**INDICATIONS AND USAGE**

To reduce the development of drug-resistant bacteria and maintain effectiveness of Doxycycline Hyclate Capsules and other antibacterial drugs, Doxycycline Hyclate Capsules should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

**Treatment**

Doxycycline is indicated for the treatment of the following infections:

- Rocky Mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsialpox, and tick-borne illnesses caused by Rickettsia species.
- Respiratory tract infections caused by Mycoplasma pneumoniae.
- Lymphogranuloma venereum caused by Chlamydia trachomatis.
- Pelvic inflammatory disease caused by Chlamydia species.
- Yersinia causes by Yersinia enterocolitica or Yersinia pseudotuberculosis.
- Bacillary angiomatosis caused by Chlamydia psittaci.
- Presepsis caused by Brucella species (in conjunction with streptomycin).
- Intra-abdominal infections caused by Klebsiella pneumoniae.

Doxycycline is also indicated for the treatment of infections caused by the following gram-negative microorganisms:

- Non-haemolytic streptococci.
- Pseudomonas aeruginosa.
- Proteus species.
- Aeromonas species.
- Hemolytic streptococci.
- Shigella species.

Doxycycline is indicated for treatment of infections caused by the following gram-positive microorganisms when bacteriologic testing indicates appropriate susceptibility to the drug:

- Enterococcus faecalis.
- Enterococcus faecium.
- Propionibacterium acnes.
- Acinetobacter species.
- Anaerobic bacteria.
- Staphylococcus epidermidis.
- Staphylococcus aureus.
- Enterococcus faecalis.
- Enterococcus faecium.
- Clostridium difficile.

Doxycycline is contraindicated in patients with known hypersensitivity to any of the tetracyclines.

**CONTRAINDICATIONS**

The drug is contraindicated in patients who have shown hypersensitivity to any of the tetracyclines.

**WARNINGS**

**The Use of Drugs in the Treatment of Tetracycline-Resistant Bacteria** (large dose of tetracyclines or prolonged treatment) may cause permanent discoloration of the teeth in children or young adolescents. Children and adolescents should be given a tetracycline drug only when the potential benefit justifies the potential risk.

**Pregnancy**

Doxycycline may cause fetal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, close surveillance is warranted, and the patient should be apprised of the potential hazard to the fetus.

**Nursing Mothers**

Doxycycline is excreted in breast milk. Because of the potential for serious adverse reactions in nursing infants from doxycycline, breastfeeding should be discontinued while receiving this medication.

**Contraception**

Before prescribing doxycycline, the practitioner should discuss contraception with women of childbearing age. If contraceptive failure is possible, a barrier method of contraception should be recommended.

**Labor**

Doxycycline Hyclate Capsules should be used with caution in the presence of renal impairment. Dosage adjustment may be necessary in patients with moderate hepatic insufficiency.

**Lactation**

The effects on nursing infants of doxycycline are not known. However, because of its potential for serious adverse reactions in nursing infants from doxycycline, breastfeeding should be discontinued while receiving this medication.

**Children**

The use of doxycycline in children has not been well established. However, in pediatrics, the most significant risk of doxycycline is the potential for irreversible discoloration of the teeth. Doxycycline should not be used in children under the age of 8 years unless the potential benefits outweigh the potential risks.

**Geriatric Use**

The need for dosage adjustment is not known. However, in geriatric patients, age-related decreases in hepatic function and reduced renal clearance may alter the elimination of doxycycline. Ofloxacin is a possible substitute for those elderly patients who are more likely to experience side effects associated with doxycycline.

**Drug Interactions**

Doxycycline has the potential to alter the results of tests for glucose tolerance. These effects are reversible. Doxycycline should be used with caution in patients receiving anticoagulant therapy, and the prothrombin time should be monitored. Doxycycline may interfere with the results of certain laboratory tests, including: prothrombin time, partial thromboplastin time, aminotransferase, alkaline phosphatase, bilirubin, blood urea nitrogen, uric acid, and serum creatinine.

**Precautions**

If prolonged treatment is required or if the patient has a gastrointestinal disorder, oral doxycycline may be substituted for parenteral administration.

**Adverse Reactions**

Adverse effects associated with doxycycline appear to be dose-related and include the following:

- Skin: Rash, maculopapular rash, pruritus, urticaria, angioneurotic edema, purpura, exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, photosensitivity reactions, photosensitivity reactions with exacerbation of lesions, photosensitivity reactions with exacerbation of lesions.
- Gastrointestinal: Nausea, vomiting, diarrhea, stomatitis, glossitis, enteritis, colitis, pseudomembranous colitis, jaundice, hepatitis, pancreatitis, biliary tract disease, cholecystitis, hepatic failure.
- Hepatic: Hepatitis, cholestasis, jaundice, hepatic failure.
- Renal: Renal failure, interstitial nephritis, pyelonephritis, renal calcification, nephrocalcinosis.
- Central nervous system: Headache, dizziness, vertigo, drowsiness, insomnia, paresthesia, convulsions, Guillain-Barré syndrome, cerebrovascular accidents, thrombophlebitis, stroke, myasthenia gravis, asterixis, tremors, ataxia, vertigo, visual disturbances, nystagmus, vertigo, diplopia, and vision loss; papilledema can be found on fundoscopy. Women of childbearing age who are pregnant while receiving this drug should be monitored for fetal effects.
- Ophthalmologic: Intraocular pressure increase, macular degeneration, cataract formation, retinal detachment, corneal ulcers, conjunctivitis, anterior uveitis, iritis, optic neuritis, papilloedema, diabetic retinopathy, retinal vein occlusion, optic neuropathy, retinal artery occlusion, retinal hemorrhage, vitreous hemorrhage, uveitis, cataracts, glaucoma.
- Cardiovascular: Hypertension, hypotension, orthostatic hypotension, tachycardia, cardiac arrhythmia, atrial fibrillation, heart block, bundle branch block, conduction abnormality, arrhythmia, angina, myocardial ischemia, myocardial infarction.
- Respiratory: Dyspnea, cough, pharyngitis, bronchitis, pneumonia, pulmonary edema, pleural effusion, pneumothorax, pulmonary embolism, interstitial lung disease, aspiration pneumonia, sinusitis, otitis media, sinusitis, rhinitis, pharyngitis, laryngitis, throat pain, sinusitis, rhinitis, pharyngitis, laryngitis, throat pain.
- Other: Photosensitivity reactions, photosensitivity reactions with exacerbation of lesions, photosensitivity reactions with exacerbation of lesions.

**Laboratory Tests**

Doxycycline may cause a decrease in serum calcium and an increase in alkaline phosphatase, serum transaminases, and serum total bilirubin. These changes are usually not clinically significant.

**Clinical Pharmacology**

**Pharmacokinetics**

Doxycycline is rapidly absorbed and distributed to body tissues in varying degree. It is concentrated in the liver, kidneys, spleen, and reticuloendothelial tissues. Doxycycline is excreted unchanged in bile, urine, and nasopharynx. Doxycycline is usually not degraded in the enterohepatic circle.

**Metabolism**

Doxycycline is not metabolized in the body.

**Excretion**

Doxycycline is eliminated primarily by renal excretion. The fraction of an oral dose of doxycycline eliminated unchanged in urine is approximately 10%, but varies with renal function from about 90% with normal renal function to about 2% with severe renal failure.

**Half-Life**

The terminal half-life is about 1-2 hours following oral administration in normal adults. The half-life is about 1-2 hours following intravenous administration in adults with normal renal function and about 12-14 hours in individuals with normal and severely impaired renal function.

**Drug Interactions**

Doxycycline is a competitive inhibitor of pepsin and should be administered at least 1 hour before or 2 hours after antacids, sucralfate, or milk to prevent decreased absorption.

**Precautions**

Doxycycline may cause a decrease in serum calcium and an increase in alkaline phosphatase, serum transaminases, and serum total bilirubin. These changes are usually not clinically significant.
ADVERSE REACTIONS

Due to oral doxycycline's virtually complete absorption, side effects of the lower bowel, particularly diarrhea, may be significant. The following adverse reactions have been observed in patients receiving tetracyclines:

Gastrointestinal: Anorexia, nausea, vomiting, diarrhea, dyspepsia, enterocolitis, and inflammatory bowel disease (including pseudomembranous colitis) have been reported. Bacterial overgrowth in the small intestine may occur resulting in flatulence, abdominal distention, and cramps.

Skin: Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, mucocutaneous and mucosal rashes, exfoliative dermatitis has been reported but is uncommon. Photosensitivity is discussed elsewhere. (See WARNINGS.)

Respiratory: Bronchitis: Rise in FVE has been reported and is apparently dose-related. (See WARNINGS.)

Immunologic: Hyperreactivity reactions including urticaria, angioedema, anaphylaxis, anaphylactoid purpura, serum sickness, pericarditis, exacerbation of systemic lupus erythematosus, and drug rash with eosinophilia and systemic symptoms (DRESS). Rashes and pruritus are frequently observed in patients receiving tetracyclines and may occur during or after discontinuation of therapy.

Blood: Hemolytic anemia, thrombocytopenia, neutropenia, and eosinophilia have been reported.

Other: Other: Bulging fontanelles in infants and hypercalcemia in neonates. (See WARNINGS - General.)

To report adverse reactions contact Cipla Limited at 1-800-604-3208 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

OVERDOSAGE

In case of overdose, discontinue treatment, treat symptomatically and institute supportive measures. Dialysis does not alter serum half-life and will not be of net benefit in treating cases of overdose.

DOSEAGE AND ADMINISTRATION

THE USUAL DOSAGE AND FREQUENCY OF ADMINISTRATION OF DOXYCYCLINE DIFFERS FROM THAT OF OTHER TETRACYCLINES. EXCEEDING THE RECOMMENDED DOSAGE MAY RESULT IN AN INCREASED INCIDENCE OF SIDE EFFECTS. Adults: The usual dose of oral doxycycline is 200 mg on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg every 12 hours. In the management of more severe infections (particularly chronic infections of the urinary tract), 100 mg every 12 hours is recommended. The therapeutic antibacterial effect usually persists for 24 hours following recommended dosage. When used in infectious diseases, therapy should be continued for 10 days. Administration of adequate amounts of fluid along with capsule and tablet forms of the tetracyclines in dosages recommended to avoid dryness and the risk of esophageal irritation and ulceration. (See ADVERSE REACTIONS.)

Gastrointestinal side effects are rarely of clinical importance, but may be pronounced in patients with renal insufficiency. Doxycycline is not nephrotoxic in patients with normal renal function.

In patients with impaired renal function, dosage adjustments should be made based on only two exposed cases. The effect of tetracyclines on labor and delivery is unknown.

Tetracyclines are excreted in human milk; however, the extent of absorption of tetracyclines, including doxycycline, by the nursing infant is not known. Caution is advised when tetracyclines are administered to individuals who may be pregnant. The antianabolic action of the tetracyclines may cause an increase in BUN. Studies to date indicate that this does not occur with the use of doxycycline in patients with impaired renal function.

Pharmacologically, manifested by an augmented bacterial activity, is observed in some individuals taking tetracyclines. Patients at risk for superinfection should be advised where this reaction may occur with tetracyclines, and treatment should be discontinued at the first evidence of drug resistance. Doxycycline offers substantial food and futile suppression of the bacterial flora of the colon. Doxycycline does not suppress P. gingivalis' sexual stage gametocytes. Studies completing this pharmacokinetic regimen may then transfer the infection to mucosal sites outside oral areas. Prescribing Doxycycline Hyclate Capsules in the absence of clinical signs or positive bacterial test results is not indicated and is not recommended. Be sure that oral doxycycline is administered at the usual dose for at least 7 days prior to and during the entire sexual activity of the infected patient. Absorption of tetracyclines is impaired by bismuth subsalicylate. (See INTERACTIONS.)

DOSAGE AND ADMINISTRATION

Dosage recommendations below are based on only two exposed cases b. The effect of the tetracyclines on labor and delivery is unknown. The antianabolic action of the tetracyclines may cause an increase in BUN. Studies to date indicate that this does not occur with the use of doxycycline in patients with impaired renal function.