Artwork Document Information	Artwork Type [Please Tick /]	Sign / Stamp
Product : T-DOXYCILLIN TAB [FRONT] SAP No. : Date : 03 September 2025	☐ Unit Box ☑ Leaflet ☐ Aluminium Foil ☐ Generic Box ☐ Outer Box ☐ Fix-A-Form ☐ Sachet ☐ Label ☐ Shipper Carton ☐ Others : _____	

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☑ RA/NPRA Artwork ☐ Recirculation Artwork ☐ Approval Copy Artwork ☐ Clean Copy
☐ Internal Artwork Circulation ☐ Previous Approved Artwork ☐ Draft Artwork
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Remarks

1. Font : Adobe Garamond Pro Regular (Spacing - 5.5pt / Size - 5pt)
2. Dimension : 170mm(w) x 197mm(h)

Colour

Black

Colours shown on this proof are to indicate correct colour separations.

Pharmacode / QR Code / Others Info

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W2	Width of thin code bar	0.35 mm
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DOXYCILLIN

DESCRIPTION

Doxycillin Tablet 100 mg
A 8 mm diameter, round, convex, film-coated, green tablet.
Each tablet contains Doxycycline HCl equivalent to Doxycycline 100 mg.

INDICATIONS

Doxycycline is indicated for treatment of the following infections: Rocky Mountain spotted fever, typhus fever and the typhus group; Q fever, rickettsial pox and tick fevers caused by *Rickettsiae*; Respiratory infections caused by *Mycoplasma pneumoniae*; Psittacosis caused by *Chlamydia psittaci*; Lymphogranuloma venereum, caused by Chlamydia trachomatis; Uncomplicated urethral, endocervical or rectal infections in adults caused by *Chlamydia trachomatis*; Trachoma caused by *Chlamydia trachomatis* although the infectious agent is not always eliminated, as judged by immunofluorescence; Inclusion conjunctivitis caused by *Chlamydia* trachomatis may be treated with oral doxycycline alone or with a combination of topical agents; Granuloma inguinale (donovanosis) caused by *Calymmatobacterium granulomatis*; Early (Stage 1) Lyme disease caused by *Borrelia burgdorferi*; Louse-borne relapsing fever caused by *Borrelia recurrentis*; Tick-borne relapsing fever caused by *Borrelia duttonii*; Non- gonococcal urethritis (NGU) caused by *Ureaplasma urealyticum* (*T-Mycoplasma*).

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

Acinetobacter species; *Bacteroides* species; *Fusobacterium* species; Brucellosis caused by *Brucella* species (in conjunction with streptomycin); Plague caused by *Yersinia pestis*; Tularemia caused by *Francisella tularensis*; Bartonellosis caused by *Bartonella bacilliformis*; *Campylobacter fetus*.

Because many strains of the following groups of microorganisms have been shown to be resistant to tetracyclines, culture and susceptibility testing are recommended.

Doxycycline is indicated for treatment of infections caused by the following gram-negative microorganisms, when bacteriologic testing indicates appropriate susceptibility to the drug: *Shigella* species; Uncomplicated gonorrhea caused by *Neisseria gonorrhoeae*; Respiratory infections caused by *Haemophilus influenzae*; Respiratory and urinary infections caused by *Klebsiella species*; *Escherichia coli*; *Enterobacter aerogenes*; *Moraxella catarrhalis*.

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

Streptococcus species: A certain percentage of strains of *Streptococcus pyogenes* and *Streptococcus faecalis* have been found to be resistant to tetracycline drugs. Tetracyclines should not be used for streptococcal infections unless the organism has been demonstrated to be sensitive.

For upper respiratory infections due to group A beta-hemolytic streptococci, penicillin is the usual drug of choice, including prophylaxis of rheumatic fever. This includes:

Upper respiratory tract infections caused by *Streptococcus pneumoniae*; Respiratory, skin and soft-tissue infections caused by *Staphylococcus aureus*. Tetracyclines are not the drug of choice in the treatment of staphylococcal infections. When penicillin is contraindicated, doxycycline is an alternative drug in the treatment of: Actinomycosis caused by *Actinomyces* species; Infections caused by *Clostridium* species; Syphilis caused by *Treponema pallidum* and yaws caused by *Treponema pertenue*; Listeriosis caused by *Listeria monocytogenes*; Vincent's infection (acute necrotizing ulcerative gingivitis) caused by *Leptotrichia buccalis* (formerly, *Fusobacterium fusiform*).

Adjunctive treatment
In acute intestinal amebiasis, doxycycline may be a useful adjunct to amebicides. In severe acne caused by *acne vulgaris*, doxycycline may be useful adjunctive therapy.

Treatment and Prophylaxis
Doxycycline is indicated for the prophylaxis and treatment of the following infections: Malaria caused by *Plasmodium falciparum* (in areas with chloroquine-resistant *P. falciparum*). Leptospirosis caused by genus *Leptospira*. Cholera caused by *Vibrio cholerae*.

Prophylaxis
Doxycycline is indicated as prophylaxis in the following conditions: Scrub typhus caused by *Rickettsia tsutsugamushi*; Traveler's diarrhea caused by enterotoxigenic *Escherichia coli*

PHARMACODYNAMICS

Doxycycline is taken up into sensitive bacterial cells by an active transport process. Once within the cell it binds reversibly to the 30S subunit of the ribosome, preventing the binding of aminoacyl transfer RNA (tRNA) to the messenger RNA (mRNA) ribosome complex and inhibiting protein synthesis and hence cell growth. Bacterial cell wall synthesis is not inhibited. Although doxycyline also inhibits protein synthesis in mammalian cells, it is not actively taken up, permitting selective effects on the infecting organism.

PHARMACOKINETICS

Doxycycline, a lipophilic analogue of tetracycline, is readily and almost completely absorbed (more than 90%) from the gastrointestinal tract and absoption is not significantly affected by the presence of food in the stomach. Admimistration of doxycycline 200 mg produces peak concentrations of about 2.6 mcg/mL 2 hours after ingestion, falling to 1.45mcg/mL at 24 hours. About 80%-95% of doxycyline is bound to plasma proteins. It is widely distributed throughout the body tissues and fluids, including bile, sinus secretions, and synovial, pleural, ascitic, and gingival crevicular fluids.

Cerebrospinal fluid (CSF) concentrations are relatively low, but may be raised if the meninges are inflamed. Concentrations in gingival crevicular fluid may be 3-7 times serum concentrations. Therapeutic concentrations are achieved in the eye while prostatic concentrations are approximately 60% of serum concentrations. Doxycycline is retained at sites of new bone formation and recent calcification, liver, spleen, tumour and in developing teeth.
Doxycycline appears in the milk of nursing mothers where concentrations may be 60% or more of those in the plasma. It diffuses across the placenta and appears in the foetal circulation in concentrations of about 25%-75% of those in the maternal blood. The normal half-life of doxycycline has been reported to be between 12-22 hours, regardless of renal function. Forty percent of a dose is excreted in the urine and urinary excretion is increased if urine is alkalinised. Doxycycline is partially inactivated by hepatic metabolism and is extensively excreted via the digestive tract where concentrations in the bile is 5-25 times those in plasma.

Gastrointestinal secretion is an important route of excretion when doxycycline is administered to patients with impaired renal function or azotemia. Doxycycline is not removed by hemodialysis or peritoneal dialysis.

DOSAGE

It must be remembered that the usual dosage and frequency of administration of doxycycline differs from that of most other tetracyclines. Exceeding the recommended dosage may result in an increased incidence of side effects. Therapy should be continued at least 24 to 48 hours after symptoms and fever have subsided. When used in streptococcal infections, therapy should be continued for 10 days to prevent the development of rheumatic fever or glomerulonephritis.

The usual dose of doxycycline in adults is 200 mg on the first day of treatment (administered as a single dose or as 100 mg every 12 hours) followed by a maintenance dose of 100 mg/day (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), 200 mg daily should be given throughout the treatment period.

For children above 8 years of age: The recommended dosage schedule for children weighing 45 kg or less is 4.4 mg/kg of body weight (given as a single daily dose or divided into two doses on the first day of treatment), followed by 2.2 mg/kg of body weight (given as a single daily dose or divided into two doses), on subsequent days. For more severe infections, up to 4.4 mg/kg of body weight may be used. For children over 45 kg, the usual adult dose should be used.

Tick- and louse-borne relapsing fevers and louse- borne typhus have been successfully treated with a single oral dose of 100 or 200 mg, according to severity. As an alternative to reduce the risk of persistence or relapse of tick-borne relapsing fever, doxycycline 100 mg every 12 hours for seven days is recommended.

Early Lyme disease (Stage 1): Doxycycline 100 mg orally twice daily for 14-60 days, according to clinical signs, symptoms and response.

Uncomplicated urethral, endocervical or rectal infection in adults caused by *Chlamydia trachomatis*: 100 mg, by mouth, twice daily for seven days.

Non-gonococcal urethritis (NGU) caused by *Chlamydia trachomatis* or *Ureaplasma* urealyticum: 100 mg, by mouth, twice daily for seven days.

Lymphogranuloma venereum caused by *Chlamydia trachomatis*: Doxycycline 100 mg orally twice daily for a minimum of 21 days.

Uncomplicated gonococcal infections of the cervix, rectum or urethra where gonococci remain fully sensitive: Doxycycline 100 mg by mouth twice daily for seven days plus co-treatment with an appropriate cephalosporin or quinolone is recommended, such as the following: Cefixime 400 mg orally in a single dose or ceftriaxone 125 mg intramuscularly (IM) in a single dose or ciprofloxacin 500 mg orally in a single dose or ofloxacin 400 mg orally in a single dose.

Uncomplicated gonococcal infections of the pharynx, where gonococci remain fully sensitive: Doxycycline 100 mg by mouth twice daily for seven days, plus co-treatment with an appropriate cephalosporin or quinolone is recommended, such as the following: ceftriaxone 125 mg IM in a single dose or ciprofloxacin 500 mg orally in a single dose or ofloxacin 400 mg orally in a single dose.

Primary and secondary syphilis: Non-pregnant penicillin-allergic patients who have primary or secondary syphilis can be treated with the following regimen: Doxycycline 100 mg orally twice daily for two weeks, as an alternative to penicillin therapy.

Latent and tertiary syphilis: Non-pregnant penicillin-allergic patients who have tertiary or secondary syphilis can be treated with the following regimen: Doxycycline 100 mg orally twice daily for two weeks, as an alternative to penicillin therapy if the duration of the infection is known to have been less than one year. Otherwise, doxycycline should be administered for four weeks.

Acute pelvic inflammatory disease (PID):

Inpatient -- Doxycycline 100 mg every 12 hours, plus cefoxitin 2 g IV every six hours or cefotetan 2 g IV every 12 hours for at least four days and at least 24 to 48 hours after patient improves. Then continue doxycycline 100 mg by mouth twice daily to complete 14 days total therapy.

Out-Patient -- Doxycycline 100 mg by mouth twice daily for 14 days as adjunctive therapy with ceftriaxone 250 mg IM once or cefoxitin 2 g IM, plus probenecid 1 g orally in a single dose concurrently once, or other parenteral third- generation cephalosporin (e.g., ceftizoxime or cefotaxime).

Acne Vulgaris: 50-100 mg daily for up to 12 weeks.

For treatment of chloroquine-resistant falciparum malaria: 200 mg daily for at least seven days. Due to the potential severity of the infection, a rapid- acting schizonticide such as quinine should always be given in conjunction with doxycycline; quinine dosage recommendations vary in different areas.

For prophylaxis of malaria: 100 mg daily in adults; for children over 8 years of age the dose is 2 mg/kg given once daily up to the adult dose. Prophylaxis can begin 1-2 days before travel to malarious areas. It should be continued daily during travel in the malarious areas and for four weeks after the traveler leaves the malarious area.

For the treatment and selective prophylaxis of cholera in adults: 300 mg in a single dose.

For the prevention of scrub typhus: 200 mg as a single oral dose.
For the prevention of traveler's diarrhea in adults: 200 mg on the first day of travel (administered as a single dose or as 100 mg every 12 hours) followed by 100 mg daily throughout the stay in the area.
Data on the use of the drug prophylactically are not available beyond 21 days.

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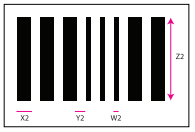

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For the prevention of Leptospirosis: 200 mg orally on a weekly basis throughout the stay in the area and 200 mg at the completion of the trip. Data on the use of the drug prophylactically are not available beyond 21 days.

For the treatment of Leptospirosis: 100 mg orally twice daily for seven days.

Studies to date have indicated that administration of doxycycline at the usual recommended doses does not lead to excessive accumulation of the antibiotic in patients with renal impairment.

OVERDOSAGE

No information available for the treatment of tetracycline overdosage. However, in the event of hypersensitivity reaction to Doxycillin, the medicine must be stopped immediately and symptomatic and supportive therapy instituted. Up-to-date information on treatment of overdose can be obtained from The National Poison Centre University Sains Malaysia.

PREGNANCY AND LACTATION

Pregnancy and Reproduction. Tetracycline crosses the placenta; use is not recommended during the last half of pregnancy since tetracyclines may cause permanent discoloration of teeth, enamel hypoplasia, and inhibition of skeletal growth in the foetus. In addition, fatty infiltration of the liver may occur in pregnant women. (FDA Pregnancy Category D).

Breast-feeding. Tetracycline are excreted in breast milk; although tetracyclines may form nonabsorbable complexes with breast-milk calcium, use is not recommended because of the possibility of their causing permanent discoloration of teeth, enamel hypoplasia, inhibition of skeletal growth, photosensitivity reactions and oral and vaginal thrush in infants.

SIDE EFFECTS

Gastrointestinal effects like diarrhoea, nausea or vomiting can follow oral administration of Doxycillin due to irritation of the mucosa. Other common side effects include dry mouth, glossitis, stomatitis and dysphagia; CNS toxicity and photosensitivity. Tetracyclines are deposited in deciduous and permanent teeth during their formation, causing discoloration and enamel hypoplasia. They are also deposited in calcifying areas in bone and the nails and interfere with bone growth when given in therapeutic doses to young infants or pregnant women. Oral candidiasis, vulvovaginitis and pruritus ani occur occasionally, mainly due to overgrowth of Candida albicans. There may also be overgrowth of resistant coliform organisms, such as Pseudomonas and Proteus spp., causing diarrhoea.

More serious superinfection with resistant staphylococci causing enterocolitis and also pseudomembranous colitis have occasionally been reported. Hyperttrophy of the papilla (darkened or discoloured tongue) occurs less frequently. An increased intracranial pressure and bulging fontanelles in infants has been reported. Hypersensitivity to tetracyclines is much less common but do occur; anaphylaxis has occurred very rarely. Abnormal pigmentation of the skin and eye, hemolytic anemia, eosinophilia, neutropenia, thrombocytopenia and hypoprothrombinemia has occurred rarely. Permanent discolouration of the cornea has been reported in infants born to mothers given tetracycline in high doses during pregnancy. Myopia in patients taking the drug may be due to transient hydration of the lens. Severe and sometimes fatal hepatotoxicity associated with fatty changes in the liver and pancreatitis has been reported in pregnant women and in patients with renal function impairment.

Immune system disorders:
Frequency not known: Jarisch- Herxheimer reaction (see Section Warnings and Precautions)

Skin and subcutaneous tissue disorders:
Frequency 'rare': Fixed eruption

CONTRAINDICATION

Doxycycline is contraindicated in patients with a history of hypersensitivity to any tetracyclines as cross-sensitivity may occur. It should be avoided in patients with systemic lupus erythematosus. Doxycycline is partially metabolised in the liver; hepatic function impairment may prolong the elimination half-life. It should not be used during pregnancy due to the risk of hepatotoxicity in the mother as well as the effects on the developing foetus. Use in pregnancy, potentially during breast-feeding and in children up to the age of 8, may result in impaired bone growth and permanent discolouration of the child's teeth.

DRUG INTERACTIONS

Potentially hepatotoxic drugs including erythromycin, chloramphenicol, isoniazid and sulphonamides should not be given concomitantly. The absorption of tetracyclines is reduced by divalent and trivalent cations such as aluminium, bismuth, calcium, iron, magnesium and zinc. Concomitant administration of tetracyclines with antacids, sucralfate, iron and calcium supplements, choline and magnesium salicylates, some foods such as milk and dairy products, other preparations containing such cations and sodium bicarbonate result in formation of nonabsorbable complexes. Concurrent use with cholestyramine and colestipol may result in binding of oral tetracyclines, thus impairing their absorption. Phenytoin, carbamazepine and barbiturates may decrease doxycycline serum concentrations due to induction of microsomal enzyme activity; adjustment of doxycycline dosage or substitution of another tetracycline may be necessary. Doxycycline may produce increased concentrations of lithium, digoxin, theophylline and oral anticoagulants. There has been reports of tetracyclines increasing the toxic effects of ergot alkaloids and methotrexate.

Long term use of tetracyclines with estrogen-containing oral contraceptives may result in reduced contraceptive reliability and increased incidence of breakthrough bleeding. Use of an alternate or additional method of contraception is advisable. Since bacteriostatic drugs may interfere with the bactericidal effects of penicillins in the treatment of meningitis or in other situations where a rapid bactericidal effect is necessary, it is best to avoid concurrent therapy.

PRECAUTION

Care should be taken if doxycycline is given to patients with impaired liver function and high doses should be avoided. Patients who may be exposed to direct sunlight should be warned of the risk of photosensitivity. Care is advisable in patients with myasthenia gravis, who may be at risk of neuromuscular blockade. Doxycillin may produce false-positive elevations of urinary catecholamines because of interfererence of fluorescence in the Hingerty method. Serum concentrations of alanine aminotransferase (ALT [SGPT]), alkaline phosphatase amylase, aspartate aminotransferase (AST [SGOT]) and bilirubin may be increased. Some patients with spirochete infections may experience a Jarisch - Herxheimer reaction shortly after doxycycline treatment is started. Patients should be reassured that this is a usually self-limiting consequence of antibiotic treatment of spirochete infections.

Geriatrics. No information is available on the relationship of age to the effects of tetracyclines in geriatric patients.

PRESENTATION

Doxycillin Tablet 100 mg } 50 x 10's, 10 x 10's
Not all pack sizes are available locally

STORAGE CONDITIONS AND USER INSTRUCTIONS

Store in a dry place below 30°C.
Protect from light.
Keep out of reach of children.
Jauhi daripada kanak-kanak.
Shelf life: please refer to outer package.
Route of administration: Oral

Take at regular intervals. Complete the prescribed course unless otherwise directed. Take with a full glass (240 mL) of water in an upright position to avoid esophageal ulceration and to decrease gastrointestinal irritation.
Maybe taken with food or milk if gastrointestinal irritation occurs.
Take at least 1 hour before retiring to bed.
Avoid too much sun or use of sunlamp.

Product Registration Holder:
Duopharma Manufacturing (Bangi) Sdn. Bhd.
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Revised Date: September 2025

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