

Vibramycin® (doxycycline)

Description: Vibramycin (doxycycline) is a new broad-spectrum antibiotic synthetically derived from tetracycline, available as Vibramycin Monohydrate (doxycycline monohydrate) and Vibramycin Hyclate (doxycycline hydrochloride hemihydrate). The chemical designation of this light-yellow crystalline powder is 4,6-dioxo-5-oxo-tetracycline. Vibramycin (doxycycline) possesses the following useful properties not observed with previously available tetracyclines: its greater absorption from the gastrointestinal tract and its capability for once-a-day maintenance dosages.

Actions: Vibramycin (doxycycline) is a broad-spectrum antibiotic and has been shown to be active *in vitro* against both gram-positive and gram-negative organisms. *In vivo* animal protection studies (PD₅₀) in mice and extensive clinical use in man have verified that Vibramycin (doxycycline) is a potent and effective antibiotic.

Vibramycin (doxycycline) differs from other tetracyclines by virtue of its greater absorption after oral administration and prolonged duration of *in vivo* antibacterial activity. Because of these factors, therapeutic effectiveness can be achieved by once-a-day maintenance dosages. Vibramycin (doxycycline) in therapeutic doses, given once daily, will produce serum activity usually persisting for 24 to 36 hours after discontinuation of therapy.

Vibramycin (doxycycline) has been administered to 60 normal volunteers for 70 days at a dose of 100 mg/day without evidence of increased toxicity.

Studies reported to date indicate that the absorption of Vibramycin (doxycycline) is not notably influenced by the ingestion of food or milk, which do impair the absorption of certain other tetracyclines.

Animal Pharmacology: As with other tetracyclines, at doses greater than those recommended for human usage, Vibramycin (doxycycline) produces discoloration of animal thyroid glands. Careful monitoring of animals and humans has disclosed no abnormalities of thyroid function studies. Also, as with other tetracyclines, at relatively high oral doses, evidence of hepatotoxicity has been noted in dogs and signs of gastrointestinal intolerance have been seen in both dogs and monkeys.

Indications: Vibramycin (doxycycline) has been found clinically effective in the treatment of a variety of infections caused by susceptible strains of gram-positive and gram-negative bacteria.

Pneumonia: Single and multiple pneumonia and bronchopneumonia due to susceptible strains of *Pneumococcus*, *Streptococcus*, *Staphylococcus*, *H. influenzae*, and *Klebsiella pneumoniae*.

Other Respiratory Tract Infections: Pharyngitis, tonsillitis, otitis media, bronchitis and sinusitis caused by susceptible strains of β -hemolytic *Streptococcus*, *Staphylococcus*, *Pneumococcus*, and *H. influenzae*. **Genitourinary Tract Infections:** Pyelonephritis, cystitis, urethritis caused by susceptible strains of the *Klebsiella-Aerobacter* group, *E. coli*, *Enterococcus*, *Staphylococcus*, *Streptococcus*, and *Neisseria gonorrhoeae*. Gonococcal urethritis in the male has been effectively treated by Vibramycin (doxycycline) at a dose of 100 mg, i.d. for a single day, but highest cure rates were achieved by a dose of 50 to 100 mg, b.i.d. for two to four days. Adult females with acute gonorrheal infections may require more extended therapy.

Soft-Tissue Infections: Impetigo, furunculosis, cellulitis, abscess, infected traumatic and postoperative wounds, paronychia caused by susceptible strains of *Staphylococcus aureus* and albus, *Streptococcus*, *E. coli*, and the *Klebsiella-Aerobacter* group. In the treatment of soft-tissue infections, indicated surgical procedures should be carried out in conjunction with Vibramycin (doxycycline) treatment.

Since Vibramycin (doxycycline) is a member of the tetracycline series of antibiotics, it may be expected to be useful in the treatment of infections which respond to other tetracyclines. These include infections caused by susceptible organisms, such as:

Ophthalmic Infections: Due to susceptible strains of *Gonococci*, *Staphylococci*, and *H. influenzae*.

Gastrointestinal Infections: Due to susceptible strains of such organisms as *E. histolytica*, pathogenic *E. coli*, and species of *Shigella* and *Salmonella*. **Miscellaneous:** Other infections due to susceptible strains of *Bacteroides*, *Pasteurella*, *Brucella* (in combination with streptomycin), *Pittacusis*, *Listeria*, *Rickettsia*, *Mycoplasma pneumoniae* (Eaton agent, PPLO), *H. parvax*, *S. enterica*, *C. welchii*, *N. meningitidis*, *Spirchetes* (Typhus), *Donaovon*, *granulomatis*, and *prostatitis* and *trigonitis* due to *Proteus* or *Pseudomonas*.

Vibramycin (doxycycline) may be useful in the treatment of acne vulgaris and acne conglobata.

Contraindications: This drug is contraindicated in individuals who have shown hypersensitivity to it.

Product Information

Warnings: If renal impairment exists, even usual doses may lead to excessive systemic accumulation of the drug and possible hepatic toxicity. Under such conditions, lower than usual doses are indicated and if treatment is prolonged, Vibramycin (doxycycline) serum level determinations may be advisable.

As with other tetracyclines, Vibramycin (doxycycline) may form a stable calcium complex in any bone-forming tissue, though *in vitro* it binds calcium less strongly than other tetracyclines.

Though not observed in clinical studies to date and until evidence to the contrary develops, it should be anticipated that, like other tetracyclines, the use of Vibramycin (doxycycline) during tooth development (last trimester of pregnancy, neonatal period, and early childhood) may cause discoloration of teeth (yellow-gray-brownish). This tetracycline effect is more commonly associated with long-term use of the drug, but has been known to occur with treatment of short duration.

Increased intracranial pressure with bulging fontanelles has been observed in infants receiving therapeutic doses of tetracyclines. Although the mechanism of this phenomenon is unknown, the signs and symptoms have disappeared rapidly upon cessation of treatment with no sequelae.

Certain hypersensitive individuals may develop a photosensitivity reaction precipitated by exposure to direct sunlight during the use of this drug. This reaction may also be produced by other tetracycline derivatives and is usually of the photoallergic type. Individuals with a history of photosensitivity reactions should be instructed to avoid exposure to direct sunlight while under treatment with tetracycline drugs, and treatment should be discontinued at first evidence of skin discomfort.

Precautions: The use of antibiotics may occasionally result in overgrowth of non-susceptible organisms. Constant observation of the patient is essential. If a resistant infection appears, the antibiotic should be discontinued and appropriate therapy instituted.

When treating gonorrhea in which lesions of primary or secondary syphilis are suspected, proper diagnostic procedures, including dark-field examinations, should be utilized. In all cases in which concomitant syphilis is suspected, monthly serological tests should be made for at least four months.

Adverse Reactions: Nausea, vomiting, diarrhea, vaginitis, and dermatitis, as well as reactions of an allergic nature, may occur but are rare. Glossitis, stomatitis, proctitis, ancylostoma and discoloration of the nails may rarely occur during tetracycline therapy as with other antibiotics. If severe adverse reactions, individual idiosyncrasy, or allergy occur, discontinue medication.

As with other tetracyclines, elevation of SGOT or SGPT values, anemia, neutropenia, eosinophilia or elevated BUN have been reported, the significance of which is not known at this time.

Dosage: The usual dose of Vibramycin (doxycycline) is 200 mg. on the first day of treatment (administered 100 mg. every 12 hours) followed by a maintenance dose of 100 mg./day. The maintenance dose may be administered as a single dose, or as 50 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 recommended dosage schedule for children weighing 100 pounds or less is 2 mg./lb. of body weight divided into two doses on the first day of treatment, followed by 1 mg./lb. of body weight given as a single daily dose or divided into two doses, on subsequent days. For more severe infections up to 2 mg./lb. of body weight may be used. For children over 100 lbs. the usual adult dose should be used.

Therapy should be continued beyond the time that symptoms and fever have subsided. It should be noted, however, that effective antibacterial levels are usually present 24 to 36 hours following discontinuation of Vibramycin (doxycycline). When used in streptococcal infections, therapy should be continued for 10 days to prevent the development of rheumatic fever or glomerulonephritis.

Studies reported to date indicate that the absorption of Vibramycin (doxycycline), unlike certain other tetracyclines, is not markedly influenced by simultaneous ingestion of food or milk.

Simultaneous administration of aluminum hydroxide gel given with tetracycline antibiotics including Vibramycin (doxycycline) has been shown to decrease absorption.

Supply: Vibramycin Hyclate (doxycycline hyclate) is available as capsules containing doxycycline hyclate equivalent to 50 mg. of doxycycline; bottles of 50. Vibramycin Monohydrate (doxycycline monohydrate) is available as a dry powder for oral suspension containing, when reconstituted, doxycycline monohydrate equivalent to 25 mg. of doxycycline/5 cc. (each teaspoonful), with a pleasant-tasting, raspberry flavor; 2 oz. bottles.

Pfizer LABORATORIES DIVISION
New York, N.Y. 10017