1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxycare Flavour 40 mg Tablets for Cats and Dogs (UK, IE)
Doxycare Vet 40 mg Tablets for Cats and Dogs (FI, SE, DK, NO)
Doxycare 40 mg Tablets for Cats and Dogs (FR, RO, HU, EE, LT, LV, PL, GR, CZ, SK, AT, CY, ES, DE, BE, PT, LU)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Active substance:
Doxycycline 40 mg
(equivalent to 47.88 mg of doxycycline hyclate)

Excipients:

Qualitative composition of excipients and other constituents
Sodium starch glycolate (type A)
Cellulose microcrystalline
Yeast extract
Magnesium stearate

Yellowish, round and convex tablet with a cross-shaped break line on one side.

Tablets can be divided into 2 or 4 equal parts.

3. CLINICAL INFORMATION

3.1 Target species

Cats and dogs.

3.2 Indications for use for each target species

Dogs
For the treatment of respiratory tract infections including rhinitis, tonsillitis and bronchopneumonia caused by *Bordetella bronchiseptica*, and *Pasteurella* spp. susceptible to doxycycline.

For the treatment of canine ehrlichiosis caused by *Ehrlichia canis*.

Cats
For the treatment of respiratory tract infections including rhinitis, tonsillitis and bronchopneumonia caused by *Bordetella bronchiseptica*, and *Pasteurella* spp. susceptible to doxycycline.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in animals with renal or hepatic insufficiency.
Do not use in animals with diseases associated with vomiting or dysphagia (see also section 3.6).
Do not use in animals with known photosensitivity (see also section 3.6).

Do not use in puppies and kittens before completion of teeth enamel formation.

3.4 Special warnings

Ehrlichia canis infection: treatment should be initiated at the onset of clinical signs. Complete eradication of the pathogen is not always achieved, but treatment for 28 days generally leads to a resolution of the clinical signs and a reduction of the bacterial load. A longer duration of treatment, based on a benefit/risk assessment by the responsible veterinarian, may be required particularly in severe or chronic ehrlichiosis. All treated patients should be regularly monitored, even after clinical cure.

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 pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at local/regional level.

Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to doxycycline and may decrease the effectiveness of treatment with other tetracyclines, due to the potential for cross-resistance. Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

Tablets should be administered with food in order to avoid vomiting and to reduce the likelihood of oesophageal irritation.

The product should be administered with caution to young animals, since tetracyclines as a class may cause permanent discolouration of the teeth, when administered during tooth development. However, human literature indicates that doxycycline is less likely than other tetracyclines to cause these abnormalities, due to its reduced ability to chelate calcium.

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

People with known hypersensitivity to doxycycline or other tetracyclines should avoid contact with the veterinary medicinal product and personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product.
In case of skin irritation, seek medical advice immediately and show the package leaflet or the label to the physician.
Accidental ingestion, especially by children, may cause adverse reactions such as emesis. To avoid accidental ingestion, blisters should be inserted back into the outer packaging and kept in a safe place. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

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

3.6 Adverse events

Cats and dogs:

Undetermined frequency (cannot be estimated from the available data):	Photosensitivity, photodermatitis[1] Dental discolouration[2]

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Gastrointestinal disorders (e.g. vomiting, nausea, hypersalivation, oesophageal irritation, diarrhoea)

[1]can occur following tetracycline therapy, after exposure to intense sunlight or ultraviolet light (See also section 3.3).
[2]use of tetracycline during the period of tooth development.

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:
Laboratory studies in rats or rabbits have not produced any evidence of teratogenic or embryotoxic effects of doxycycline. The safety of the veterinary medicinal product has not been established during pregnancy, therefore, the use is not recommended during pregnancy.
Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Doxycycline should not be used concurrently with other antibiotics, especially bactericidal drugs such as the ß-lactams. Cross-resistance to tetracyclines can occur.

The half-life of doxycycline is reduced by concurrent administration of barbiturates, phenytoin and carbamazepine.

Dosage adjustments may be necessary in subjects under anticoagulant therapy, as tetracyclines depress the plasma activity of prothrombin.
Simultaneous administration of oral absorbents, antacids and preparations including multivalent cations should be avoided as they reduce doxycycline availability.

3.9 Administration routes and dosage

Oral use.
The dosage is 10 mg doxycycline per kilogram of bodyweight per day.
To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid overdosing or underdosing. In order to adjust the dosage, the tablets can be divided into 2 or 4 equal parts. Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface. The dosage can be divided into two daily administrations. The duration of treatment might be adapted depending on the clinical response, after benefit/risk assessment by the veterinarian.

Disease	**Dosage regimen**	**Duration of treatment**
Respiratory tract infection	10 mg/kg per day	5-10 days
Canine ehrlichiosis	10 mg/kg per day	28 days

Halves: press down with your thumbs or fingers on both sides of the tablet.
Quarters: press down with your thumb or finger in the middle of the tablet.

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

Vomiting may occur in dogs with 5 times the recommended dose. Increased levels of ALT, GGT, ALP and total bilirubin were reported in dogs at 5-fold overdose.

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

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:
QJ01AA02

4.2 Pharmacodynamics

Doxycycline is a broad-spectrum tetracycline-class antibiotic active against a large number of gram positive and gram negative bacteria including both aerobic and anaerobic species.

Doxycycline inhibits bacterial protein synthesis by binding to the 30-S ribosomal 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 has a predominantly bacteriostatic activity.

The penetration of doxycycline into the bacterial cell takes place by both active transport and passive diffusion.
The main mechanisms of acquired resistance to tetracycline class antibiotics include active efflux and ribosomal protection. A third mechanism is enzymatic degradation. The genes mediating resistance may be carried on plasmids or transposons, as for example, *tet*(M), *tet*(O), and *tet*(B) that can be found in both gram-positive and gram-negative organisms including clinical isolates.

Cross-resistance to other tetracyclines is common but depends on the mechanism conferring resistance. Due to the greater liposolubility and greater ability to pass through cell membranes (in comparison to tetracycline), doxycycline retains a certain degree of efficacy against microorganisms with acquired resistance to tetracyclines via efflux pumps. However, resistance mediated by ribosomal protection proteins confer cross-resistance to doxycycline.

The following MIC values for the targeted bacteria were collected between 2017 and 2018 as a part of ongoing European surveillance studies:

Bacterial pathogen	Origin (number of strains tested)	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)
Bordetella bronchiseptica	Dog – respiratory tract (38)	0.12	0.5
Bordetella bronchiseptica	Cat – respiratory tract (11)	0.12	0.12
Pasteurella spp.	Dog – respiratory tract (27)	0.12	0.25
Pasteurella spp.	Cat– respiratory tract (77)	0.12	0.25

Antibiotic susceptibility data for *Ehrlichia canis* are limited.

4.3 Pharmacokinetics

Absorption

After oral administration, the bioavailability of doxycycline is approximately 45% in dogs and cats. Peak concentrations of 1.4 μg/ml (dogs) and 4.3 μg/ml (cats) are reached within 3 hours after oral administration, supporting that doxycycline is rapidly absorbed from the gastro-intestinal tract.

Distribution
Doxycycline is broadly distributed throughout the organism due to its physicochemical characteristics, as it is highly liposoluble. Protein binding in dogs is reported as 91.75 % ± 0.63 and 91.4% in the literature. In cats a publication reports a protein binding of 98.35% (+/-0.24).
The tissue concentrations, with the exception of the skin, are generally higher than the plasma levels, including the excretion organs (liver, kidney and intestines) and for the lungs.

Elimination
After a single administration, the half-life elimination (T1/2) is 8.37 hours in cats. Excretion occurs in an unchanged active form (90%) via the faeces (approximately 75%), via the urine (approximately 25%) and less than 5% via the bile ducts.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.
Any remaining tablet portion should be returned to the blister and given at the next administration.

5.4 Nature and composition of immediate packaging

OPA/Aluminium/PVC foil and Aluminium foil blister containing 10 tablets

Pack sizes:
Cardboard box of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, or 250 tablets.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Ecuphar NV

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

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

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

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

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxycare Flavour 40 mg Tablets (UK, IE)
Doxycare Vet 40 mg Tablets (FI, SE, DK, NO)
Doxycare 40 mg Tablets (FR, RO, HU, EE, LT, LV, PL, GR, CZ, SK, AT, CY, ES, DE, BE, PT, LU)

2. STATEMENT OF ACTIVE SUBSTANCES

Each tablet contains

Active substance:
Doxycycline 40 mg (equivalent to 47.88 mg of doxycycline hyclate)

3. PACKAGE SIZE

10 tablets
20 tablets
30 tablets
40 tablets
50 tablets
60 tablets
70 tablets
80 tablets
90 tablets
100 tablets
250 tablets

4. TARGET SPECIES

Cats and Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Oral use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE CONDITIONS

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

Ecuphar
An Animalcare Company

14. MARKETING AUTHORISATION NUMBERS

15. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BLISTERS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Doxycare Flavour (UK, IE)
Doxycare Vet (FI, SE, DK, NO)
Doxycare (FR, RO, HU, EE, LT, LV, PL, GR, CZ, SK, AT, CY, ES, DE, BE, PT, LU)

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Doxycycline 40 mg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Doxycare Flavour 40mg Tablets for Cats and Dogs (UK, IE)
Doxycare Vet 40 mg Tablets for Cats and Dogs (FI, SE, DK, NO)
Doxycare 40 mg Tablets for Cats and Dogs (FR, RO, HU, EE, LT, LV, PL, GR, CZ, SK, AT, CY, ES, DE, BE, PT, LU)

2. Composition

Each tablet contains:

Active substance:
Doxycycline 40 mg
(equivalent to 47.88 mg of doxycycline hyclate)

Yellowish, round and convex tablet with a cross-shaped break line on one side.

Tablets can be divided into 2 or 4 equal parts.

3. Target species

Cats and dogs.

4. Indications for use

Dogs
For the treatment of respiratory tract infections including rhinitis, tonsillitis and bronchopneumonia caused by *Bordetella bronchiseptica* and *Pasteurella* spp. susceptible to doxycycline.

For the treatment of canine ehrlichiosis (a disease transmitted by ticks) caused by *Ehrlichia canis*.

Cats
For the treatment of respiratory tract infections including rhinitis, tonsillitis and bronchopneumonia caused by *Bordetella bronchiseptica* and *Pasteurella* spp. susceptible to doxycycline.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or any of the excipients.
Do not use in animals with renal or hepatic insufficiency.
Do not use in animals with diseases associates with vomiting or dysphagia (difficulty to swallow) (see also section ‘Adverse events’).
Do not use in animals with known photosensitivity (see also section ‘Adverse events’).
Do not use in puppies and kittens before completion of teeth enamel formation.

6. Special warnings

Special warnings:

Ehrlichia canis infection: treatment should be initiated at the onset of clinical signs. Complete eradication of the pathogen is not always achieved, but treatment for 28 days generally leads to a resolution of the clinical signs and a reduction of the bacterial load. A longer duration of treatment, based on a benefit/risk assessment by the responsible veterinarian, may be required particularly in

severe or chronic ehrlichiosis. All treated patients should be regularly monitored, even after clinical cure.

Special precautions for safe use in the target species:

Tablets should be administered with food in order to avoid vomiting and to reduce the likelihood of oesophageal irritation.

The product should be administered with caution to young animals, since tetracyclines as a class may cause permanent discolouration of the teeth, when administered during tooth development. However, human literature indicates that doxycycline is less likely than other tetracyclines to cause these abnormalities, due to its reduced ability to chelate calcium.

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at local/regional level.
Use of the veterinary medicinal product deviating from the instructions given in the leaflet may increase the prevalence of bacteria resistant to doxycycline and may decrease the effectiveness of treatment with other tetracyclines, due to the potential for cross resistance.
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:

People with known hypersensitivity to doxycycline or other tetracyclines should avoid contact with the veterinary medicinal product and personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product.
In case of skin irritation, seek medical advice immediately and show the package leaflet or the label to the physician.
Accidental ingestion, especially by children, may cause adverse reactions such as emesis. To avoid accidental ingestion, blisters should be inserted back into the outer packaging and kept in a safe place. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy:

Laboratory studies in rats and rabbits have not produced any evidence of teratogenic or embryotoxic effects (malformations or deformities) of doxycycline. The safety of the veterinary medicinal product has not been established during pregnancy, therefore the use is not recommended during pregnancy. Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:

Doxycycline should not be used concurrently with other antibiotics especially bactericidal drugs such as the ß-lactams (for example penicillin, ampicillin). Cross-resistance to tetracyclines may occur.

The half-life of doxycycline is reduced by concurrent administration of barbiturates (some types of sedatives or tranquilisers), phenytoin and carbamazepine (two types of anti-epileptic medications). Dosage adjustments may be necessary in subjects under anticoagulant therapy (blood thinners), as tetracyclines depress the plasma activity of prothrombin.
Simultaneous administration of oral absorbents, antacids (protectants for the stomach) and preparations including multivalent cations should be avoided as they reduce doxycycline availability.

Overdose:

Vomiting may occur in dogs with 5 times the recommended dose. Increased levels of ALT, GGT, ALP and total bilirubin were reported in dogs at 5-fold overdose.

7. Adverse events

Cats and dogs:

Undetermined frequency (cannot be estimated from the available data):	Photosensitivity, photodermatitis[1] Dental discolouration[2]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Gastrointestinal disorders (e.g. vomiting, nausea, hypersalivation, oesophageal irritation, diarrhoea)

[1]can occur following tetracycline therapy, after exposure to intense sunlight or ultraviolet light (See also section 'contraindications').
[2]use of tetracycline during the period of tooth development.

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: <{national system details}>

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

Oral use.
The dosage is 10 mg doxycycline per kilogram of bodyweight per day.
The dosage can be divided into two daily administrations. The duration of treatment might be adapted depending on the clinical response, after benefit/risk assessment by the veterinarian.

Disease	**Dosage regimen**	**Duration of treatment**
Respiratory tract infection	10 mg/kg per day	5-10 days
Canine ehrlichiosis	10 mg/kg per day	28 days

Tablets can be divided into 2 or 4 equal parts to ensure accurate dosing. Place the tablet on a flat surface, with its scored side facing up and the convex (rounded) side facing the surface.

Halves: press down with your thumbs or fingers on both sides of the tablet.
Quarters: press down with your thumb or finger in the middle of the tablet.

9. Advice on correct administration

To ensure a correct dosage, bodyweight should be determined as accurately as possible to avoid overdosing or underdosing. In order to adjust the dosage, the tablets can be divided into 2 or 4 equal parts. Tablets should be administered with food in order to avoid vomiting.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Any remaining tablet portion should be given at the next administration.

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

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

12. Special precautions for the 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

Cardboard box of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, or 250 tablets

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

MM/YYYY

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 and contact details to report suspected adverse reactions:

Ecuphar NV
Legeweg 157-I
B-8020,
Oostkamp,
Belgium

Manufacturer responsible for batch release:

Lelypharma B.V.
Zuiveringsweg 42
8243 PZ

Lelystad
The Netherlands