PRESCRIBING INFORMATION

TETRACYCLINE

Tetracycline Hydrochloride Capsules USP

250 mg

Antibiotic

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THERAPEUTIC CLASSIFICATION

Antibiotic

INDICATIONS AND CLINICAL USE

Many strains of bacteria have been shown to be resistant to the tetracyclines. These include certain strains of streptococci, staphylococci, pneumococci, gonococci, and many other gram negative organisms. Therefore, culture and sensitivity testing are advised to determine the susceptibility of the infecting organisms to tetracyclines.

Chemotherapy should not be initiated until all the necessary bacteriological investigations have been started.

Microorganisms that have become insensitive to one tetracycline invariably exhibit cross resistance to other tetracyclines.

Some cross resistance between the tetracyclines and chloramphenicol for gram-negative organisms but not for gram-positive ones has been reported. Tetracycline resistant organisms are most likely to be acquired from other individuals in a population where tetracyclines have been widely used.

The tetracyclines are indicated in infections caused by the following microorganisms:

Rickettsiae (Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox, tick fevers), *M. pneumoniae* (PPLO, Eaton agent), agents of psittacosis and ornithosis, agents of *L. venereum* and *G. inguinale*, and the spirochetal agent of relapsing fever (*B. recurrentis*).

The following gram-negative organisms: *H. ducreyi* (chancroid), *P. pestis* and *P. tularensis*, *B. bacilliformis*. Bacteroides, *V. comma* and *K. fetus*, and Brucella organisms (in conjunction with streptomycin).

The following gram-negative organisms, when bacteriologic testing indicates appropriate susceptibility to the drug: *E. coli*, *A. aerogenes*, Shigella, Mima, Herellea, *H. influenzae* (respiratory infections), and Klebsiella infections (respiratory and urinary).

The following gram-positive organisms when bacteriologic testing indicates appropriate susceptibility to the drug: anaerobic streptococci, *S. pyogenes* (for upper respiratory infections due to Group A beta-hemolytic streptococci, penicillin is the drug of choice including prophylaxis of rheumatic fever), *S. pneumoniae*, and *S. aureus*.

The frequency of resistance to tetracyclines in hemolytic streptococci is highest in strains from infections of the ear, wounds and skin. Tetracyclines should not be prescribed for acute throat infections; also, they are not the drugs of choice in any staphylococcal infection.

When penicillin is contraindicated, tetracyclines are alternative drugs in the treatment of infections due to: *N. gonorrhoeae*, *T. pallidum* and *T. pertenue* (syphilis and yaws), *L. monocytogenes*, Clostridia, *B. anthracis*, Fusobacterium (Vincent's infection), and Actinomyces.

In acute intestinal amebiasis, the tetracyclines may be a useful adjunct to amebicides. In severe acne, the tetracyclines may be useful adjunctive therapy.

Tetracyclines are indicated in the treatment of trachoma, although the infectious agent is not always eliminated, as judged by immunofluorescence.

Inclusion conjunctivitis may be treated with oral tetracyclines or with a combination of oral and topical agents.

Because tetracycline tends to accumulate in certain neoplastic cells and to exhibit a brilliant, yellow gold fluorescence when exposed to ultraviolet light, it may be useful in experienced hands for the diagnosis of malignancy.

CONTRAINDICATIONS

TETRACYCLINE (tetracycline hydrochloride) is contraindicated in patients with hypersensitivity to any of the tetracyclines and in patients with severe renal or hepatic disease.

Pregnancy and Lactation

TETRACYCLINE is not recommended for use in pregnant or lactating women unless the potential benefit to the patient outweighs the risk to the fetus or child.

Children

TETRACYCLINE is contraindicated in children under 12 years of age for therapy of common infections or for any condition in which a bactericidal effect is essential (bacterial endocarditis).

Avoid prophylactic administration to surgical cases, if possible.

PRECAUTIONS

The use of tetracyclines during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent tooth discoloration (yellow gray

brown). This reaction is more common during long-term use of the tetracyclines, but has been observed following short-term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should **not** be used in this age group unless other drugs are not likely to be effective or are contraindicated.

If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such conditions, lower than usual doses are indicated and, if therapy is prolonged, serum level determinations of the drug may be advisable.

The antianabolic action of tetracycline may cause an increase in BUN. While this is not a problem in those with normal renal function, in patients with significantly impaired function, higher serum levels of tetracycline may lead to azotemia, hyperphosphatemia, and acidosis. Consequently, increasing levels of BUN may not accurately reflect changes in renal function; the serum creatinine will provide a more reliable index.

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients should be warned to avoid exposure to direct sunlight and/or ultraviolet light while under treatment with tetracycline drugs, and treatment should be discontinued at the first evidence of skin discomfort.

Tetracyclines form a stable calcium complex in any bone forming tissue. A decrease in the fibula growth rate has been observed in prematures given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued.

Tetracycline administration may result in overgrowth of non-susceptible organisms. Superinfections due to staphylococci and other organisms may occur during oral but rarely during parenteral administration.

C. albicans can produce effects at three levels: proliferation in the mouth can cause disturbances ranging from simple soreness to frank and extensive thrush, which may spread to the pharynx and possibly the bronchi; in the bowel, it can be manifested by diarrhea; also, pruritus ani occurs frequently.

Proteus and Pseudomonas species resistant to tetracyclines may become predominant in the bowel and diarrhea is common. Periodic microbiologic examination of materials, such as stool and sputum, during tetracycline therapy may alert one to changes in flora indicating bacteriologic superinfection in time to avert progression to clinical disease.

If superinfections are encountered, tetracyclines should be discontinued and appropriate therapy started. Superinfection of the bowel by staphylococci may be life threatening.

Adhere closely to expiration dates; ingestion of deteriorated tetracyclines has produced kidney damage corresponding clinically to the acute Fanconi syndrome (nausea, vomiting, albuminuria, glycosuria, aminoaciduria, hypophosphatemia, hypokalemia, and acidosis). Such damage is usually reversed slowly after withdrawal of the deteriorated tetracycline, although fatal reactions have been reported.

Before treating gonorrhea, a darkfield examination should be made from any lesion suggesting concurrent syphilis. Serological tests for syphilis should be made for at least 4 months afterwards.

Because the tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage. Interference with vitamin K synthesis by microorganisms in the gut has been reported.

Concurrent use of methoxyflurane and tetracyclines has been reported to impair renal function seriously, leading in some cases to death. Such use of these two drugs is therefore not recommended unless the benefits outweigh the risks.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline in conjunction with penicillin.

During long-term therapy, periodic laboratory evaluation of organ systems, including hematopoietic, renal and hepatic studies should be performed.

All infections due to Group A beta-hemolytic streptococci should be treated for at least 10 days.

Since sensitivity reactions are more likely to occur in persons with a history of allergy, asthma, hay fever, or urticaria, the preparations should be used with caution in such individuals. Cross sensitization among the various tetracyclines is extremely common.

When it is essential to administer any of the tetracyclines i.v., the blood concentration should not be permitted to exceed 15 µg/mL and, if possible, other potentially hepatotoxic drugs should be avoided. Presumably, large doses may be expected to have comparable toxicity by either the i.m. or oral route if renal or hepatic insufficiency is present.

ADVERSE EFFECTS

Gastrointestinal

Anorexia, epigastric distress, nausea, vomiting, diarrhea, bulky loose stools, stomatitis, sore throat, glossitis, black hairy tongue, dysphagia, hoarseness, enterocolitis, and inflammatory lesions (with candidal overgrowth) in the anogenital region, including proctitis and pruritus ani. These reactions have been caused by both the oral and parenteral administration of tetracyclines but are less frequent after parenteral use.

Skin

Maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Onycholysis and discolouration of the nails have been reported rarely. Photosensitivity has occurred (see PRECAUTIONS).

Renal Toxicity

Rise in BUN has been reported and is apparently dose-related (see PRECAUTIONS).

Hepatic cholestasis has been reported rarely, and is usually associated with high dosage levels of tetracycline. Hepatic toxicity, associated with pancreatitis in some cases, has been attributed to the long-term use of doses larger than those recommended in patients with renal insufficiency or to the concomitant administration of other potentially hepatotoxic drugs. This serious reaction has occurred most often in pregnant or postpartum patients with pyelonephritis.

Hypersensitivity Reactions

Urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus, and serum sickness like reactions, as fever, rash, and arthralgia. When given over prolonged periods, tetracyclines have been reported to produce brown black microscopic discolouration of thyroid glands. No abnormalities of thyroid function studies are known to occur.

Bulging fontanels have been reported in young infants following full therapeutic dosage. This sign disappeared rapidly when the drug was discontinued.

Blood

Anemia, hemolytic anemia, thrombocytopenia, thrombocytopenic purpura, neutropenia and eosinophilia have been reported.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Treatment

If ingested, gastric lavage when necessary.

DOSAGE AND ADMINISTRATION

Adults should receive an average daily dose of 250 mg 4 times a day. Higher dosages, such as 500 mg 4 times a day may be required for severe infections. In general, the pediatric dosage should supply 22 to 44 mg of tetracycline/kg/day, in divided doses, depending on the type and severity of the infection.

Antacids, containing aluminum, calcium, or magnesium and iron salts impair absorption and should not be given to patients taking oral tetracyclines. Foods and some dairy products also interfere with absorption. Oral forms of tetracycline should be given 1 hour before or 2 hours after meals.

AVAILABILITY OF DOSAGE FORM

Each orange and yellow no. 2 capsule, identified 250, contains tetracycline HCI 250 mg. Available in bottles of 100, 1000, and 3000.