SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DFV DOXIVET 500 mg/g, powder for use in drinking water for pigs and chickens.

CZ: DFV DOXYCYCLINE 500 mg/g, oral powder for use in drinking water for pigs and chickens.

IT: Doxycycline 500 mg/g DFV, oral powder for use in drinking water for pigs and chickens

DK: Doxycycline Divasa-Farmavic Vet.

SE: Doxycycline Divasa-Farmavic 500 mg/g pulver för användning I dricksvatten

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition for 1 g:

Active substance:
Doxycycline hyclate 500 mg
(equivalent to 433 mg doxycycline base)

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

3. PHARMACEUTICAL FORM

Powder for use in drinking water
Yellow to pale yellow powder.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs and chickens (broiler, pullet, breeder).

4.2 Indications for use, specifying the target species

Pigs: For the treatment of the clinical signs associated with porcine respiratory disease caused by *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, and *Mycoplasma hyopneumoniae* susceptible to doxycycline.
Chickens: Where clinical disease is present in the flock, to reduce mortality, morbidity, and clinical signs and to reduce lesions due to Pasteurellosis caused by *Pasteurella multocida* or to reduce morbidity and lesions in respiratory infections caused by *Ornithobacterium rhinotracheale (ORT)*.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with an impaired liver function.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

4.5.i Special precautions for use in animals

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, especially susceptibility of *A. pleuropneumoniae* and *O. rhinotracheale* may differ from country to country and even farm to farm, bacteriological sampling and susceptibility testing are recommended.
Use of the product should be based on culture and sensitivity of micro-organisms from diseased cases on farm. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
As eradication of the target pathogens may not be achieved, medication should therefore be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking.

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

If you know you are allergic to the tetracycline class of antibiotics, special care should be taken when handling this product or the medicated solution.
During preparation and administration of the medicated drinking water, skin contact with the product and inhalation of dust particles should be avoided. Wear impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) when applying the product.
In the event of eye or skin contact, rinse the affected area with large amounts of clean water and if irritation occurs, seek medical attention. Wash hands and contaminated skin immediately after handling the product.
If you develop symptoms following exposure such as skin rash, you should seek medical advice and show this warning to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.
Do not smoke, eat or drink while handling the product.
Take measures to avoid producing dust when incorporating the product into water. Avoid direct contact with skin and eyes when handling the product to prevent sensitisation and contact dermatitis.

4.6 Adverse reactions (frequency and seriousness)

Tetracyclines may - in very rare cases - induce photosensitivity and allergic reactions. If suspected adverse reactions occur, treatment should be discontinued. Inform your veterinary surgeon if adverse reactions occur that are not stated.

4.7 Use during pregnancy, lactation or lay

Doxycycline has a low affinity for forming complexes with calcium and studies have demonstrated that doxycycline scarcely affects skeleton formation. No negative effects were observed in poultry after the administration of therapeutic doses of doxycycline.
In the absence of specific studies the use of the product is not recommended during pregnancy or lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Do not combine with antibiotics that are bacteriocidal e.g. penicillins or cephalosporins.
Absorption of doxycycline can be decreased in the presence of high quantities of calcium, iron, magnesium or aluminium in the diet. Do not administered together with antacids, kaolin and iron preparations.
It is advised that the interval between the administration of other products containing polyvalent cations should be 1-2 hours because they limit the absorption of tetracyclines.
Doxycycline increases the action of anticoagulants.
The solubility of the product is pH dependent and will precipitate if mixed in alkaline solution.
Do not store the drinking water in metallic containers.

4.9 Amounts to be administered and administration route

Administration orally with the drinking water.

The recommended dose in pigs is:
12.5 mg doxycycline hyclate (25 mg product) per kg body weight per day for 4 consecutive days. If no improvement in clinical signs is seen within this time, the diagnosis should be reviewed and treatment changed. In case of severe infections the medication period may be prolonged for a maximum of 8 consecutive days as determined by the attending veterinary surgeon.

The recommended dose in chickens is:
10 mg doxycycline hyclate (20 mg product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *P. multocida* and 20 mg doxycycline hyclate (40 mg product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *O. rhinotracheale.*

Based on the dose to be used, and the number and weight of the animals to be treated, the exact daily amount of product can be calculated. The following formula can be used to calculate the concentration of the product in drinking water:

$$\frac{\text{..... mg product/ kg body weight / day} \times \text{mean body weight (kg) of animals to be treated}}{\text{mean daily water consumption (l) per animal}} = \text{.... mg product per l drinking water}$$

To ensure a correct dosage body weight should be determined as accurately as possible. The uptake of medicated drinking water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of doxycycline has to be adjusted accordingly. The use of suitably calibrated weighing equipment is recommended if part packs are used. The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be refreshed or replaced every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 100 grams product per litre drinking water - and to dilute this further to therapeutic concentrations if required. Alternatively, the concentrated solution can be used in a proportional water medicator. Solubility of the product is pH dependent and it may precipitate if it is mixed in hard alkaline drinking water. Use at minimum concentrations of 200 mg powder per litre drinking water in areas with hard alkaline drinking water (hardness above 10.2 °d and pH more than 8.1). During the treatment period animals should not have access to other water sources than the medicated water.

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

Overdoses up to 1.6 times the label recommended dose resulted in no clinical signs that could be attributed to treatment. Poultry tolerate double overdoses of doxycycline (40 mg/kg body weight) without any clinical effect.

4.11 Withdrawal periods

Pigs:
- Meat and offal: 4 days

Chickens:
- Meat and offal: 3 days, following a dose rate of 10 mg/kg body weight for 4 days.
- Meat and offal: 12 days, following a dose rate of 20 mg/kg body weight for 4 days.
- Eggs: Not authorised for use in laying birds producing eggs for human consumption.

Do not use within 4 weeks of onset of the laying period

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiinfectives for systemic use, antibacterials for systemic use, tetracycline, doxycycline
ATCvet code: QJ01AA02

5.1 Pharmacodynamic properties

Doxycycline belongs to the group of the tetracycline antibiotics. These antibiotics have a broad spectrum of antimicrobial activity, sharing the same basic structure of polycyclic naphthacenecarboxamide.
Doxycycline is primarily a bacteriostatic drug. It exerts its action by inhibiting the protein synthesis of the bacterial cell. Inhibition of bacterial protein synthesis results in disturbance of all functions necessary for the life of bacteria. Especially cell-division and the formation of the cell wall are impaired.
Doxycycline is a broad-spectrum antibiotic, active against a large number of Gram-positive and Gram-negative, aerobe and anaerobe micro-organisms, Mycoplasmata, Chlamydiae and Rickettsia.
For *Ornithobacterium* rhinotracheale results demonstrate a great variation from high to low susceptibility, depending on the geographical region where isolates came from.
In pig pathogens resistance against doxycycline may also vary; especially susceptibility figures of *A. pleuropneumoniae* may differ from country to country and even farm to farm.
Four resistance mechanisms acquired by microorganisms against tetracyclines in general have been reported: Decreased accumulation of tetracyclines (decreased permeability of the bacterial cell wall and active efflux), protein protection of the bacterial ribosome, enzymatic inactivation of the antibiotic and rRNA mutations (preventing the tetracycline binding to ribosome). Tetracycline resistance is usually acquired by means of plasmids or other mobile elements (e.g. conjugative transposones). Cross resistance between tetracyclines has also been described. Due to the greater liposolubility and greater facility to pass through cell membranes (in comparison to tetracycline), doxycycline retains a certain degree of efficacy against microorganisms with acquired resistance to tetracyclines.

5.2 Pharmacokinetic properties

Doxycycline is absorbed in the stomach and the first part of the duodenum. Compared to the older tetracyclines the absorption of doxycycline is less affected by the presence of bivalent cations in food. Bioavailability in non-fasted pigs is approximately 21%.
Following oral administration at a dose of 12.8 mg/kg body weight, steady state concentrations during medication range between a C_{min} of 0.40 µg/ml in the early morning to a C_{max} of 0.87 µg/ml in the late afternoon in pigs.
Following administration of doxycycline hyclate at an actual dose of 21 mg/kg body weight to chickens mean plasma concentrations above 1 µg/ml were reached within 6 hours and lasted for 6 hours after cessation of medication. From 24 h up to 96 h after start of treatment the doxycycline plasma concentrations exceeded 2 µg/ml. Following administration of doxycycline hyclate at an actual dose of 10 mg/kg body weight steady state plasma concentrations ranged from 0.75 to 0.93 µg/g between 12 and 96 hours after start of medication.
Because doxycycline is highly lipid soluble, it has a good tissue penetration. Respiratory tract tissue: plasma ratios of 1.3 (healthy lungs), 1.9 (pneumonic lungs) and 2.3 (nasal mucosa) have been reported for doxycycline. Plasma protein binding is high (over 90%).
Doxycycline is scarcely metabolised. Doxycycline is primarily excreted with the faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica colloidal anhydrous
Citric acid anhydrous

6.2 Incompatibilities

Solubility of doxycycline is pH dependent. Precipitation will occur in an alkaline solution. In the absence of compatibility studies, this 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: 2 years.
Shelf-life after first opening the immediate packaging: 12 months.
Shelf-life after dilution or reconstitution according to directions: 24 hours after dilution in drinking water.

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Nature of container:
Bag formed of polyester/aluminium/polyethylene laminate.

Package sizes:
Carton box 10 x 100 g
Carton box 50 x 100 g
Carton box 250 x 100 g
Bag 1 kg
Bag 2.5 kg

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 product

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

DIVASA-FARMAVIC S.A.
Ctra. Sant Hipòlit, km 71
08503 Gurb-Vic
Barcelona (Spain)

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<{DD/MM/YYYY}> <{DD month YYYY}>…

10 DATE OF REVISION OF THE TEXT

{MM/YYYY} or <month YYYY>

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

PRODUCT LITERATURE

<PARTICULARS TO APPEAR ON THE OUTER PACKAGE>

CARTON BOX: 10 X 100 g – 50 X 100 g – 250 X 100 g

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DFV DOXIVET 500 mg/g, powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

CZ: DFV DOXYCYCLINE 500 mg/g, oral powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

IT: Doxycycline 500 mg/g DFV, oral powder for use in drinking water for pigs and chickens
Doxycycline hyclate

DK: Doxycycline Divasa-Farmavic Vet.
Doxycycline hyclate

SE: Doxycycline Divasa-Farmavic 500 mg/g pulver för användning I dricksvatten
Doxycycline hyclate

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 g of powder contains 500 mg of doxycycline hyclate (equivalent to 433 mg doxycycline base).

3. PHARMACEUTICAL FORM

Yellow to pale yellow powder for use in drinking water.

4. PACKAGE SIZE

10 x 100 g
50 x 100 g
250 x 100 g

5. TARGET SPECIES

Pigs and chickens (broiler, pullet, breeder).

6. INDICATIONS

Read the package leaflet before use

7. METHOD AND ROUTE OF ADMINISTRATION

Administration route: In drinking water use.
Pigs: 12,5 mg doxycycline hyclate per kg bw / day for 4 days
Chickens: Pasteurellosis: 10 mg doxycycline hyclate per kg bw / day for 3-4 days.
ORT: 20 mg doxycycline hyclate per kg bw / day for 3-4 days.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Pigs:
- Meat and offal: 4 days
Chickens:
- Meat and offal: 3 days, following a dose rate of 10 mg/kg body weight for 4 days.
- Meat and offal: 12 days, following a dose rate of 20 mg/kg body weight for 4 days.
- Eggs: Not authorised for use in laying birds producing eggs for human consumption.
Do not use within 4 weeks of onset of the laying period

9. SPECIAL WARNINGS, IF NECESSARY

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10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the immediate packaging: 12 months.
Shelf-life after dilution in drinking water: 24 hours.

11. SPECIAL STORAGE CONDITIONS

This veterinary medicinal product does not require any special storage conditions.

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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

DIVASA-FARMAVIC S.A.
Ctra. Sant Hipòlit, km 71
08503 Gurb-Vic - Barcelona (Spain)

16. MARKETING AUTHORISATION NUMBER(S)

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17. MANUFACTURER'S BATCH NUMBER

Batch {number}

PARTICULARS TO APPEAR ON THE INMEDIATE PACKAGE

LABEL/LEAFLET: BAG of 1 kg AND 2.5 kg

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

Marketing authorisation holder and manufacturer for the batch release:

DIVASA-FARMAVIC S.A.
Ctra. Sant Hipòlit, km 71
08503 Gurb-Vic
Barcelona (Spain)

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

DFV DOXIVET 500 mg/g, powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

CZ: DFV DOXYCYCLINE 500 mg/g, oral powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

IT: Doxycycline 500 mg/g DFV, oral powder for use in drinking water for pigs and chickens
Doxycycline hyclate

DK: Doxycycline Divasa-Farmavic Vet.
Doxycycline hyclate

SE: Doxycycline Divasa-Farmavic 500 mg/g pulver för användning I dricksvatten
Doxycycline hyclate

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

1 g of powder contains 500 mg of doxycycline hyclate (equivalent to 433 mg doxycycline base)

Yellow to pale yellow powder for use in drinking water

4. INDICATIONS

Pigs: For the treatment of the clinical signs associated with porcine respiratory disease caused by *Actinobacillus pleuropneumoniae, Pasteurella multocida*, and *Mycoplasma hyopneumoniae* susceptible to doxycycline.
Chickens: Where clinical disease is present in the flock, to reduce mortality, morbidity, and clinical signs and to reduce lesions due to Pasteurellosis caused by *Pasteurella multocida* or to reduce morbidity and lesions in respiratory infections caused by *Ornithobacterium rhinotracheale (ORT)*.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with an impaired liver function.

6. ADVERSE REACTIONS

Tetracyclines may - in very rare cases - induce photosensitivity and allergic reactions. If suspected adverse reactions occur, treatment should be discontinued. If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Pigs and chickens (broiler, pullet, breeder).

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

Administration orally with the drinking water.

The recommended dose in pigs is:
12.5 mg doxycycline hyclate (25 mg product) per kg body weight per day for 4 consecutive days. If no improvement in clinical signs is seen within this time, the diagnosis should be reviewed and treatment changed. In case of severe infections the medication period may be prolonged for a maximum of 8 consecutive days as determined by the attending veterinary surgeon.

The recommended dose in chickens is:
10 mg doxycycline hyclate (20 mg product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *P. multocida* and 20 mg doxycycline hyclate (40 mg product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *O. rhinotracheale*.

Based on the dose to be used, and the number and weight of the animals to be treated, the exact daily amount of product can be calculated. The following formula can be used to calculate the concentration of the product in drinking water:

$$\frac{\text{..... mg product/ kg body weight / day} \times \text{mean body weight (kg) of animals to be treated}}{\text{mean daily water consumption (l) per animal}} = \text{.... mg product per l drinking water}$$

To ensure a correct dosage body weight should be determined as accurately as possible. The uptake of medicated drinking water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of doxycycline has to be adjusted accordingly. The use of suitably calibrated weighing equipment is recommended if part packs are used. The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be refreshed or replaced every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 100 grams product per litre drinking water - and to dilute this further to therapeutic concentrations if required. Alternatively, the concentrated solution can be used in a proportional water medicator. Solubility of the product is pH dependent and it may precipitate if it is mixed in hard alkaline drinking water. Use at minimum concentrations of 200 mg powder per litre drinking water in areas with hard alkaline drinking water (hardness above 10.2 °d and pH more than 8.1). During the treatment period animals should not have access to other water sources than the medicated water.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIODS

Pigs:
- Meat and offal: 4 days
Chickens:
- Meat and offal: 3 days, following a dose rate of 10 mg/kg body weight for 4 days.
- Meat and offal: 12 days, following a dose rate of 20 mg/kg body weight for 4 days.
- Eggs: Not authorised for use in laying birds producing eggs for human consumption.

Do not use within 4 weeks of onset of the laying period

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.

This veterinary medicinal product does not require any special storage conditions.

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

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf-life after first opening the immediate packaging: 12 months.
Shelf-life after dilution or reconstitution according to directions: 24 hours after dilution in drinking water.

12. SPECIAL WARNINGS

Special precautions for use in animals

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, especially susceptibility of *A. pleuropneumoniae* and *O. rhinotracheale* may differ from country to country and even farm to farm, bacteriological sampling and susceptibility testing are recommended. Use of the product should be based on culture and sensitivity of micro-organisms from diseased cases on farm. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
As eradication of the target pathogens may not be achieved, medication should therefore be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking

User Warning

If you know you are allergic to the tetracycline class of antibiotics, special care should be taken when handling this product or the medicated solution.
During preparation and administration of the medicated drinking water, skin contact with the product and inhalation of dust particles should be avoided. Wear impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) when applying the product.
In the event of eye or skin contact, rinse the affected area with large amounts of clean water and if irritation occurs, seek medical attention. Wash hands and contaminated skin immediately after handling the product.
If you develop symptoms following exposure such as skin rash, you should seek medical advice and show this warning to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.
Do not smoke, eat or drink while handling the product.
Take measures to avoid producing dust when incorporating the product into water. Avoid direct contact with skin and eyes when handling the product to prevent sensitisation and contact dermatitis.

Use during pregnancy, lactation or lay

Doxycycline has a low affinity for forming complexes with calcium and studies have demonstrated that doxycycline scarcely affects skeleton formation. No negative effects were observed in poultry after the administration of therapeutic doses of doxycycline.
In the absence of specific studies the use of the product is not recommended during pregnancy or lactation

Interaction with other medicinal products and other forms of interactions

Do not combine with antibiotics that are bacteriocidal e.g. penicillins or cephalosporins.

Absorption of doxycycline can be decreased in the presence of high quantities of calcium, iron, magnesium or aluminium in the diet. Do not administered together with antacids, kaolin and iron preparations.
It is advised that the interval between the administration of other products containing polyvalent cations should be 1-2 hours because they limit the absorption of tetracyclines.
Doxycycline increases the action of anticoagulants.
The solubility of the product is pH dependent and will precipitate if mixed in alkaline solution.
Do not store the drinking water in metallic containers.

Overdose

Overdoses up to 1.6 times the label recommended dose resulted in no clinical signs that could be attributed to treatment. Poultry tolerate double overdoses of doxycycline (40 mg/kg body weight) without any clinical effect.

Incompatibilities

Solubility of doxycycline is pH dependent. Precipitation will occur in an alkaline solution. In the absence of compatibility studies, this product must not be mixed with other veterinary medicinal products.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT 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.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pharmaceutical form
Yellow to pale yellow powder for use in drinking water

Pack size
Box 10 x 100 g – 50 x 100 g and 250 x 100 g
Bag 1000 and 2500 g.
Not all pack sizes may be marketed.

For animal treatment only – to be supplied only on veterinary prescription.
Authorisation number:
EXP {month/year}
Batch {number}
Once broached, use by …

<PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE>

LABEL SACHET 100 g

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DFV DOXIVET 500 mg/g, powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

CZ: DFV DOXYCYCLINE 500 mg/g, oral powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

IT: Doxycycline 500 mg/g DFV, oral powder for use in drinking water for pigs and chickens
Doxycycline hyclate

DK: Doxycycline Divasa-Farmavic Vet.
Doxycycline hyclate

SE: Doxycycline Divasa-Farmavic 500 mg/g pulver för användning I dricksvatten
Doxycycline hyclate

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

1 g of powder contains 500 mg of doxycycline hyclate (equivalent to 433 mg doxycycline base).

3. PHARMACEUTICAL FORM

Yellow to pale yellow powder for use in drinking water.

4. PACKAGE SIZE

100 g

5. TARGET SPECIE

Pigs and chickens (broiler, pullet, breeder).

6. INDICATION(S)

Pigs: For the treatment of the clinical signs associated with porcine respiratory disease caused by *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, and *Mycoplasma hyopneumoniae* susceptible to doxycycline.
Chickens: Where clinical disease is present in the flock, to reduce mortality, morbidity, and clinical signs and to reduce lesions due to Pasteurellosis caused by *Pasteurella multocida* or to reduce morbidity and lesions in respiratory infections caused by *Ornithobacterium rhinotracheale (ORT)*.

7. METHOD AND ROUTES OF ADMINISTRATION

Administration route: In drinking water use.
Pigs: 12,5 mg doxycycline hyclate per kg bw / day for 4 days
Chickens: Pasteurellosis: 10 mg doxycycline hyclate per kg bw / day for 3-4 days.
ORT: 20 mg doxycycline hyclate per kg bw / day for 3-4 days.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Pigs:
- Meat and offal: 4 days
Chickens:
- Meat and offal: 3 days, following a dose rate of 10 mg/kg body weight for 4 days.
- Meat and offal: 12 days, following a dose rate of 20 mg/kg body weight for 4 days.
- Eggs: Not authorised for use in laying birds producing eggs for human consumption.
Do not use within 4 weeks of onset of the laying period

9. SPECIAL WARNING(S), IF NECESSARY

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10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the immediate packaging: 12 months.
Once broached, use by …
Shelf-life after dilution in drinking water: 24 hours.

11. SPECIAL STORAGE CONDITIONS

This veterinary medicinal product does not require any special storage conditions.

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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

DIVASA-FARMAVIC S.A.
Ctra. Sant Hipòlit, km 71
08503 Gurb-Vic / Barcelona (Spain)

16. MARKETING AUTHORISATION NUMBER(S)

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17. MANUFACTURER'S BATCH NUMBER

Batch {number}

LEAFLET

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

Marketing authorisation holder and manufacturer for the batch release:

DIVASA-FARMAVIC S.A.
Ctra. Sant Hipòlit, km 71
08503 Gurb-Vic
Barcelona (Spain)

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

DFV DOXIVET 500 mg/g, powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

CZ: DFV DOXYCYCLINE 500 mg/g, oral powder for use in drinking water for pigs and chickens.
Doxycycline hyclate

IT: Doxycycline 500 mg/g DFV, oral powder for use in drinking water for pigs and chickens
Doxycycline hyclate

DK: Doxycycline Divasa-Farmavic Vet.
Doxycycline hyclate

SE: Doxycycline Divasa-Farmavic 500 mg/g pulver för användning I dricksvatten
Doxycycline hyclate

3. STATEMENT OF THE ACTIVE SUBSTANCE AND OTHER INGREDIENTS

1 g of powder contains 500 mg of doxycycline hyclate (equivalent to 433 mg doxycycline base).

4. INDICATIONS

Pigs: For the treatment of the clinical signs associated with porcine respiratory disease caused by *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, and *Mycoplasma hyopneumoniae* susceptible to doxycycline.
Chickens: Where clinical disease is present in the flock, to reduce mortality, morbidity, and clinical signs and to reduce lesions due to Pasteurellosis caused by *Pasteurella multocida* or to reduce morbidity and lesions in respiratory infections caused by *Ornithobacterium rhinotracheale (ORT)*.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with an impaired liver function.

6. ADVERSE REACTIONS

Tetracyclines may - in very rare cases - induce photosensitivity and allergic reactions. If suspected adverse reactions occur, treatment should be discontinued. If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Pigs and chickens (broiler, pullet, breeder).

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

Administration orally with the drinking water.

The recommended dose in pigs is:
12.5 mg doxycycline hyclate (25 mg product) per kg body weight per day for 4 consecutive days. If no improvement in clinical signs is seen within this time, the diagnosis should be reviewed and treatment changed. In case of severe infections the medication period may be prolonged for a maximum of 8 consecutive days as determined by the attending veterinary surgeon.

The recommended dose in chickens is:
10 mg doxycycline hyclate (20 mg product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *P. multocida* and 20 mg doxycycline hyclate (40 mg product) per kg body weight per day for 3-4 consecutive days in case of infections caused by *O. rhinotracheale.*

Based on the dose to be used, and the number and weight of the animals to be treated, the exact daily amount of product can be calculated. The following formula can be used to calculate the concentration of the product in drinking water:

$$\frac{\text{..... mg product/ kg body weight / day} \times \text{mean body weight (kg) of animals to be treated}}{\text{mean daily water consumption (l) per animal}} = \text{.... mg product per l drinking water}$$

To ensure a correct dosage body weight should be determined as accurately as possible. The uptake of medicated drinking water depends on the clinical condition of the animals. In order to obtain the correct dosage the concentration of doxycycline has to be adjusted accordingly. The use of suitably calibrated weighing equipment is recommended if part packs are used. The daily amount is to be added to the drinking water such that all medication will be consumed in 24 hours. Medicated drinking water should be refreshed or replaced every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 100 grams product per litre drinking water - and to dilute this further to therapeutic concentrations if required. Alternatively, the concentrated solution can be used in a proportional water medicator. Solubility of the product is pH dependent and it may precipitate if it is mixed in hard alkaline drinking water. Use at minimum concentrations of 200 mg powder per litre drinking water in areas with hard alkaline drinking water (hardness above 10.2 °d and pH more than 8.1). During the treatment period animals should not have access to other water sources than the medicated water.

9. ADVICE ON CORRECT ADMINISTRATION

10. WITHDRAWAL PERIODS

Pigs:
- Meat and offal: 4 days

Chickens:
- Meat and offal: 3 days, following a dose rate of 10 mg/kg body weight for 4 days.
- Meat and offal: 12 days, following a dose rate of 20 mg/kg body weight for 4 days.
- Eggs: Not authorised for use in laying birds producing eggs for human consumption.

Do not use within 4 weeks of onset of the laying period

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.

This veterinary medicinal product does not require any special storage conditions.
Do not use after the expiry date stated on the label.

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf-life after first opening the immediate packaging: 12 months.
Shelf-life after dilution or reconstitution according to directions: 24 hours after dilution in drinking water.

12. SPECIAL WARNINGS

Special precautions for use in animals

Due to likely variability (time, geographical) in susceptibility of bacteria for doxycycline, especially susceptibility of *A. pleuropneumoniae* and *O. rhinotracheale* may differ from country to country and even farm to farm, bacteriological sampling and susceptibility testing are recommended. Use of the product should be based on culture and sensitivity of micro-organisms from diseased cases on farm. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
As eradication of the target pathogens may not be achieved, medication should therefore be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking

User Warning

If you know you are allergic to the tetracycline class of antibiotics, special care should be taken when handling this product or the medicated solution.
During preparation and administration of the medicated drinking water, skin contact with the product and inhalation of dust particles should be avoided. Wear impermeable gloves (e.g. rubber or latex) and an appropriate dust mask (e.g. disposable half-mask respirator conforming to European Standard EN149) when applying the product.
In the event of eye or skin contact, rinse the affected area with large amounts of clean water and if irritation occurs, seek medical attention. Wash hands and contaminated skin immediately after handling the product.
If you develop symptoms following exposure such as skin rash, you should seek medical advice and show this warning to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.
Do not smoke, eat or drink while handling the product.
Take measures to avoid producing dust when incorporating the product into water. Avoid direct contact with skin and eyes when handling the product to prevent sensitisation and contact dermatitis.

Use during pregnancy, lactation or lay

Doxycycline has a low affinity for forming complexes with calcium and studies have demonstrated that doxycycline scarcely affects skeleton formation. No negative effects were observed in poultry after the administration of therapeutic doses of doxycycline.
In the absence of specific studies the use of the product is not recommended during pregnancy or lactation

Interaction with other medicinal products and other forms of interactions

Do not combine with antibiotics that are bacteriocidal e.g. penicillins or cephalosporins.
Absorption of doxycycline can be decreased in the presence of high quantities of calcium, iron, magnesium or aluminium in the diet. Do not administered together with antacids, kaolin and iron preparations.

It is advised that the interval between the administration of other products containing polyvalent cations should be 1-2 hours because they limit the absorption of tetracyclines.
Doxycycline increases the action of anticoagulants.
The solubility of the product is pH dependent and will precipitate if mixed in alkaline solution.
Do not store the drinking water in metallic containers.

Overdose

Overdoses up to 1.6 times the label recommended dose resulted in no clinical signs that could be attributed to treatment. Poultry tolerate double overdoses of doxycycline (40 mg/kg body weight) without any clinical effect.

Incompatibilities

Solubility of doxycycline is pH dependent. Precipitation will occur in an alkaline solution. In the absence of compatibility studies, this product must not be mixed with other veterinary medicinal products.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT 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.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pharmaceutical form
Yellow to pale yellow powder for use in drinking water

Pack size
Box 10 x 100 g – 50 x 100 g and 250 x 100 g
Bag 1000 and 2500 g.
Not all pack sizes may be marketed.
For animal treatment only – to be supplied only on veterinary prescription.
Authorisation number: