SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BayCubis, 325 mg/g powder for oral solution for chickens (NL)
BayCubis, 325 mg/g Pulver zum Eingeben über das Trinkwasser (DE)
BayCubis, 293 mg/g powder for oral solution for chickens (FR, IT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Per gram:

Active substance:

Phenoxymethylpenicillin	293 mg
equivalent to potassium phenoxymethylpenicillin	325 mg

Excipient:
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral solution.
White to off-white powder.

4. CLINICAL PARTICULARS

4.1 Target species

Chickens.

4.2 Indications for use, specifying the target species

Prevention of mortality at a group level from necrotic enteritis in chickens caused by *Clostridium perfringens* susceptible to phenoxymethylpenicillin.

4.3 Contraindications

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

4.4 Special warnings for each target species

The administration of the product may lead to an increase in medicated water consumption.

4.5 Special precautions for use

Special precautions for use in animals

Use of the product should be based on susceptibility testing of the bacteria isolated from chickens that have already died on the farm.
The product should not be used to compensate for poor hygiene and management of the chicken houses.

Official, national and regional 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 phenoxymethylpenicillin and may decrease the effectiveness of treatment with phenoxymethylpenicillin or other penicillins, due to the potential for crossresistance.

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.

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 to the physician.

People with known hypersensitivity to penicillins or cephalosporins should avoid contact with the product. In case of development of hypersensitivity symptoms following exposure to the product, all further contact with the product (and other medicines containing other penicillins or cephalosporins) should be avoided.

Handle this product with great care to avoid exposure, taking all recommended precautions. Wear 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 when mixing and handling the product. Wash hands immediately after handling the product..

4.6 Adverse reactions (frequency and seriousness)

Although no adverse reactions have been seen after the administration of the product, penicillins may cause vomiting, diarrhoea and alter gut flora with selecting resistant bacteria.

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals and humans have not produced any evidence of effects on reproductive function or foetal development.

4.8 Interaction with other medicinal products and other forms of interaction

Do not combine with bacteriostatic antibiotics.

4.9 Amounts to be administered and administration route

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

Method of administration: oral use, dissolve in drinking water and use within 24 hours.
The maximum solubility is 250 g of the product per litre of drinking water.

The following calculation should be made to determine the quantity in gram of the product to be added in 1000 litres of water:

$$\frac{\text{mg product/ kg body weight/day x mean body weight of individual animals (kg) x number of animals}}{\text{Total water consumption of the house (litres) at the previous day}}$$

= mg product/l x 1000 = g product/1000 l water

In dispensing the weight of the product to be used, the use of calibrated weighing equipment is recommended.
Taking into account that sick animals may drink less, it is recommended to start therapy with the higher dose, to compensate for a possible lower intake of medicated water.
To ensure correct dosage, the body weight of the animals should be determined as accurately as possible to avoid underdosing.
No other source of drinking water should be available during the medication period.
In cases of altered drinking water consumption in poultry, the concentration should be adjusted so that the recommended dosage is achieved.

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

Phenoxymethylpenicillin has a high therapeutic index. 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.

4.11 Withdrawal period

Meat and offal:	2 days.
Eggs:	zero days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins

ATCvet-code: QJ01CE02

5.1 Pharmacodynamic properties

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. Cross resistance exists between phenoxymethylpenicillin and other beta-lactam antibiotics.

Minimum Inhibitory Concentrations (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.

5.2 Pharmacokinetic properties

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 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%.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

6.2 Incompatibilities

Do not mix with other veterinary medicinal products.
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.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
Securitainer: 60 months.
Composite can: 3 years
Shelf life after first opening the immediate packaging: 3 months.
Shelf life after reconstitution in drinking water according to directions: 24hours.

6.4. Special precautions for storage

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

6.5 Nature and composition of immediate packaging

- Securitainer: white PP 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 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 product.

Not all pack sizes may be marketed

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

[to be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[to be completed nationally]

9. DATE OF THE FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

[to be completed nationally]

10. DATE OF REVISION OF THE TEXT

[to be completed nationally]

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE / ON THE IMMEDIATE PACKAGE

Securitainer, Composite can

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BayCubis, 325 mg/g powder for oral solution for chickens (NL)
BayCubis, 325 mg/g Pulver zum Eingeben über das Trinkwasser (DE)
BayCubis, 293 mg/g powder for oral solution for chickens (FR, IT)

Potassium phenoxymethylpenicillin

2. STATEMENT OF THE ACTIVE AND OTHER SUBSTANCES

Per gram:

Active substance:
Phenoxymethylpenicillin 293 mg
equivalent to potassium phenoxymethylpenicillin 325 mg

3. PHARMACEUTICAL FORM

Powder for oral solution

4. PACKAGE SIZE

250 gram or 1 kg.

5. TARGET SPECIES

Chickens

6. INDICATION

Prevention of mortality at a group level from necrotic enteritis in chickens caused by *Clostridium perfringens* susceptible to phenoxymethylpenicillin.

7. METHOD AND ROUTE OF ADMINISTRATION

Oral use, after dissolution in drinking water
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Meat and offal: 2 days.
Eggs: zero days.

9. SPECIAL WARNING(S)

Read the package leaflet before use.

10. EXPIRY DATE

Exp <<EXP month/year>>

Shelf life after first opening of the container: 3 months
Shelf life after reconstitution in drinking water according to directions: 24hours.

Once opened, use by:

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bayer B.V. – Animal Health Division
Energieweg 1
3641 RT Mijdrecht The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch <<partijnummer>>

For Italy only:

Name of Manufacturer responsible for the batch release: Dopharma B.V., Zalmweg 24, 4941 VX Raamsdonksveer - The Netherlands

B. PACKAGE LEAFLET

PACKAGE LEAFLET

BayCubis, 325 mg/g powder for oral solution for chickens (NL)
BayCubis, 325 mg/g Pulver zum Eingeben über das Trinkwasser (DE)
BayCubis, 293 mg/g powder for oral solution for chickens (FR, IT)

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
[to be completed nationally]

Manufacturer responsible for the batch release:
Dopharma B.V.
Zalmweg 24
4941 VX Raamsdonksveer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

BayCubis, 325 mg/g powder for oral solution for chickens
Potassium phenoxymethylpenicillin

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Per gram

Active substance:
Phenoxymethylpenicillin 293 mg
equivalent to potassium phenoxymethylpenicillin 325 mg

White to off-white powder

4. INDICATION

Prevention of mortality at a group level from necrotic enteritis in chickens caused by *Clostridium perfringens* susceptible to phenoxymethylpenicillin.

5. CONTRAINDICATIONS

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

6. ADVERSE REACTIONS

Although no adverse reactions have been seen after the administration of the product, penicillins may cause vomiting, diarrhoea and alter gut flora with selecting resistant bacteria.
If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Chickens

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD(S) OF ADMINISTRATION

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

This product is administered to the chickens after dissolution in drinking water.

The following calculation should be made to determine the quantity in gram of the product to be added in 1000 litres of water:

$$\frac{\text{mg product/ kg body weight/day x mean body weight of individual animals (kg) x number of animals}}{\text{Total water consumption of the house (litres) at the previous day}}$$

= mg product/l x 1000 = g product/1000 l water

In dispensing the weight of the product to be used, the use of calibrated weighing equipment is recommended.

9. ADVICE ON CORRECT ADMINISTRATION

Taking into account that sick animals may drink less, it is recommended to start therapy with the higher dose, to compensate for a possible lower intake of medicated water.
To ensure correct dosage, the body weight of the animals should be determined as accurately as possible to avoid underdosing.
The maximal solubility is 250 g of the product per litre of drinking water.
No other source of drinking water should be available during the medication period.
In cases of altered drinking water consumption in poultry the concentration should be adjusted so that the recommended dosage is achieved.
Only sufficient medicated drinking water should be prepared to cover daily requirements.
Medicated drinking water should be refreshed or replaced every 24 hours.

10. WITHDRAWAL PERIOD

Meat and offal: 2 days.
Eggs: zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

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

Do not use after the expiry date stated on the label after exp.

Shelf-life after first opening of the container: 3 months.
Shelf-life after reconstitution in drinking water according to directions: 24 hours.

When the container is opened for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

12. SPECIAL WARNINGS

Special warnings for each target species
The administration of the product may lead to an increase in medicated water consumption.

Special precautions for use in animals
Use of the product should be based on susceptibility testing of the bacteria isolated from chickens that have already died on the farm.
The product should not be used to compensate for poor hygiene and management of the chicken houses.

Official, national and regional 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 phenoxymethylpenicillin and may decrease the effectiveness of treatment with phenoxymethylpenicillin or other penicillins, due to the potential for crossresistance.

Operator warnings
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.
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 to the physician.
People with known hypersensitivity to penicillins or cephalosporins should avoid contact with the product. In case of development of hypersensitivity symptoms following exposure to the product, all further contact with the product (and other medicines containing other penicillins or cephalosporins) should be avoided.
Handle this product with great care to avoid exposure, taking all recommended precautions. Wear 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 when mixing and handling the product. Wash hands immediately after handling the product.

Use during pregnancy, lactation or lay
Studies in laboratory animals and humans have not produced any evidence of effects on reproductive function or foetal development.

Interactions with other medicinal products and other forms of interaction
Do not use the product in combination with bacteriostatic antibiotics.

Overdose (symptoms, emergency procedures, antidotes)
Phenoxymethylpenicillin has a high therapeutic index. 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.

Incompatibilities
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.

Do not mix the product with other veterinary medicinal products.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.
Ask your veterinary surgeon to dispose of medicinal products no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

List of pack sizes: 250 gram, 1 kg.

Not all pack sizes may be marketed.