SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

TAF 25%, 250 mg/g solution to be used in drinking water for pigs, poultry, turkeys, ducks and geese.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of product contains:

Active substance:
Thiamphenicol 250 mg

Qualitative composition of excipients and other constituents
N,N-dimethylacetamide
Propylene glycol

Clear colourless or slightly yellow solution

3. CLINICAL INFORMATION

3.1 Target species

Pigs (fattening pigs), poultry (broilers), turkeys, ducks and geese.

3.2 Indications for use for each target species

Pigs: for the treatment of bacterial infections of the respiratory tract sustained by *Actinobacillus pleuropneumoniae, Bordetella bronchiseptica and Pasteurella multocida* and of intestinal infections caused by *Escherichia coli*.
Broilers: treatment of bacterial diseases of the respiratory and intestinal tract, in chronic respiratory diseases and fowl coryza, sustained by Gram-positive *(Staphylococcus aureus)*, Gram-negative *(Ornithobacterium rhinotracheale, Pasteurella multocida), Salmonella (S. typhimurium, S. enteriditis* and *S. gallinarum),* rickettsiae and chlamydiae, *Clostridium perfrigens* and *Mycoplasma (gallisepticum* and *synoviae*).
Turkeys: treatment of infections sustained by Gram-positive *(Staphylococcus aureus*), Gram-negative *(Ornithobacterium rhinotracheale, Pasteurella multocida, Salmonella spp.*), *Clostridium perfringens* and *Mycoplasma (gallisepticum, synoviae, meleagridis)*.
Ducks and geese: treatment of infections sustained by sensitive microorganisms, such as Gram-positive *(Staphylococcus aureus),* Gram-negative *(Pasteurella multocida*, *Riemerella anatipestifer), Salmonella (blockey, enteriditis, heidelberg, infantis, kentucky, livingstone, mbandaka, tiphymurium, virchow), Clostridium perfringens* and *Mycoplasma (anatis, anseris, cloacale, imitans)*.

3.3 Contraindications

Do not use in case of hypersensitivity to the active principle or to one of the excipients.
The use of the product is contraindicated in cases of known resistance to thiamphenicol.

3.4 Special warnings

The intake of the medicine by the animals may be altered after the disease.
For those subjects with a low water intake, proceed with the parenteral administration, by using a suitable injectable product which is prescribed by a veterinary surgeon.
Repeated or prolonged use of the product must be avoided, by improving the management practice and through cleaning and disinfection operations.
Cross-resistance between chloramphenicol and thiamphenicol is possible.
The use of thiamphenicol must be carefully considered when sensitivity testing has shown resistance to phenols, as its efficacy may be reduced.

3.5 Special usage precautions

Special precautions for safe use in the target species:
The use of the veterinary medicine in poultry must be compliant with EC Regulation No. 1177/2006 of the Commission. Do not leave the medicated liquid or medicated liquid feed available to other animals.
Do not mix in solid feeds.
An antibiotic with a lower risk of selecting antimicrobial resistance (lower AMEG category) should be used for first-line treatment if the sensitivity test suggests that this approach is likely to be effective.
The use of the veterinary medicine must be based on identification and sensitivity tests on bacteria isolated from the animals. If this is not possible, the therapy should be based on local (regional, farm-related) epidemiological information regarding the sensitivity of the target bacteria. The use of the product must comply with official, national and regional antimicrobial policies.
Use of the veterinary medicinal product contrary to the instructions provided in the SPC may increase the prevalence of thiamphenicol-resistant bacteria and may reduce the efficacy of treatment with amphenicols due to potential cross-resistance. In addition to medical treatment, it is important to ensure proper farm conditions including good hygiene, adequate ventilation and avoidance of crowded conditions.
Do not use in prophylaxis/metaphylaxis.

Special precautions to be taken by the person administering the veterinary medicine to the animals:
Direct contact with the product must be avoided while handling it.
People with known hypersensitivity to thiamphenicol must avoid any contact with the veterinary medicine.
Do not swallow. In case of accidental ingestion, immediately seek medical attention, possibly showing the product's label.
Do not eat, drink or smoke while handling the product. Wash your hands after use.

Special precautions for environmental protection:
Not applicable.

3.6 Adverse events

Pigs (fattening pigs), poultry (broilers), turkeys, ducks and geese.

Very rare (less than 1 out of 10,000 treated animals, including isolated cases)	Diarrhoea, nausea, vomiting*. Localised rash*.

* However such symptoms disappear after the treatment end.

The reporting of adverse events is important, as it allows continuous monitoring of the safety of a veterinary medicine. Reports should be sent, preferably by a veterinary surgeon, to the marketing authorisation holder or the national competent authority through the national reporting system. See also the combined label/package leaflet for the respective contact details.

3.7 Usage during pregnancy, lactation and egg laying

The safety of the veterinary medicine during pregnancy and lactation was not established.

Pregnancy, lactation and fertility
Laboratory studies have shown no teratogenic effects, while some evidence (especially at high dosage) of embryonic and foetal toxicity, as well as possible reduction in male fertility, have been reported.
Only use in compliance with the benefit/risk ratio issued by the veterinary surgeon in charge.

Egg-laying birds
Do not administer to birds in egg-laying phase producing eggs for human food consumption.

3.8. Interactions with other medicines and further forms of interaction

Do not administer together with chemoantibiotics with bactericidal action, such as penicillins and cephalosporins.

3.9 Routes of administration and dosage

The product should be administered per os in drinking water or liquid feed, according to the instructions of the veterinary surgeon, taking care not to exceed the authorised daily dosage in mg of active principle/kg b.w.
To ensure consumption of the medicated water, animals must not have access to other water sources during the treatment period.
In order to ensure a proper dosage, determine the body weight as precisely as possible. The intake of water containing the medicinal product depends on the animals' clinical conditions. In order to obtain the correct dosage, the concentration of thiamphenicol may need to be adjusted accordingly.
In order to ensure adequate intake of the water containing the medicinal product, the animals to be treated must have sufficient access to the water supply system.

Carefully dilute the product in drinking water at the following dosage:
Fowl: 1.6-2.0 ml veterinary medicine/10 kg b.w. (equal to 40-50 mg of thiamphenicol/kg b.w.), that is about 80-125 ml/100 litres of water for 3-5 consecutive days.
Pigs: 1.2-1.6 ml veterinary medicine/10 kg b.w. (equal to 30-40 mg of thiamphenicol/kg b.w.) for 3-5 consecutive days.
According to the recommended dosage and to the number and weight of the animals to be treated, the exact daily concentration of the veterinary medicine must be calculated according to the following formula:

$$\frac{\text{ml of medicine/kg b.w.} \times \text{Average weight of animals to be treated per day (kg)} \times \text{Number of animals to be treated}}{\text{Mean water consumption (l)}} = \text{ml of medicine/litre of water}$$

Dissolve the medicine in drinking water. Then the drinking water may be added to the liquid feed. The liquid feed mixed with the diluted medicine must be used immediately and not stored. Dispose of any residual liquid medicated feed before re-feeding.
Remove the non-medicated drinking water from the troughs and administer the medicated one for the time that is specified. Restore the non-medicated drinking water at the end of the therapy period. The water medicated with the veterinary medicine must be disposed of 12 hours after its preparation.

3.10 Overdosage symptoms (and, if relevant, emergency procedures and antidotes)

Do not exceed the recommended dosage.
In turkeys receiving a higher dose than 5 times the one specified for 10 consecutive days the following symptoms were noted: depression, motor incoordination, permanent decubitus, weight loss; anatomopathological lesions such as: focal liver lesions, ulcers in the proventriculus and gizzard, catarrhal duodenitis.
Clinical symptoms such as anorexia, depression, diarrhoea and weight loss occurred in pigs receiving 3-5 times the recommended dosage for a longer time (15 days) than recommended.

3.11 Special restrictions on use and special conditions for use, including restrictions on the use of antimicrobial drugs and of veterinary pesticides to control the risk of developing resistance

Do not use for prophylaxis.

3.12 Withdrawal times

Meat and offal:
Pigs: 6 days.
Broilers: 4 days.
Turkeys: 6 days.
Ducks: 4 days.
Geese: 4 days.
Do not use in birds that produce eggs or are intended to produce eggs for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCVet Code: QJ01BA02

4.2 Pharmacodynamics

TAF 25% is a veterinary medicine containing as sole pharmacologically active substance, thiamphenicol, which is a semisynthetic antibiotic analogous to chloramphenicol.
Thiamphenicol is obtained by replacing the *p*-nitro group of the benzene ring of chloramphenicol with a *p*-methyl-sulphonic group. It has a bacteriostatic action which can become bactericidal generally at much higher concentrations than the minimum inhibiting concentrations. It acts by binding to the 50S ribosome subunit, in such a way as to inhibit the movement of the ribosomes along the m-RNA and to block the last phase of the protein synthesis.
Thiamphenicol has a very wide antibacterial spectrum, which is similar to the one of chloramphenicol.
It is active towards many Gram-positive and Gram-negative bacteria. In particular *Erysipelotrix, Streptococcus, Brucella, Pasteurella, Pseudomonas, Shigella* are sensitive. Intermediate sensitivity for *Corynebacterium, Listeria, Staphylococcus*, *Klebsiella*, *Proteus*, *Salmonella*. A fairly good efficacy is noted towards mycoplasms, treponemas and rickettsiae.
Thiamphenicol is indicated in the bacterial infections of the respiratory and intestinal tracts of poultry, turkeys, ducks , geese and pigs.
The range of MIC values recorded for different strains of microorganisms is
Staphylococcus aureus: 0.50 - 4 μg/ml; *Ornithobacterium rhinotracheale*: 0.125 - 2 μg/ml; *Pasteurella multocida*: 0.125 - 1 μg/ml; *Clostridium perfrigens*: 0.50 - 4 μg/ml; *Mycoplasma gallisepticum*: 0.25 - 2 μg/ml; *Mycoplasma synoviae*: 0.25 - 4 μg/ml; *Mycoplasma meleagridis*: 0.50-2 μg/ml.
The range of MIC values recorded for different strains of swine origin is
Staphylococcus aureus: 1 - 16 μg/ml; *Streptococcus suis*: 0.5 - 8 μg/ml; *Actinobacillus spp*.: 0.5 - 8 μg/ml; *Bordetella bronchiseptica*: 0.25 - 4 μg/ml; *Escherichia coli*: 1 - 16 μg/ml; *Haemophilus parasuis*: 0.5 - 2 μg/ml; *Klebsiella pneumoniae*: 2 - 16 μg/ml; *Pasteurella multocida*: 0.25 - 2 μg/ml; *Salmonella infantis*: 2 - 16 μg/ml; *Clostridium perfrigens*: 0.5 - 2 μg/ml; *Mycoplasma hyopneumoniae*: 0.5-2 μg/ml.

Breakpoint values for thiamphenicol are not currently available. To assess the sensitivity of the isolated strains, the published values for chloramphenicol were used (Sensitive ≤8 μg/ml, Intermediate 16 μg/ml, Resistant ≥32 μg/ml).

The main mechanism of resistance is the inactivation of thiamphenicol by acetylation by the enzyme chloramphenicol-acetyltransferase (CAT). CAT-related genes are common in Enterobacteriaceae and Pasteurellaceae. The cross-resistance between chloramphenicol and thiamphenicol is complete in bacteria with CAT.

4.3 Pharmacokinetics

Thiamphenicol has a good bioavailability through the oral route (80-90%). It binds little to the plasma proteins (5-15%) and penetrates rather well the tissues, thus reaching the highest concentrations in a few organs and tissues such as heart, lung and muscles, together with the plasma peaks that may be noted 3-4 hours after the administration. It is little metabolised by liver and is eliminated mainly through the renal route, less through the biliary route, in unmetabolised form, thus still provided with antibiotic activity.
The main pharmacokinetic parameters after oral administration in poultry species are: maximum plasma concentration (Cmax): 2.9 μg/ml; time at which the maximum concentration is reached (Tmax): 2 hours; area under the curve (concentration/time ratio: AUC_{0-24}): 116.9 μg/ml. After the oral administration in ducks the maximum plasma concentration was higher (Cmax 35 μg/ml) and it was reached more rapidly (Tmax 0.5 h).

<u>Pigs</u>
In pigs, oral thiamphenicol has a good bioavailability (27.84% ± 15.5). The maximum concentration after a single dose of 40 mg/kg (Cmax) of 6.1 μg/ml is reached in 2 h (Tmax) and the elimination time averages 2.5 h (t ½ elim). Glucuronidation is the main metabolic pathway, particularly after the oral administration.

Environmental properties:
The conscious and prudent use of antibiotic medication contributes to limiting and combating the phenomenon of antimicrobial resistance and to safeguarding public, animal and environmental health, according to the One Health principle.

5. PHARMACEUTICAL INFORMATION

5.1 Main incompatibilities

As there are no compatibility studies available, do not mix this product with other veterinary medicinal products.

5.2 Shelf-life

Shelf-life of the veterinary medicinal product, as packaged for selling purposes: 36 months.
Shelf-life after first opening of primary packaging: 3 months.
Shelf-life after dilution as per instructions: 12 hours.

5.3 Special storage precautions

This veterinary medicinal product requires no special storage conditions.

5.4 Nature and composition of primary packaging

80 ml bottle, 1000 ml bottle and 5 litre tanks in HDPE for food use. The cap in HDPE is provided with seal in HDPE, which is irreparably torn when opening the container, and with (multilayer) undercap glued to the package.

It is possible that not all packages will be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or wastes resulting from their use

Medicinal products must not be disposed of in waste water or household waste.
Use collection systems for the disposal of unused veterinary medicinal products or wastes resulting from the use of such medicinal products in accordance with local regulations and any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER
Chemifarma S.p.A.

7. MARKETING AUTHORISATION NUMBERS

Cardboard box containing an 80 ml bottle: MA No. 103552016
1 litre bottle: MA No. 103552028
5 litre tank: MA No. 103552030

8. FIRST AUTHORISATION DATE

First authorisation date: 01/06/2006.

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

03/ 2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
To be sold by medical-veterinary prescription only, in three copies, not reproducible.

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

chemifarma® S.p.A. INDUSTRIA FARMACEUTICA VETERINARIA