Approved Package Insert for Medicines for Human Use:

DOXYTET

SCHEDULING STATUS

S4

NAME OF THE MEDICINE

DOXYTET (CAPSULES)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule content contains:

Doxycycline hyclate equivalent to doxycycline 100 mg

Other ingredients: Magnesium stearate, microcrystalline cellulose (pH 102), sodium lauryl sulphate.

Capsule shell: sunset yellow C.I 15985, patent blue VC.I. 42051, quinoline yellow C.I. 47005, titanium dioxide C.I. 77891 and dry gelatin.

Sugar free.

For the full list of excipients, see section 6.1.

PHARMACOLOGICAL CLASSIFICATION

A 20.1.1 Broad spectrum antibiotics

PHARMACOLOGICAL ACTION:

Mechanism of Action:

Doxycycline is bacteriostatic antibiotic which inhibits bacterial growth by binding to the 30S ribosomal sub-unit with consequent misreading of information for protein synthesis.

Antimicrobial Spectrum:

Doxycycline is effective in vitro against the following organism (in vitro activity does not necessarily imply in vivo efficacy) : Vibrio cholerae, Ureaplasma urealyticum, Mycoplasma pneumoniae, Chlamydia trachomatis, Chlamydia psittaci, Borrelia recurrentis, Calymmatobacterium granulomatis, Borrelia burgdorferi, penicillin-sensitive Neisseria gonorrhoea and Rickettsiae.

It is also effective against the following organisms in vitro: Haemophilus ducreyi, Actinomyces israelii, Francisella tularensis, Treponema pertenue.

The resistant pathogens include Staphylococci, Enterococci, Proteus vulgaris, Fungi and yeasts (except Actinomyces), Pseudomonas aeroginosa (all strains), E. coli, Shigella and Streptococcus.

PHARMACOKINETICS

Doxycycline hyclate is almost completely (90 – 100%) absorbed from the gastrointestinal tract and the absorption is not significantly different whether doxycycline is administered on an empty stomach or after a meal. After a 200 mg oral dose of doxycycline, a mean peak plasma concentration of 2,6 microgram/ml is reached by the end of two hours. About 80-95% of doxycycline is bound to plasma proteins.

Doxycycline is widely distributed in body tissues and fluids and is concentrated by the liver in bile. It is partially inactivated by hepatic metabolism. As doxycycline is partially metabolised in the liver, hepatic function impairment may prolong the elimination half-life. Doxycycline is excreted in the urine and faeces at high concentrations in a biologically active form. It is excreted in the faeces as a conjugate.

About 40% of an administered dose is excreted in the urine. The plasma elimination half - life varies from 15 – 25 hours. In patients with severe renal insufficiency excretion of doxycycline is reduced. The plasma half-life of doxycycline does not alter in renal failure;

this is because it is also eliminated through the biliary tract and with the faeces under this circumstances. There is no evidence suggesting that doxycycline accumulates significantly in patients with impaired renal function.

INDICATIONS

Infections caused by susceptible strains of pathogens:

Upper and lower respiratory tract infections: Sinusitis, pharyngitis, Mycoplasma Pneumonia, psittacosis and chronic bronchitis.

Genito-urinary tract infections: Non specified urethritis (Only if the strain is sensitive), lymphogranuloma venereum, chancroid and granuloma inguinale, gonococcal salpingitis, epididymitis, acute epididymoorchitus, endocervical infections, syphilis and gonorrhoea (in case of penicillin allergy).

Soft tissue: Acne

Ophthalmic: Trachoma and inclusion conjunctivitis.

Intestinal: Cholera, Whipple's disease and tropical sprue.

Miscellaneous: Rickettsial infections, brucellosis, tularemia, actinomycosis, Lyme disease, yaws, relapsing fever, leptospirosis during the early infective phase.

Malaria prophylaxis: For short-term prophylaxis of malaria in area where a high level of chloroquine resistance has been reported and the traveller who can not tolerate mefloquine or other agents for the prophylaxis of malaria.

CONTAINDICATIONS:

- Allergy to any tetracycline.
- Doxycycline should not be given in pregnancy as it crosses the placenta and get deposited in foetal bones and teeth.
- Pregnant women are particularly susceptible to severe doxycycline-induced liver

damage.

- Should not be given to lactating women or to children younger than 12 years of age as permanent discoloration of the child's teeth may occur.
- Should not be given to patients with systemic lupus erythematosus.

WARNING AND SPECIAL PRECAUTIONS:

- Use with care in patients with liver function impairment.
- Frail or elderly patients are susceptible to the hepatotoxic and anti-anabolic effect.
- Do not use concomitantly with hepatotoxic medicines.
- Symptoms of Myasthenia gravis may be aggravated.
- Photosensitivity may occur (see side-effects and special precautions)
- Raised intracranial pressure may occur particularly in infants and especially if Vitamin A or other retinoids are given concomitantly.

Precautions:

Doxycycline is not indicated for treating commonly occurring infections in children under 12 years of age.

Increased severity of uraemia and hepatotoxicity in patients with renal disease when given high doses.

Vitamin deficiencies may occur.

A Jarisch-Heryxheimer -like reaction has been reported in patients with relapsing fever treated with doxycycline.

The use of expired doxycycline may lead to Fanconi-type syndrome, which is characterised by polyuria and polydipsia with nausea, vomiting, proteinuria, glucosuria, acidosis, aminociduria, hypophosphatemia and hypocalcemia.

In the elderly a negative nitrogen balance may be induced.

Interaction:

- Absorption of doxycycline is diminished by milk, alkalis, aluminium hydroxide and other di-and trivalent cations such as calcium, iron and magnesium, if they are given concomitantly.
- Doses of anticoagulants may need to be reduced if given concomitantly.
- Penicillin should not be given concomitantly with doxycycline as antagonism in action may occur.
- Doxycycline may diminish the effectiveness of oral contraceptives.
- Methoxyflurane: Serious nephrotoxicity may follow concomitant use.

Laboratory value alterations:

SGOT, SGPT, alkaline phosphatase, serum amylase, serum bilirubin and urinary catecholamine levels may be increased when patients are on doxycycline.

PREGNANCY AND LACTATION:

DOXYTET must not be taken during pregnancy or to be used by mothers who are breastfeeding their babies (see **"CONTRAINDICATIONS"**).

DOSAGE AND DIRECTIONS FOR USE:

Should be taken either one hour before meals or two hours after meals.

Should be taken with adequate liquid to avoid lodging of capsules in the distal oesophagus as this may result in local corrosive irritation and ulceration.

Usual dose for the commonly occurring infections, depending	100 mg every twelve hours.

on the severity of the infection.	
Uncomplicated gonorrhoea, non-gonococcal urethral, endocervical and rectal infections	100 mg every twelve hours for seven days.
Malaria prophylaxis:	For adults, the recommended dose in 100 mg daily. For children over 8 years of age, the recommended dose is 2 mg/kg given once daily up to the adult dose. Prophylaxis should begin 1 – 2 days before travel to the malaria area. Prophylaxis should be continued daily during travel in the malaria area and for 4 weeks after the traveller leaves the malaria area.

Readjustment of doses is not required in renal impairment.

SIDE EFFECTS:

Gastrointestinal : Nausea, vomiting, diarrhoea, glossitis, dysphagia related to oesophagitis enterocolitis.

Secondary-fungal overgrowth (Candida albicans): Oral candidiasis, vulvovaginitis, pruritis ani.

Secondary bacterial overgrowth infections may occur: Resistant conliform organism such as proteus spp. May cause diarrhoea. *Pseudomembranous colitis due to Clostridium*

difficile may occur, super-infection due to resistant staphylococci may cause fulminating enteritis.

Blood abnormalities: Haemolytic anaemia, eosinophilia, neutropenia, thrombocytopenia.
Allergic (hypersensitivity) reactions: Urticaria, maculopapular and erythematous rashes, exfoliative dermatitis, exacerbation of systemic lupus erythematosus, pericarditis, Henoch-Schonlein purpura (anaphylactoid purpura), angioneurotic oedema, anaphylaxis.
Photosensitivity of the skin and nails: Onycholysis and nail discoloration may occur.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See “Side-effects and special precautions”. Treatment is symptomatic and supportive.

IDENTIFICATION:

Opaque, hard gelatin, self -locked capsules of size ‘2’ with green cap and green body, containing a yellow granular powder.

PRESENTATION:

Carton containing 10 or 100 capsules in blister strips [Al foil/PVC (PVDC coated)] of 10 capsules each.
Carton containing 28 capsules in blister strips [Al foil/PVC (PVDC coated)] of 14 capsules each.
Milky white HDPE bottle containing 100 capsules.
Milky white HDPE bottle containing 500 capsules.
Opaque white HDPE round shape container containing 1 000 capsules.
White polyethylene polymer plastic Patient Ready Packs containing 14 or 28 capsules.

STORAGE INSTRUCTIONS:

Store at or below 25 ºC, protected from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

32/20.1.1/0254

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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