1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ASHIDOX 500 mg/g, powder for use in drinking water/milk for cattle (pre-ruminant), pigs and chickens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substance:
Doxycycline 433 mg
(equivalent to 500 mg Doxycycline Hyclate)

After reconstitution the concentration is 100 mg/ml.

Excipients:

Qualitative composition of excipients and other constituents
Citric Acid Anhydrous
Lactose Monohydrate

Pale yellow to yellow granular powder.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (pre-ruminant), pigs, chickens.

3.2 Indications for use for each target species

For the treatment of the following specified infections of the respiratory tract and the alimentary tract.
Cattle (pre-ruminant):
- Bronchopneumonia and pleuropneumonia caused by *Pasteurella* spp., *Streptococcus* spp., *Arcanobacterium pyogenes*, *Histophilus somni* and *Mycoplasma* spp..
Pigs:
- Atrophic rhinitis caused by *Pasteurella multocida* and *Bordetella bronchiseptica*;
- Bronchopneumonia caused by *Pasteurella multocida*, *Streptococcus suis* and *Mycoplasma hyorhinis*;
- Pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.
Chickens:
- Infections of the respiratory tract caused by *Mycoplasma* spp., *Escherichia coli*, *Haemophilus paragallinarum* and *Bordetella avium*;
- Enteritis caused by *Clostridium perfringens* and *Clostridium colinum*.

3.3 Contraindications

Do not use in cases of hypersensitivity to tetracyclines or to any of the excipients.
Do not use in animals with severe liver- or kidney insufficiency.

3.4 Special warnings

A high resistance rate of *E. coli*, isolated from chickens, against tetracyclines has been documented. Therefore, the veterinary medicinal product should be used for the treatment of infections caused by *E. coli* only after susceptibility testing has been carried out. Resistance to tetracyclines has also been

reported in pig respiratory pathogens (*A. pleuropneumoniae*, *S. suis*) and calf pathogens (*Pasteurella spp*) in some EU countries.
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.

3.5 Special precautions for use

Special precautions for safe use in the target species:
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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
During the handling of the veterinary medicinal product, skin contact and inhalation has to be avoided, taking into account the risk of sensitization and contact dermatitis. For that purpose wear gloves and a dust mask.
People with known hypersensitivity to tetracyclines should avoid contact with the veterinary medicinal product.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

None known.

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

Pregnancy and lactation:
Due to deposit of doxycycline in young bone tissue, use of the veterinary medicinal product should be limited during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

Do not use in conjunction with bactericidal antibiotics, such as penicillins and cephalosporins.
Tetracyclines can chelate cations (e.g. Mg, Mn, Fe and Al) and this may lead to decreased bioavailability.

3.9 Administration routes and dosage

To be administered orally through the milk-replacer and/or the drinking water.

Cattle (pre-ruminant): 10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days, divided over 2 administrations.
Pigs: 10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.
Chickens: 25 mg doxycycline hyclate / kg body weight / day, corresponding to 50 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.

For the administration through the drinking water, the exact daily amount of product should be calculated, based on the recommended dose, and the number and weight of the animals to be treated, according to the following formula:

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

To ensure a correct dosage body weight should be determined as accurately as possible.
The intake of medicated water depends on the clinical conditions of the animals. In order to obtain the correct dosage, the concentration in drinking water may have 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 freshly prepared every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 100 grams of veterinary medicinal 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.

To prepare the solution in milk replacer, weigh the appropriate quantity of the product according to the bodyweight of the animal. Dissolve this quantity in 500 ml water. Add 130g milk replacer, make up the final volume to 1 litre with water and mix thoroughly.
The medicated milk replacer should be used immediately.

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

In cattle (pre-ruminant) acute, sometimes fatal myocardial degeneration can occur following single or multiple dosages. Since mostly this is caused by overdosage, it is important to measure the dosage accurately.

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:
Cattle (pre-ruminant): 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing eggs for human consumption.
Not authorised for use in animals producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QJ01AA02.

4.2 Pharmacodynamics

Doxycycline is a broad spectrum antibiotic. It inhibits bacterial protein synthesis intracellularly by binding on the 30-S ribosome subunits. This interferes with binding of aminoacetyl-tRNA to the

acceptor site on the mRNA ribosome complex and prevents coupling of amino acids to the elongating peptide chains.
Doxycycline inhibits bacteria, Mycoplasma, Chlamydia, Rickettsia, and certain Protozoa.
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.

4.3 Pharmacokinetics

Doxycycline is quickly and almost completely absorbed from the intestine. The presence of food in the intestine has no effect on the actual absorption of doxycycline. The distribution of doxycycline and penetration of doxycycline throughout most body tissues is good.
Following absorption, tetracyclines are hardly metabolized. In contrast to the other tetracyclines, doxycycline is mainly excreted via the faeces.

Cattle (pre-ruminant)
After a dosage of 10 mg/kg body weight/day during 5 days, an elimination halftime varying between 15 and 28 hours was found. The doxycycline plasma level reached an average of 2.2 to 2.5 µg/ml.

Pigs
In pigs, no accumulation of doxycycline in plasma was found after treatment via the drinking water. Mean plasma values of 0.44 ± 0.12 µg/ml after 3 days of medication with an average dose of 10 mg/kg body weight were found.

Poultry
Steady state plasma concentrations of 2.05 ± 0.47 µg/ml were reached within 6 hours after start of the medication and varied between 1.28 and 2.18 µg/ml with a dosage of 25 mg/kg body weight during 5 days.

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.
No information is available on potential interactions or incompatibilities of this veterinary medicinal product administered orally by mixing into drinking water or milk replacer containing biocidal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening of the immediate packaging: 3 months.
Shelf life after reconstitution in drinking water: 24 hours.
Shelf life after reconstitution in milk replacer: use immediately.

5.3 Special precautions for storage

Store below 30ºC.
Do not refrigerate or freeze.
Protect from frost.

Store in the original container in order to protect from light.

5.4 Nature and composition of immediate packaging

Sachet pack: Carton box of 10 x 100 g powder in a sachet: Poly laminated aluminium silver coloured foil.
Pouch pack: 1000 g powder in a pouch: Poly laminated aluminium silver coloured pouch.

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

Ashish Life Science Holding B.V.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: <{DD/MM/YYYY}> <{DD month YYYY}.>

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

<{MM/YYYY}>

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - <u>COMBINED LABEL AND PACKAGE LEAFLET</u>

1000g POUCH

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ASHIDOX 500 mg/g, powder for use in drinking water/milk for cattle (pre-ruminant), pigs and chickens

2. COMPOSITION

Each gram contains:

Active substance :
Doxycycline 433 mg
(equivalent to 500 mg Doxycycline Hyclate)

After reconstitution the concentration is 100 mg/ml.

Pale yellow to yellow granular powder.

3. PACKAGE SIZE

1000 g

4. TARGET SPECIES

Cattle (pre-ruminant), pigs, chickens.

5. INDICATIONS FOR USE

For the treatment of the following specified infections of the respiratory tract and the alimentary tract.
Cattle (pre-ruminant):
- Bronchopneumonia and pleuropneumonia caused by *Pasteurella* spp., *Streptococcus* spp., *Arcanobacterium pyogenes*, *Histophilus somni* and *Mycoplasma* spp..

Pigs:
- Atrophic rhinitis caused by *Pasteurella multocida* and *Bordetella bronchiseptica*;
- Bronchopneumonia caused by *Pasteurella multocida*, *Streptococcus suis* and *Mycoplasma hyorhinis*;
- Pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.

Chickens:
- Infections of the respiratory tract caused by *Mycoplasma* spp., *Escherichia coli*, *Haemophilus paragallinarum* and *Bordetella avium*;
- Enteritis caused by *Clostridium perfringens* and *Clostridium colinum*.

6. CONTRAINDICATIONS

Do not use in cases of hypersensitivity to tetracyclines or to any of the excipients.
Do not use in animals with severe liver- or kidney insufficiency.

7. SPECIAL WARNINGS

<u>Special warnings:</u>

A high resistance rate of *E. coli*, isolated from chickens, against tetracyclines has been documented. Therefore, the veterinary medicinal product should be used for the treatment of infections caused by *E. coli* only after susceptibility testing has been carried out. Resistance to tetracyclines has also been reported in pig respiratory pathogens (*A. pleuropneumoniae*, *S. suis*) and calf pathogens (*Pasteurella* spp) in some EU countries.

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

Special precautions for safe use in the target species:
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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
During the handling of the veterinary medicinal product, skin contact and inhalation has to be avoided, taking into account the risk of sensitization and contact dermatitis. For that purpose wear gloves and a dust mask.
People with known hypersensitivity to tetracyclines should avoid contact with the veterinary medicinal product.

Special precautions for the protection of the environment:
Not applicable.

Pregnancy and lactation:
Due to deposit of doxycycline in young bone tissue, use of the veterinary medicinal product should be limited during pregnancy and lactation.

Interactions with other medicinal products and other forms of interaction:
Do not use in conjunction with bactericidal antibiotics, such as penicillins and cephalosporins.
Tetracyclines can chelate cations (e.g. Mg, Mn, Fe and Al) and this may lead to decreased bioavailability.

Overdose:
In cattle (pre-ruminant) acute, sometimes fatal myocardial degeneration can occur following single or multiple dosages. Since mostly this is caused by overdosage, it is important to measure the dosage accurately.

Special restrictions for use and special conditions for use:
Not applicable.

8. ADVERSE EVENTS

Adverse events
None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or its local representative using the contact details on this label, or via your national reporting system.

9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

Dosage for each species, routes and method of administration
To be administered orally through the milk-replacer and/or the drinking water.

Cattle (pre-ruminant): 10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days, divided over 2 administrations.

Pigs: 10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.

Chickens: 25 mg doxycycline hyclate / kg body weight / day, corresponding to 50 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.

For the administration through the drinking water, the exact daily amount of product should be calculated, based on the recommended dose, and the number and weight of the animals to be treated, according to the following formula:

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

10. ADVICE ON CORRECT ADMINISTRATION

Advice on correct administration
To be administered orally through the milk-replacer and/or the drinking water.
To ensure a correct dosage body weight should be determined as accurately as possible.
The intake of medicated water depends on the clinical conditions of the animals. In order to obtain the correct dosage, the concentration in drinking water may have 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 freshly prepared every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 100 grams of veterinary medicinal 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.
To prepare the solution in milk replacer, weigh the appropriate quantity of the product according to the bodyweight of the animal. Dissolve this quantity in 500 ml water. Add 130g milk replacer, make up the final volume to 1 litre with water and mix thoroughly.
The medicated milk replacer should be used immediately.

11. WITHDRAWAL PERIODS

Withdrawal periods
Meat and offal:
Cattle (pre-ruminant): 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing eggs for human consumption.
Not authorised for use in animals producing milk for human consumption.

12. SPECIAL STORAGE PRECAUTIONS

Special storage precautions
Keep out of the sight and reach of children.

Store below 30ºC.
Do not refrigerate or freeze.
Protect from frost.
Store in the original container in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

13. SPECIAL PRECAUTIONS FOR DISPOSAL

Special precautions for disposal
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 applicable national collection systems. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Classification of veterinary medicinal products
Veterinary medicinal product subject to prescription.

15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

EU/0/00/000/000

1000 g.

16. DATE ON WHICH THE LABEL WAS LAST REVISED

Date on which the label was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database. (https://medicines.health.europa.eu/veterinary).

17. CONTACT DETAILS

Contact details
Marketing authorisation holder:
Ashish Life Science Holding B.V.
Herengracht 454
Amsterdam
Noord-Holland
1017 CA
Netherlands

Manufacturer responsible for batch release:
Pantex Holland B.V.
Smaragdweg 15
Hapert
5527 LA
Netherlands

<Local representatives <and contact details to report suspected adverse reactions>:>

18. OTHER INFORMATION

19. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

20. EXPIRY DATE

Exp {mm/yyyy}

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening of the immediate packaging: 3 months.
Shelf life after reconstitution in drinking water: 24 hours.
Shelf life after reconstitution in milk replacer: use immediately.

21. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON BOX (10 x 100 g)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ASHIDOX 500 mg/g, powder for use in drinking water/milk.

2. STATEMENT OF ACTIVE SUBSTANCES

Each gram contains:

Active substance:
Doxycycline: 433 mg
(equivalent to 500 mg Doxycycline Hyclate)

After reconstitution the concentration is 100 mg/ml.

3. PACKAGE SIZE

10 x 100 g

4. TARGET SPECIES

Cattle (pre-ruminant), pigs, chickens.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

Meat and offal:
Cattle (pre-ruminant): 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing eggs for human consumption.
Not authorised for use in animals producing milk for human consumption.

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened, use within 3 months.
Once reconstituted in drinking water, use within 24 hours.
Once reconstituted in milk replacer, use immediately.

9. SPECIAL STORAGE PRECAUTIONS

Store below 30ºC.
Do not refrigerate or freeze.
Protect from frost.
Store in the original container in order to protect from light.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Ashish Life Science Holding B.V.

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

100g Pouch

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ASHIDOX 500 mg/g, powder for use in drinking water/milk.

2. STATEMENT OF ACTIVE SUBSTANCES

Doxycycline Hyclate 500 mg/g.

3. TARGET SPECIES

Cattle (pre-ruminant), Pigs, Chickens.

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Meat and offal:
Cattle (pre-ruminant): 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing eggs for human consumption.
Not authorised for use in animals producing milk for human consumption.

6. EXPIRY DATE

Exp. {mm/yyyy}

Once opened, use within 3 months.
Once reconstituted in drinking water, use within 24 hours.
Once reconstituted in milk replacer, use immediately.

7. SPECIAL STORAGE PRECAUTIONS

Store below 30ºC.
Do not refrigerate or freeze.
Protect from frost.
Store in the original container in order to protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Ashish Life Science Holding B.V.

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

ASHIDOX 500 mg/g, powder for use in drinking water/milk for cattle (pre-ruminant), pigs and chickens

2. Composition

Each gram contains:

Active substance:
Doxycycline 433 mg
(equivalent to 500 mg Doxycycline Hyclate)

After reconstitution the concentration is 100 mg/ml.

Pale yellow to yellow granular powder.

3. Target species

Cattle (pre-ruminant), pigs, chickens.

4. Indications for use

For the treatment of the following specified infections of the respiratory tract and the alimentary tract.
Cattle (pre-ruminant):
Bronchopneumonia and pleuropneumonia caused by *Pasteurella spp*., *Streptococcus spp.*, *Arcanobacterium pyogenes*, *Histophilus somni* and *Mycoplasma spp*..
Pigs:
Atrophic rhinitis caused by *Pasteurella multocida* and *Bordetella bronchiseptica*;
Bronchopneumonia caused by *Pasteurella multocida*, *Streptococcus suis* and *Mycoplasma hyorhinis*;
Pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.
Chickens:
Infections of the respiratory tract caused by *Mycoplasma spp*., *Escherichia coli*, *Haemophilus paragallinarum* and *Bordetella avium*;
Enteritis caused by *Clostridium perfringens* and *Clostridium colinum*.

5. Contraindications

Do not use in cases of hypersensitivity to tetracyclines or to any of the excipients.
Do not use in animals with severe liver- or kidney insufficiency.

6. Special warnings

A high resistance rate of *E. coli*, isolated from chickens, against tetracyclines has been documented. Therefore, the veterinary medicinal product should be used for the treatment of infections caused by *E. coli* only after susceptibility testing has been carried out. Resistance to tetracyclines has also been reported in pig respiratory pathogens (*A. pleuropneumoniae, S. suis*) and calf pathogens (*Pasteurella* spp) in some EU countries.
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.

Special precautions for safe use in the target species:
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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
During the handling of the veterinary medicinal product, skin contact and inhalation has to be avoided, taking into account the risk of sensitization and contact dermatitis. For that purpose, wear gloves and a dust mask.
People with known hypersensitivity to tetracyclines should avoid contact with the veterinary medicinal product.

Special precautions for the protection of the environment:
Not applicable.

Pregnancy and lactation:
Due to deposit of doxycycline in young bone tissue, use of the veterinary medicinal product should be limited during pregnancy and lactation.

Interactions with other medicinal products and other forms of interaction:
Do not use in conjunction with bactericidal antibiotics, such as penicillins and cephalosporins.
Tetracyclines can chelate cations (e.g. Mg, Mn, Fe and Al) and this may lead to decreased bioavailability.

Overdose:
In cattle (pre-ruminant) acute, sometimes fatal myocardial degeneration can occur following single or multiple dosages. Since mostly this is caused by overdosage, it is important to measure the dosage accurately.

Special restrictions for use and special conditions for use:
Not applicable.

7. Adverse events

None known.
Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

To be administered orally through the milk-replacer and/or the drinking water.

Cattle (pre-ruminant): 10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days, divided over 2 administrations.

Pigs: 10 mg doxycycline hyclate / kg body weight / day, corresponding to 20 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.

Chickens: 25 mg doxycycline hyclate / kg body weight / day, corresponding to 50 mg of veterinary medicinal product per kg body weight, for 3-5 consecutive days.

For the administration through the drinking water, the exact daily amount of veterinary medicinal product should be calculated, based on the recommended dose, and the number and weight of the animals to be treated, according to the following formula:

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

9. Advice on correct administration

To be administered orally through the milk-replacer and/or the drinking water.
To ensure a correct dosage body weight should be determined as accurately as possible.
The intake of medicated water depends on the clinical conditions of the animals. In order to obtain the correct dosage, the concentration in drinking water may have 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 freshly prepared every 24 hours. It is recommended to prepare a concentrated pre-solution - approximately 100 grams of veterinary medicinal 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.
To prepare the solution in milk replacer, weigh the appropriate quantity of the product according to the bodyweight of the animal. Dissolve this quantity in 500 ml water. Add 130g milk replacer and make up the final volume to 1 litre with water and mix thoroughly.
The medicated milk replacer should be used immediately.

10. Withdrawal periods

Meat and offal:
Cattle (pre-ruminant): 7 days
Pigs: 8 days
Chickens: 5 days
Not for use in birds producing eggs for human consumption.
Not authorised for use in animals producing milk for human consumption.

11. Special storage precautions

Keep out of the sight and reach of children.
Store below 30ºC.
Do not refrigerate or freeze.
Protect from frost.
Store in the original container in order to protect from light.

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening of the immediate packaging: 3 months.
Shelf life after reconstitution in drinking water: 24 hours.
Shelf life after reconstitution in milk replacer: use immediately.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

12. Special precautions for disposal

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Carton box containing 10 x 100 g sachets: poly-laminated aluminium silver coloured foil.
Poly-laminated aluminium silver coloured pouch containing 1000 g powder.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder:

Ashish Life Science Holding B.V.
Herengracht 454
Amsterdam
Noord-Holland
1017 CA
Netherlands

Manufacturer responsible for batch release:
Pantex Holland B.V.
Smaragdweg 15
Hapert
5527 LA
Netherlands

<Local representatives <and contact details to report suspected adverse reactions>:>