SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

HYPERSOL 500 mg/g Powder for use in Drinking water

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of product contains:

Active substance
Oxytetracycline (as hydrochloride) 500 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

- Powder for use in drinking water
- Yellow powder

4. CLINICAL PARTICULARS

4.1 Target species

Chickens (broilers, breeding hens) and pigs.

4.2 Indications for use, specifying the target species

In chickens (broilers, breeding hens) and pigs:
-Treatment and metaphylaxis at the group level of septicaemia, respiratory and gastrointestinal infections caused by bacteria sensitive to oxytetracycline.

The presence of disease in the herd/group should be established before the product is used.

4.3 Contraindications

Do not use in cases of hypersensitivity to oxytetracycline or any other substance from tetracyclines group.
Do not use in cases of known tetracycline resistance.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

i) Special precautions for use in animals

This powder should be dissolved in water, before use.

Use of the product should be based on susceptibility testing of bacteria isolates from the animal. If not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.
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 the oxytetracycline and may decrease the effectiveness of treatment with tetracyclines, due to the potential for cross-resistance.

Prolonged or repeated use should be avoided as these practises can enforce development and spread of the bacterial resistance. This is particularly likely in enterobacteria and *Salmonella spp.*, many of which are already resistant.
As eradication of the target pathogens may not be achieved, medication should be combined with good management practices, e.g. good hygiene, proper ventilation, no overstocking.

Extensive resistance to oxytetracycline has been recognised in porcine and poultry isolates of strains form *E. Coli*, *Salmonella spp.*, *Campylobacter spp.*, and *Enterococcus spp*. The product should only be used where culture and sensitivity testing have demonstrated that it is likely to be effective.

Sick animals may have a reduced appetite and an altered drinking pattern and should, if necessary, be medicated parenterally.

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

People with known hypersensitivity to tetracyclines should avoid contact with the veterinary medicinal product.
Avoid inhaling dust when handling the product until complete solubilisation in water.
Use in a well-ventilated area away from draughts.
Avoid contact with skin and eyes.
Personal protective equipment consisting of latex and nitrile gloves, eye protection dust mask (either a disposal half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143) and suitable protective clothing should be worn when handling the veterinary medicinal product. In case of accidental eye or skin contact, rinse the affected area with large amounts of clean water. If irritation occurs, seek medical advice immediately and show the label to the physician.
Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.
Wash hands and contaminated skin immediately after handling the product.
Do not smoke, eat or drink while handling the product.

iii) Other precautions

None.

4.6 Adverse reactions (frequency and seriousness)

As for all other tetracyclines, side effects such as gastro-intestinal disorder and less frequently, allergic and photosensitivity reactions are very rare according to phamacovigilance data.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Laboratory studies in animals have not produced any evidence of embryotoxicity or teratogenic effects.
In mammals, oxytetracycline passes the placental barrier, resulting in staining of teeth and slow foetal growth.
Tetracyclines are found in breast milk.

Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

Divalent or trivalent cations (Mg, Fe, Al, Ca) may chelate with tetracyclines. The tetracylines should not be administered with antacids, gels containing aluminium, preparations containing vitamins or minerals as insoluble complexes will be formed, which decreases the absorption of the antibiotic.

4.9 Amount(s) to be administered and administration route

The uptake of medicated drinking water depends on the clinical and physiological conditions of the animals. In order to obtain the correct dosage, the concentration of oxytetracycline must be adjusted by calculating the required mean daily water consumption.
The duration of treatment is 3 to 5 days, for both chickens and pigs.

Dosing is presented in the following table:

Species	Expressed in mg of oxytetracycline / kg of bodyweight / day	Expressed in mg of ORAL POWDER / 10 kg of bodyweight / day	Estimated water consumption (L / kg of bodyweight)	Expressed in mg of ORAL POWDER / L of drinking water
Pigs	20 mg	400 mg of ORAL POWDER	1 L / 10 kg of bodyweight	400 mg of ORAL POWDER
Chickens	20 mg	400 mg of ORAL POWDER	1 L / 5 kg of bodyweight	200 mg of ORAL POWDER

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

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

To ensure a correct dosage, body weight should be determined as accurately as possible to avoid under dosing.

The use of suitability 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.

For full advantages of solubility qualities, it is recommended to prepare a concentrated pre-solution – approximately 400 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.

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

None known

4.11 Withdrawal period

Meat and offal: 7 days
Eggs: do not use in laying birds producing eggs intended for human consumption

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, tetracycline
ATCvet code: QJ01AA06.

5.1 Pharmacodynamic properties

The oxytetracycline links reversibly to the ribosomal subunit 30S receptors, this leading to a blockage of the union between aminoacyl-tRNA to the site corresponding to the mRNA-ribosome complex messenger.
It results in an inhibition of the protein synthesis and inhibits bacterial growth. The mainly bacteriostatic activity of oxytetracycline involves uptake of the substance into the bacterial cell which occurs by both passive and active diffusions. The main mechanism of resistance is due to the possible presence of a R factor responsible for a decrease in the active transport of oxytetracycline.

Oxytetracycline is a broad-spectrum antibiotic. It is mainly active against Gram-positive and Gram negative bacteria, aerobic and anaerobic, as well as against mycoplasma, the Chlamydia and Rickettsiae.

Acquired resistance to oxytetracycline has been reported. This resistance is usually of plasmid origin. Cross-resistance to other tetracyclines is possible. The prolonged or repeated use of oxytetracycline as well as continuous treatment with low doses of oxytetracycline may also cause increased resistance to other antibiotics due to potential co-resistance with other antimicrobials

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 ribosome).

5.2 Pharmacokinetic particulars

The oral absorption of oxytetracycline is low. The mean values of oral absorption of oxytetraycline are 3-5% in pigs and 48% in turkeys.

This bioavailability can be reduced in the presence of food in the stomach as oxytetracycline leads to the formation of insoluble chelates with divalent or trivalent cations (Mg, Fe, Al, Ca).
In pigs, the influence of food is negligible on the bioavailability of oxytetracycline which is less than 5%.
The oxytetracycline binds variably to plasma proteins according to the species (75%). Its distribution is large. The oxytetracycline diffuses throughout the body, the highest concentrations have been found in the kidneys, liver, spleen and lungs. The oxytetracycline crosses the placental barrier.

Oxytetracycline is excreted unchanged mainly via urine. It is also excreted via bile but a high proportion of oxytetracycline is reabsorbed by the small intestine (enterohepatic cycle).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid, anhydrous.

6.2 Major 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:
- 1 kg jar and 5 kg bucket: 2 years
- 5 kg and 10 kg bags: 18 months

Shelf life after first opening:
- 1 kg jar and 5 kg bucket: 6 months
- 5 kg and 10 kg bags: 3 months

Shelf life after dissolution in drinking water: 24 hours

6.4 Special precautions for storage

For 5 kg and 10 kg bags: Do not store above 25°C
For 1 kg jar and 5 kg bucket: No special storage conditions are required.

6.5 Nature and composition of immediate packaging

- 1 kg jar: Jar made of high density polyethylene (in contact with the veterinary medicinal product) with a screw cap made of low density polyethylene / aluminium / cardboard operculum / polypropylene
- 5 kg bucket: internal bag made of low density polyethylene (in contact with the veterinary medicinal product) in a bucket made of polypropylene – cover made of polypropylene
- 5 kg and 10 kg bags: Bag made of low density polyethylene (in contact with the veterinary medicinal product) / paper / paper

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 products, if appropriate

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

7. MARKETING AUTHORISATION HOLDER

Huvepharma SA
34 Rue Jean Monnet
ZI d'Etriché
Segré
49500 Segré-en-Anjou Bleu
France

8. MARKETING AUTHORISATION NUMBER

Vm 41623/5001

9. DATE OF FIRST AUTHORISATION

10 May 2013

10. DATE OF REVISION OF THE TEXT

March 2020

Approved: 26 March 2020