

TABI

PROPOSED GENERIC LABELING

ACTIVE INGREDIENTS: Generic amoxicillin trihydrate/clavulanate potassium (AT/CP) tablets are available in the following strengths:

Each 125 mg tablet contains amoxicillin trihydrate equivalent to 100 mg of amoxicillin activity and 25 mg of clavulanic acid as the potassium salt. For use in dogs and cats.

Each 250 mg tablet contains amoxicillin trihydrate equivalent to 200 mg of amoxicillin activity and 50 mg of clavulanic acid as the potassium salt. For use in dogs only.

Each 500 mg tablet contains amoxicillin trihydrate equivalent to 400 mg of amoxicillin activity and 100 mg of clavulanic acid as the potassium salt. For use in dogs only.

Each 750 mg tablet contains amoxicillin trihydrate equivalent to 600 mg of amoxicillin activity and 150 mg of clavulanic acid as the potassium salt. For use in dogs only.

INDICATIONS: Generic AT/CP tablets are indicated in the treatment of:

Dogs: Skin and soft tissue infections such as wounds, abscesses, cellulites, superficial/juvenile and deep pyoderma due to susceptible strains of the following organisms: β -lactamase-producing *Staphylococcus aureus*, non- β -lactamase-producing *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp. And *E. coli*.

Periodontal infections due to susceptible strains of both aerobic and anaerobic bacteria.

Generic AT/CP has been shown to be clinically effective for treating cases of canine periodontal disease.

Cats: Skin and soft tissue infections such as wounds abscesses, and cellulites/dermatitis due to susceptible strains of the following organisms: β -lactamase-producing *Staphylococcus aureus*, non- β -lactamase-producing *Staphylococcus aureus*, *Staphylococcus* spp., *Streptococcus* spp., *E. coli*, and *Pasteurella* spp.

Urinary tract infections (cystitis) due to susceptible strains of *E. coli*.

Therapy may be initiated with generic AT/CP prior to obtaining results from bacteriological and susceptibility studies. A culture should be obtained prior to treatment to determine susceptibility of the organisms to generic AT/CP.

Following determination of susceptibility results and clinical response to medication, therapy may be reevaluated.

PHARMACOLOGY: Description: Generic AT/CP is an orally administered formulation comprised of the broad-spectrum antibiotic amoxicillin trihydrate and the β -lactamase inhibitor, clavulanate (the potassium salt of clavulanic acid).

Amoxicillin trihydrate is a semisynthetic antibiotic with a broad spectrum of bactericidal activity against many gram-positive and gram-negative, aerobic and anaerobic microorganisms. It does not restrict destruction by β -lactamases; therefore it is not effective against β -lactamase-producing bacteria. Chemically, it is D(-)- α -amino-p-hydroxybenzyl-penicillin trihydrate.

Clavulanic acid, an inhibitor of β -lactamase enzymes, is produced by the fermentation of *Streptomyces clavuligerus*. Clavulanic acid by itself has only weak antibacterial activity. Chemically, clavulanate potassium is potassium a-(3R,5R)-2- β -hydroxyethylidene clavam-3-carboxylate.

Action: Generic AT/CP is stable in the presence of gastric acid and is not significantly influenced by gastric or intestinal contents. The 2 components are rapidly absorbed resulting in amoxicillin and clavulanic acid concentrations in serum, urine, and tissues similar to those produced when each is administered alone.

Amoxicillin and clavulanic acid diffuse readily into most body tissues and fluids with the exception of brain and spinal fluid, which amoxicillin penetrates adequately when meninges are inflamed. Most of the amoxicillin is excreted unchanged in the urine. Clavulanic acid's penetration into spinal fluid is unknown at this time. Approximately 15% of the administered dose of clavulanic acid is excreted in the urine within the first 6 hours.

Generic AT/CP combines the distinctive properties of a broad-spectrum antibiotic and a β -lactamase inhibitor to effectively extend the antibacterial spectrum of amoxicillin to include β -lactamase-producing as well as non- β -lactamase-producing aerobic and anaerobic organisms.

Microbiology: Amoxicillin is bactericidal in action and acts through the inhibition of biosynthesis of cell wall mucopeptide of susceptible organisms. The action of clavulanic acid extends the antimicrobial spectrum of amoxicillin to include organisms resistant to amoxicillin and other β -lactam antibiotics. Amoxicillin/clavulanate has been shown to have a wide range of activity which includes β -lactamase-producing strains of both gram-positive and gram-negative aerobes, facultative anaerobes and obligate anaerobes. Many strains of the following organisms, including β -lactamase-producing strains, isolated from veterinary sources, were found to be susceptible to amoxicillin/clavulanate *in*

vitro but the clinical significance of this activity has not been demonstrated for some of these organisms in animals.

Anaerobic bacteria, including *Staphylococcus aureus**, β -lactamase-producing *Staphylococcus aureus** (penicillin resistant), *Staphylococcus* species*, *Staphylococcus epidermidis*, *Staphylococcus intermedius*, *Streptococcus* species*, *Corynebacterium pyogenes*, *Corynebacterium* species, *Erysipelothrix rhusiopathiae*, *Bordetella bronchiseptica*, *Escherichia coli**, *Proteus mirabilis*, *Proteus* species, *Enterobacter* species, *Klebsiella pneumoniae*, *Salmonella dublin*, *Salmonella typhimurium*, *Pasteurella multocida**, *Pasteurella hemolytica*, *Pasteurella* species*.

*The susceptibility of these organisms has also been demonstrated in *in vivo* studies.

Studies have demonstrated that both aerobic and anaerobic flora are isolated from gingival cultures of dogs with clinical evidence of periodontal disease. Both gram-positive and gram-negative aerobic and anaerobic subgingival isolates indicate sensitivity to amoxicillin/clavulanate acid during antimicrobial susceptibility testing.

Susceptibility Test: The recommended quantitative disc susceptibility method (Federal Register 37:20527-29; Baur AW, Kirby WMM, Sherris JC, *et al*: Antibiotic susceptibility testing by standardized single disc method. Am J Clin Path 45:493, 1966) utilized 30 μ g Augmentum® (AMC) discs for estimating the susceptibility of bacteria to generic AT/CP tablets.

DOSAGE AND ADMINISTRATION:

Dogs: The recommended dosage is 12.5 mg/lb of body weight once a day.

Skin and soft tissue infections such as abscesses, cellulitis, wounds, superficial/juvenile pyoderma and periodontal infections should be treated for 5-7 days or for 48 hours after all symptoms have subsided. If no response is seen after 5 days of treatment, therapy should be discontinued and the case reevaluated. Deep pyoderma may require treatment for 21 days; the maximum duration of treatment should not exceed 30 days.

Cats: The recommended dosage is 125 mg once a day.

Skin and soft tissue infections such as abscesses, cellulitis/dermatitis should be treated for 5-7 days or for 48 hours after all symptoms have subsided not to exceed 30 days. If no response is seen after 3 days of treatment, therapy should be discontinued and the case reevaluated.