Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

GalluDoxx 500 mg/g powder for use in drinking water/milk replacer for calves, chickens and turkeys

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:

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

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

3 PHARMACEUTICAL FORM

Powder for use in drinking water/milk replacer.
Yellowish powder.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle (pre-ruminant calves)
Chickens (broilers, breeders, replacement pullets) and turkeys.

4.2 Indications for use, specifying the target species

Cattle (pre-ruminant calves)
For the treatment of:
- Pneumonia and shipping fever caused by *Pasteurella* spp and *Mannheimia haemolytica* infections.

Chickens (broilers, breeders, replacement pullets) and turkeys
For the treatment of:
- Ornithosis caused by *Chlamydophila psittaci* in turkeys;
- Colibacillosis caused by *E. coli* in chickens and turkeys;
- Chronic Respiratory Disease caused by *Mycoplasma gallisepticum* in chickens and turkeys.

4.3 Contraindications

Do not use in cases of known hypersensitivity to tetracyclines or the excipient.
Do not administer to animals with severe liver or kidney insufficiency.
Do not use when tetracycline resistance has been detected in the herd/flock due to the potential for cross resistance

4.4 Special warnings for each target species

The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of drinking water or medicated milk replacer, animals should be treated parenterally. It is necessary to administer medicated milk to calves on an individual basis.

4.5 Special precautions for use

Special precautions for use in animals

Due to variability (time, geographical) in susceptibility of bacteria for doxycycline, bacteriological sampling and susceptibility testing of micro-organisms from diseased animals on farm are highly recommended.

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

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.

Official, national and regional antimicrobial policies should be taken into account when the product is used.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to doxycycline and may decrease the effectiveness of treatment with other tetracyclines due to the potential for cross-resistance.

Resistance to tetracyclines has also been reported in calf pathogens (*Pasteurella* spp.) in some EU countries.

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

During the handling of the product, skin contact and inhalation has to be avoided, taking into account the risk of sensitisation and contact dermatitis.
People with known hypersensitivity to tetracyclines should not handle the product. 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. Do not smoke, eat or drink while handling 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.

4.6 Adverse reactions (frequency and seriousness)

Tetracyclines may in rare cases induce photosensitivity and allergic reactions. If suspected adverse reactions occur, treatment should be discontinued.

4.7 Use during pregnancy, lactation or lay

Laboratory studies with doxycycline in rats and rabbits has not produced any evidence of teratogenic, embryotoxic or foetotoxic effects.
The safety of the product has not been assessed in breeder chickens. Use only accordingly to benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Do not use in conjunction with bactericidal antibiotics, such as penicillins and cephalosporins.

Do not administer concurrently with feed overloaded with polyvalent cations such as Ca^{2+}, Mg^{2+}, Zn^{2+} and Fe^{3+} because the formation of doxycycline complexes with these cations is possible. Do not administer together with antacids, kaolin and iron preparations. It is advised that the interval between administration of the product and administration of products containing polyvalent cations should be 1-2 hours because the latter limit the absorption of doxycycline.

Doxycycline increases the action of anticoagulants.

4.9 Amounts to be administered and administration route

Route of administration:

Calves: To be administered in drinking water/milk replacer Chickens and turkeys: In drinking water use

Dosing

Calves:
Doxycycline hyclate 5 mg per kg body weight, twice a day, equivalent to 10 mg of the product per kg of animal body weight, twice a day, for 4-7 successive days.

Chickens and turkeys:
20 mg doxycycline hyclate per kg of body weight per day, corresponding to 40 mg of the product per kg of animal body weight, for 4-7 consecutive days.

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

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

To ensure a correct dosage body weight should be determined as accurately as possible.
The uptake of medicated water is dependent on the clinical conditions of the animals. In order to obtain the correct dosage, the concentration in drinking water may have to be adjusted.
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 12 hours. Medicated drinking water should be freshly prepared every 12 hours. It is recommended to prepare a concentrated pre-solution - not exceeding 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. The water should be stirred until full dissolution of the product is obtained. The solubility of doxycycline decreases at higher pH. Therefore the product should not be used in hard alkaline water since precipitation might occur depending on the product concentration. Delayed precipitation might also occur.
Milk replacer: The veterinary medicinal product must first be dissolved in warm water before adding the milk powder - the maximal concentration to be used is 100 grams of product per litre of water. The obtained milk replacer solution must be homogenised and heated to feeding temperature prior to administration. The medicated milk replacer should be freshly prepared prior to use, used immediately and be constantly stirred to avoid sedimentation of the active substance. If a concentration greater than 200 mg per litre of milk is required, animals should be treated parenterally.
Sufficient access to the system of water supply should be available for the animals to be treated to ensure adequate water consumption. No other source of drinking water should be available during the medication period. At the end of treatment period the water supply should be cleaned adequately to avoid the uptake of remaining quantities in sub-therapeutic doses.

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

In calves acute, sometimes fatal cardiac muscle degeneration may occur after one or more administrations. Since this is usually related to overdosing, it is important to calculate the dose correctly.

If suspected toxic reactions do occur due to extreme overdose, the medication should be discontinued and appropriate symptomatic treatment should be initiated if necessary.

4.11 Withdrawal Period(s)

Calves:	Meat and offal: 28 days
Turkeys:	Meat and offal: 28 days
Chickens	Meat and offal: 14 days

Not authorised for use in birds producing eggs for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-infectives for systemic use, Tetracyclines.
ATCvet code: QJ01AA02.

5.1 Pharmacodynamic properties

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, mycoplasmae, chlamydiae, rickettsiae, and certain protozoa.
Organisms other than streptococci with MIC values ≤ 4µg/ml are considered sensitive, at 8 µg/ml intermediate susceptible and with MIC values ≥16µg/ml resistant to doxycycline, according to the CLSI data.
For cattle MIC90 values for *Pasteurella multocida* of 0.5 µg/ml and of 2µg/ml for *Mannheimia haemolytica* have been reported in literature (2014). Resistance varies for both organisms between 0 and 22% in relation to the geographical origin of the strains (2014)
In poultry literature indicates that *Mycoplasma* spp. (2008) and C*hlamydophila psittaci* (2013) demonstrate good susceptibility. Resistance rate for *M. gallisepticum* is low (0-6%).

Four resistance mechanisms acquired by micro-organisms 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 transposons). 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 micro-organisms with acquired resistance to tetracyclines.

5.2 Pharmacokinetic properties

Doxycycline is quickly and almost completely absorbed from the intestine. The distribution of doxycycline and penetration of doxycycline throughout most body tissues is good.
Following absorption, tetracyclines are hardly metabolised. In contrast to the other tetracyclines, doxycycline is mainly excreted via the faeces.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal 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: 18 months.
Shelf life after first opening 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 store.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special temperature storage conditions. After first opening keep the bag tightly closed in order to protect from moisture.

6.5 Nature and composition of immediate packaging

Bag formed from polyethylene/aluminium/polyethylene terephthalate laminate.

Pack sizes:
Bag of 1 kg
Bag of 5 kg

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerp
Belgium

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10782/023/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th February 2017

10 DATE OF REVISION OF THE TEXT