For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

Rx Doxycycline for Injection USP

WINDOXY™

Sterile
For IV Infusion only
Lyophilized

Composition :
Each vial contains
Doxycycline Hyclate (Sterile) IP
Eq. to Doxycycline 100 mg

PHARMACEUTICAL FORM
Powder for solution for Injection.
THERAPEUTIC INDICATION
To reduce the development of drug-resistant bacteria and maintain effectiveness of doxycycline for injection and other antibacterial drugs, doxycycline for injection 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.
Doxycycline is a broad spectrum antibiotic, indicated for treatment of infections caused by the gram negative and gram positive microorganisms when bacteriologic testing indicates appropriate susceptibility to the drug or as directed by the Physician.
DOSAGE AND ADMINISTRATION
Note: Rapid administration is to be avoided. Parenteral therapy is indicated only when oral therapy is not indicated. Oral therapy should be instituted as soon as possible. If intravenous therapy is given over prolonged periods of time, thrombophlebitis may result.
The usual dosage and frequency of administration of doxycycline I.V. (100-200 mg/day) differs from that of the other tetracyclines (1-2 g/day). Exceeding the recommended dosage may result in an increased incidence of side effects.
Studies to date have indicated that Doxycycline at the usual recommended doses does not lead to excessive accumulation of doxycycline in patients with renal impairment.
Posology
Adults: The usual dosage of Doxycycline I.V. is 200 mg on the first day of treatment administered in one or two infusions. Subsequent daily dosage is 100 to 200 mg depending upon the severity of infection, with 200 mg administered in one or two infusions or as directed by the Physician.
Parenteral therapy is only indicated when oral therapy is not indicated and should not be continued over a prolonged period of time. Oral therapy should be instituted as soon as possible.
General
The duration of infusion may vary with the dose (100 to 200 mg per day), but is usually one to four hours. A recommended minimum infusion time for 100 mg of a 0.5 mg/mL solution is one hour. Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided. The therapeutic antibacterial serum activity will usually persist for 24 hours following recommended dosage.
Method of administration: For IV Infusion Only.
Method of Preparation:
To prepare a solution containing 10 mg/mL, the contents of the vial should be reconstituted with 10 mL (for the 100 mg/vial container) of Sterile Water for Injection or any of the ten intravenous infusion solutions listed below. Each 100 mg of doxycycline (i.e., withdraw entire solution from the 100 mg vial) is further diluted with 100 mL to 1000 mL of the intravenous solutions listed below: Sodium Chloride Injection, 5% Dextrose Injection, Ringer's solution, Lactated Ringer's solution, Dextrose 5% in Lactated Ringer's, Plasma-Lyte in 5% Dextrose. This will result in desired concentrations of 0.1 to 1.0 mg/ml. Concentrations lower than 0.1 mg/mL or higher than 1.0 mg/mL are not recommended.
During infusion, the solution must be protected from direct sunlight. Solutions must be used freshed or within the time period as directed by the physician.
CONTRAINDICATIONS
Doxycycline is contraindicated in patients with known hypersensitivity to any of the tetracyclines or to any of the component of this formulation.
SPECIAL WARNINGS AND PRECAUTIONS FOR USE
The use of drugs of the tetracycline class during tooth development (Last half of Pregnancy, Infancy and Childhood to the age of 8 Years) may cause permanent discoloration of the teeth (Yellow-Gray-Brown). This adverse reaction is more common during long-term use of the drugs but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should not be used in this age group, except for anthrax, including inhalational anthrax (post-exposure), unless other drugs are not likely to be effective or are contraindicated.
Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with tetracycline drugs, and treatment should be discontinued at the first evidence of skin erythema.
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including doxycycline for injection, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.
C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.
If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.
Severe skin reactions, such as exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in patients receiving doxycycline (see ADVERSE REACTIONS). If severe skin reactions occur, doxycycline should be discontinued immediately and appropriate therapy should be instituted.
The anti-anabolic 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.
Precautions
As with other antibacterial drugs, use of Doxycycline may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, Doxycycline should be discontinued and appropriate therapy instituted.
Intracranial hypertension (IH, pseudotumor cerebri) has been associated with the use of tetracyclines including Doxycycline. Clinical manifestations of IH include headache, blurred vision, diplopia, vision loss, and papilledema. Women of childbearing age who are overweight or have a history of IH are at greater risk for developing tetracycline associated IH. Concomitant use of isotretinoin and Doxycycline should be avoided because isotretinoin is also known to cause pseudotumor cerebri.
Although IH typically resolves after discontinuation of treatment, it is possible that permanent visual loss can occur. If visual symptoms develop during treatment, prompt ophthalmologic evaluation is warranted. Since intracranial pressure can remain elevated for weeks after drug cessation patients should be monitored until they stabilize.
In venereal diseases when coexistent syphilis is suspected, a dark field examination should be done before treatment is started and the blood serology repeated monthly for at least 4 months.
Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.
In long-term therapy, periodic laboratory evaluation of organ systems, including hematopoietic, renal, and hepatic studies should be performed.
All infections due to group beta-hemolytic streptococci should be treated for at least 10 days.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline in conjunction with penicillin.
Doxycycline has not been studied in pregnant patients. It should not be used in pregnant women unless, in the judgement of the physician, it is essential for the welfare of the patient. Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals, treated early in pregnancy.
Information for Patients
Patients taking doxycycline should be advised:
To avoid excessive sunlight or artificial ultraviolet light while receiving doxycycline and to discontinue therapy if phototoxicity (e.g., skin eruption, etc.) occurs. Sunscreen or sunblock should be considered. (See Warnings)
The use of doxycycline might increase the incidence of vaginal candidiasis.
Patients should be counseled that antibacterial drugs, including doxycycline should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When doxycycline is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by doxycycline or other antibacterial drugs in the future.
Diarrhea is a common problem caused by antibacterial drugs, which usually ends when the antibacterials are discontinued. Sometimes after starting treatment with antibacterial drugs, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibacterial drug. If this occurs, patients should contact their physician as soon as possible.
Laboratory Tests
In venereal diseases when coexistent syphilis is suspected, a dark field examination should be done before treatment is started and the blood serology repeated monthly for at least 4 months. In long-term therapy, periodic laboratory evaluation of organ systems, including hematopoietic, renal, and hepatic studies should be performed.
DRUG INTERACTION
Because tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving tetracycline in conjunction with penicillin.
Barbiturates, carbamazepine, and phenytoin decrease the half-life of doxycycline.
The concurrent use of tetracycline and methoxyflurane has been reported to result in fatal renal toxicity.
Concurrent use of tetracycline may render oral contraceptives less effective.
USE IN SPECIAL POPULATION
Pregnancy
Teratogenic Effects: Pregnancy Category D.
There are no adequate and well-controlled studies on the use of doxycycline in pregnant women. The vast majority of reported experience with doxycycline during human pregnancy is short-term, first trimester exposure. There are no human data available to assess the effects of long-term therapy of doxycycline in pregnant women such as that proposed for treatment of anthrax exposure. An expert review of published data on experiences with doxycycline use during pregnancy by TERIS - the Teratogen Information System - concluded that therapeutic doses during pregnancy are unlikely to pose a substantial teratogenic risk (the quantity and quality of data were assessed as limited to fair), but the data are insufficient to state that there is no risk.
(See above Warnings about use during tooth development.)
Doxycycline Intravenous has not been studied in pregnant patients. It should not be used in pregnant women unless, in the judgment of the physician, it is essential for the welfare of the patient.
Results of animal studies indicate that tetracyclines cross the placenta, are found in fetal tissues and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Evidence of embryotoxicity has also been noted in animals treated early in pregnancy.
Labor and Delivery
The effect of tetracyclines on labor and delivery is unknown.
Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals to evaluate carcinogenic potential of doxycycline have not been conducted. However, there has been evidence of oncogenic activity in rats in studies with the related antibacterial drugs, oxytetracycline (adrenal and pituitary tumors), and minocycline (thyroid tumors). Likewise, although mutagenicity studies of doxycycline have not been conducted, positive results in in vitro mammalian cell assays have been reported for related antibacterial drugs (tetracycline, oxytetracycline).
Doxycycline administered orally at dosage levels as high as 250 mg/kg/day had no apparent effect on the fertility of female rats. Effect on male fertility has not been studied.
Nursing Mothers
Tetracyclines are excreted in human milk, however, the extent of absorption of tetracyclines, including doxycycline, by the breastfed infant is not known. Short-term use by lactating women is not necessarily contraindicated; however, the effects of prolonged exposure to doxycycline in breast milk are unknown. Because of the potential for adverse reactions in nursing infants from doxycycline, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Tetracyclines are present in the milk of lactating women who are taking a drug in this class.
Paediatric population
The use of Doxycycline Intravenous in children under 8 years is not recommended because safe conditions for its use have not been established.
(See above Warnings about use during tooth development.)
As with other tetracyclines, doxycycline forms 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.
For all pediatric patients weighing less than 45 kg with severe or life-threatening infections, the recommended dosage is 2.2 mg/kg of body weight administered every 12 hours. Children weighing 45 kg or more should receive the adult dose.
EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
No studies have been performed on the ability to drive and use machines. However, patients must refrain from driving or operating machinery.
UNDESIRABLE EFFECTS
The followings are adverse drug reactions have been reported with doxycycline.
Gastrointestinal: Anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, and inflammatory lesions (with monilial overgrowth) in the anogenital region.
Hepatotoxicity has been reported rarely. These reactions have been caused by both the oral and parenteral administration of tetracyclines.
Skin: Maculopapular and erythematous rashes. Exfoliative dermatitis has been reported but is uncommon. Photosensitivity is discussed above. (See Warnings.)
Renal toxicity: Rise in BUN has been reported and is apparently dose related. (See Warnings.)
Immune: Hypersensitivity reactions including urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus, and drug rash with eosinophilia and systemic symptoms (DRESS).
Bulging fontanels in infants and benign intracranial hypertension in adults have been reported in individuals receiving full therapeutic dosages. These conditions disappeared rapidly when the drug was discontinued.
Blood: Hemolytic anemia, thrombocytopenia, neutropenia and eosinophilia have been reported.
When given over prolonged periods, tetracyclines have been reported to produce brownblack microscopic discoloration of thyroid glands. No abnormalities of thyroid function studies are known to occur.
OVERDOSE
In case of overdosage, discontinue medication, treat symptomatically and institute supportive measures. Dialysis does not alter serum half-life and thus would not be of benefit in treating cases of overdosage.
PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Tetracyclines.
The tetracyclines, including doxycycline, are mainly bacteriostatic and are thought to exert antimicrobial effects by the inhibition of protein synthesis. Bacteriostatic antibiotics suppress the growth of bacteria, or keep them in the stationary phase of growth. The tetracyclines, including doxycycline, have a similar antimicrobial spectrum of activity against a variety of gram-positive and gram-negative microorganisms, treating numerous infectious diseases. Cross-resistance of these microorganisms to tetracyclines is a common occurrence. Doxycycline shows favorable intra-cellular penetration, with bacteriostatic activity on a wide range of bacteria.
Doxycycline is primary bacteriostatic and thought to exert its antimicrobial effect by the inhibition of protein synthesis. Doxycycline is active against a wide range of gram-positive and gram-negative organisms.
Mechanism of Action
Doxycycline inhibits bacterial protein synthesis by binding to the 30S ribosomal subunit. Doxycycline has bacteriostatic activity against a broad range of Gram-positive and Gram-negative bacteria.
Tetracyclines such as doxycycline are thought to inhibit translation by binding to the 16S rRNA portion of the ribosome, preventing binding of tRNA to the RNA-30S bacterial ribosomal subunit, which is necessary for the delivery of amino acids for protein synthesis. As a result of the above actions, the initiation of protein synthesis by polyribosome formation is blocked. This stops the replication of bacteria and produces a bacteriostatic effect.
Pharmacokinetic Properties
Tetracyclines are readily absorbed and are bound to plasma proteins in varying degrees. They are concentrated by the liver in the bile, and excreted in the urine and feces at high concentrations and in a biologically active form.
Following a 100 mg single dose administered in a concentration of 0.4 mg/mL in a one-hour infusion, normal adult volunteers averaged a peak of 2.5 mcg/mL, while 200 mg of a concentration of 0.4 mg/mL administered over two hours average a peak of 3.6 mcg/mL.
Excretion of doxycycline by the kidney is about 40 percent/72 hours in individuals with normal function (creatinine clearance about 75 mL/min). This percentage of excretion may fall as low as 1 to 5 percent/72 hours in individuals with severe renal insufficiency (creatinine clearance below 10 mL/min). Studies have shown no significant difference in serum half-life of doxycycline (range 18 to 22 hours) in individuals with normal and severely impaired renal function.
Hemodialysis does not alter this serum half-life of doxycycline
INCOMPATIBILITY
Doxycycline solution for injection must not be mixed with other medicinal products.
STORAGE INSTRUCTIONS
Store below 25°C. Protected from light.
Keep medicine out of reach of children.
SHELF LIFE : 24 months
PRESENTATION
This Pack contains Injection 100mg vial and Accompanying with Sterile Water for Injection IP 10 mL.

Manufactured by :
Protech Telelinks
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