ATTACHMENT 1

OTC WATER SOLUBLE POWDER 500MG/G

Ingredient(s): Each gram contains:
Oxytetracycline (as hydrochloride) … 500mg

Pharmacology (Summary of Pharmacodynamics and Pharmacokinetics):
Pharmacodynamics
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).

Pharmacokinetics
The oral absorption of oxytetracycline is low. The mean values of oral absorption of oxytetracycline 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).

Indications
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 veterinary medicinal product is used.

Dosage and Administration
In drinking water use.
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 OTC-50/ 10 kg of bodyweight / day	Estimated water consumption(L / kg of bodyweight)	Expressed in mg of OTC-50 / L of drinking water
Pigs	20 mg	400 mg of OTC-50	1 L / 10 kg of bodyweight	400 mg of OTC-50
Chickens	20 mg	400 mg of 0TC-50	1 L / 5 kg of bodyweight	200 mg of OTC-50

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:

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

To ensure a correct dosage, body weight should be determined as accurately as possible.
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 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.

Target Species
Chickens (broilers, breeding hens) and pigs.

Mode of Administration
Orally via drinking water.

Contraindication
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.

ATTACHMENT 2

Precaution(s) / Warning(s):
Special precautions for use in animals
This powder should be dissolved in water, before use.
Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogen(s). If not possible, therapy should be based on local 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. Use of the veterinary medicinal 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 practices 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 recognized in porcine and poultry isolates of strains form E. Coli, Salmonella spp., Campylobacter spp., and Enterococcus spp. The veterinary medicinal 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals.
People with known hypersensitivity to tetracyclines should avoid contact with the veterinary medicinal product.
Avoid inhaling dust when handling the veterinary medicinal product until complete solubilization 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 veterinary medicinal product.
Do not smoke, eat or drink while handling the veterinary medicinal product.

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

Pregnancy and Lactation:
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 fetal growth.
Tetracyclines are found in breast milk.
Use only according to the benefit/risk assessment by the responsible veterinarian.

Side Effect / Adverse Reactions:
Chickens and pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic and photosensitivity reactions [1]
Undetermined frequency	Digestive tract disorder [1]

[1]Common effect for all tetracyclines.

Environmental Property:
For the environmental protection, medicines should not be disposed of via wastewater or household waste. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

Symptoms and Treatment for Overdosage, and Antidotes:
None known.

Storage Conditions:
Store under 30ºC at a dry place. Protect from light.

Shelf-life:
2 years.
Shelf life after dissolution in drinking water: 24 hours.

Product description and Packing:
Yellow color powder.
Aluminum Pouch of 100g, 500g, 1kg.

For food producing animal product:
Withdrawal Periods
Meat and offal: 7 days
Eggs: do not use in laying birds producing eggs intended for human consumption.

Maximum Residual Limit (MRL)
Kidney of chickens/ swine: 1.2 ppm.
Liver of chickens/ swine: 0.6 ppm.
Muscle of chickens/ swine: 0.2 ppm.

Made in Vietnam
Manufacturer:
Y.S.P. INDUSTRIES VIETNAM CO., LTD.
Road No. 6, Nhon Trach Industrial Zone 3, Nhon Trach Dist.,
Dong Nai Province, Vietnam. Tel: +84251 3569 993

Product Registration Holder:
Y.S.P. INDUSTRIES (M) SDN. BHD.
Lot 3, 5, 7, 12 & 14, Jalan P/7, Section 13, Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor Darul Ehsan Malaysia.
Ordering Line : 1 800 88 3027 Product Info: 1 800 88 3679

Insert OTP5 – MY v1 Size 260mm x 110 mm