

Pigs: 15 mg phenoxymethylpenicillin per kg of body weight per day,
corresponding with 51 mg of the veterinary medicinal product per kg of body weight per day, for 5 days.

Chickens: 13.5 – 20 mg phenoxymethylpenicillin per kg of body weight per day,
corresponding with 46 – 68 mg of the veterinary medicinal product per kg of body weight per day, for 5 days.

Medicated drinking water should be refreshed every 12 hours.
The maximum solubility is 250 g of the veterinary medicinal product per litre of drinking water.

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:

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

The medicated water solution should be prepared to provide a volume to be fully consumed over 12 hours. Any unused medicated water should be discarded after 12 hours, and freshly medicated water should be prepared for the next 12 hours.
This may be achieved by dividing the total daily dose and the daily water consumption by 2 to reach the same concentration of medicated water as if calculated over 24 hours.

The use of suitably calibrated measuring equipment is recommended.
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 phenoxymethylpenicillin may need to be adjusted accordingly.
No other source of drinking water should be available during the medication period.

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

Phenoxymethylpenicillin has a high therapeutic index.
Pigs: the administration of the medicated drinking water up to five times the recommended therapeutic dose for three times the recommended duration of treatment was well tolerated. However, at five times

the recommended therapeutic dose a reduction in water intake and temporary redness of the skin were observed.
Chickens: the administration of the medicated drinking water at two and five times the recommended therapeutic dose for twice the recommended duration of treatment did not reveal any adverse effects. In some individuals, administration of five times the recommended therapeutic dose for twice the recommended duration of treatment led to an increase in water consumption, a decrease in feed intake and watery faeces.

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

Pigs: Meat and offal: 4 days.
Chickens: Meat and offal: 2 days.
Eggs: zero days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code :
QJ01CE02

4.2 Pharmacodynamics

Phenoxymethylpenicillin is a narrow-spectrum penicillin with activity mainly against gram-positive bacteria.

Phenoxymethylpenicillin as all other penicillins, exerts a bactericidal action on bacteria during the stage of active multiplication. It forms an irreversible binding to penicillin-binding-proteins (PBPs), enzymes that facilitate the formation of cross-links of peptidoglycan chains in the synthesis of the bacterial cell wall. This results in abnormal cell growth and cytolysis of the cell.

Phenoxymethylpenicillin is an acid-stable derivate of benzylpenicillin and has a largely comparable spectrum of activity.

Development of resistance is mainly based on the formation of beta-lactamase, an enzyme that breaks open the beta-lactam ring, rendering the antibiotic ineffective.
Other resistance mechanisms include the acquisition of penicillin binding proteins (PBPs) with reduced affinity to β-lactam antibiotics, mutations in the PBPs, but also reduced β-lactam uptake due to alterations in the outer membrane of Gram-negative bacteria or export by multidrug transporters.
Cross resistance exists between phenoxymethylpenicillin and other beta-lactam antibiotics.
Minimum Inhibitory Concentrations (MICs) were determined against *Streptococcus suis* isolates from diseased pigs in Europe (2019-2024). Most of the isolates showed a MIC of ≤ 0.0625 µg/ml. Clinical breakpoints established by CLSI Vet01S in 2015 for penicillinase labile penicillins (Penicillin G) in pigs for respiratory infections; *Streptococcus suis*: S: ≤0.25 µg/ml; I: 0.5 µg/ml; R: ≥1 µg/ml.

MICs of phenoxymethylpenicillin were determined against *Clostridium perfringens* isolates from clinical cases of necrotic enteritis in chickens during 1998 and 1999. The MIC for *C. perfringens* isolated from faeces, liver and caecum samples were < 0.01 – 0.05 µg/ml.

4.3 Pharmacokinetics

The most important advantage of phenoxymethylpenicillin in comparison with penicillin G is that it is more stable in an acid environment and it is therefore better absorbed from the gastrointestinal tract.

Following oral use, phenoxymethylpenicillin for the most part escapes decomposition by gastric juices, as it is stable at a low pH.
Phenoxymethylpenicillin is well distributed over most of the tissues, leading to a high concentration in the kidneys and the liver. Phenoxymethylpenicillin is partially decomposed in the gastrointestinal tract. A small portion of the absorbed amount is metabolised in the body. For the most part, phenoxymethylpenicillin is excreted in unaltered active form in urine and faeces.

Following a single administration of the veterinary medicinal product in pigs at a dose of 15 mg of phenoxymethylpenicillin potassium/kg bodyweight, average maximum plasma concentrations of 2.04 mg/l (range 0.67 – 4.12 mg/l) were achieved 0.50 hours (range 0.25 – 1.48 hours) after administration. The absolute bioavailability phenoxymethylpenicillin after oral administration to pigs showed to be approximately 21.1%.

Following a single administration of the veterinary medicinal product in poultry at a dose of 15 mg of phenoxymethylpenicillin potassium/kg bodyweight by oral gavage, maximum plasma concentrations of 0.40 ± 0.15 mg/l are achieved within 1.7 ± 1.0 hours after administration. Phenoxymethylpenicillin is well absorbed and has an absolute bioavailability of 69%.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product.
Contact of penicillin containing solutions with metals and the use of metal systems for their administration is known to adversely influence penicillin stability. Therefore, such systems should be avoided and they should not be used for the storage of solutions.
No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water containing biocidal products, feed additives or other substances used in drinking water.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
- Securitainer: 3 years.
- Composite can: 3 years.
- Bucket: 2 years.

Shelf life after first opening of the immediate packaging: 3 months.
Shelf life after dissolution in drinking water according to directions: 12 hours.

5.3 Special precautions for storage

Store below 25 ºC.
Do not refrigerate or freeze.
Protect from frost.
Store in the original package.

5.4 Nature and composition of immediate packaging

- Securitainer: white polypropylene cylindrical container, with white HDPE/LDPE closure, with thumb-tab for opening. This type of container has two different sizes (650 ml, 1875 ml) with a content of 250 g, 1000 g veterinary medicinal product respectively.
- Composite can: three-layered rectangular container, which consists of a cardboard base with an inner lining of aluminium-paper and with label on the outside. This type of container has a content of 1 kg of veterinary medicinal product.
- Bucket: white polypropylene bucket provided with a polypropylene lid. The bucket contains 1, 2.5 or 5 kg of veterinary medicinal product.

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

Dopharma Research B.V.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

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

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).