SUMMARY OF PRODUCT CHARACTERISTICS DOXYLINE CAPSULES

1 Name of the Medicinal Product

1.1 Proprietary Name

Doxyline Capsules 100mg

1.2 Strength

Each capsule contains;
Doxycycline hyclate
Equivalent to doxycycline……100mg

1.3 Pharmaceutical form

Capsules

2 Qualitative and Quantitative Composition

2.1 Qualitative declaration

Name of active ingredients
Doxycycline

2.2 Quantitative declaration

Name of ingredient	**Quantity/Tablet (mg)**
Doxycycline	100mg

Excipients with known effect:

Qualitative declaration

Name of Excipient
Lactose BP

Quantitative declaration

Name of Excipient	Quantity/tablet (mg)
Lactose BP	30.000mg

For full list of Excipients, see section 6.1

3 Pharmaceutical Form

Capsules

Product description
Creamish white to light orange, free-flowing powder, free from visible evidence of contamination, with fruity odour.

4 Clinical Particulars

4.1 Therapeutic Indications

- 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 and certain other micro-organisms.
- Doxycycline Capsules are indicated for prophylaxis in the following conditions: Scrub typhus, travellers' diarrhoea (enterotoxigenic Escherichia coli), leptospirosis.

4.2 Posology and Method of administration

Posology

Posology Adults

The usual dosage of Doxycycline for the treatment of acute infections in adults is 200mg on the first day (as a single dose or in divided doses) followed by a maintenance dose of 100mg/day. In the management of more severe infections (particularly chronic infections of the urinary tract), 200mg daily should be given throughout the treatment.

Method of Administration

The capsules should be swallowed with plenty of fluid in either the resting or standing position and well before going to bed for the night to reduce the likelihood of oesophageal irritation and ulceration.

If gastric irritation occurs, it is recommended that Doxycycline Capsules be given with food or milk.

4.3 Contraindication

Persons who have shown hypersensitivity to doxycycline or any of the excipients listed or to any of the tetracyclines.

Pregnancy

Doxycycline is contraindicated in pregnancy. It appears that the risks associated with the use of tetracyclines during pregnancy are predominantly due to effects on teeth and skeletal development.

Nursing mothers

Tetracyclines are excreted into milk and are therefore contraindicated in nursing mothers.
Children under 12 years of age

Doxycycline is contraindicated in children under the age of 12 years. As with other tetracyclines.

4.4 Special warnings and precautions for use

Use in patients with impaired hepatic function

Doxycycline should be administered with caution to patients with hepatic impairment or those receiving potentially hepatotoxic drugs.
Use in patients with renal impairment

Excretion of doxycycline by the kidney is about 40%/72 hours in individuals with normal renal function. This percentage excretion may fall to a range as low as 1-5%/72 hours in individuals with severe renal insufficiency (creatinine clearance below 10ml/min).
Photosensitivity

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines, including doxycycline.

Patients likely 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.
Microbiological overgrowth

The use of antibiotics may occasionally result in overgrowth of non-susceptible organisms including Candida. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.
Oesophagitis

Instances of oesophagitis and oesophageal ulcerations have been reported in patients receiving capsule and tablet forms of drugs in the tetracycline class, including doxycycline. Most of these patients took medications immediately before going to bed or with inadequate amounts of fluid.
Bulging fontanelles

Bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults have been reported in individuals receiving full therapeutic dosages. These conditions disappeared rapidly when the drug was discontinued.
Porphyria

There have been rare reports of porphyria in patients receiving tetracyclines.
Venereal disease
When treating venereal disease, where co-existent syphilis is suspected, proper diagnostic procedures, including dark-field examinations, should be utilised. In such cases monthly serological tests should be performed for at least four months.

Beta-haemolytic streptococci infections

Infections due to Group A beta-haemolytic streptococci should be treated for at least 10 days.
Myasthenia gravis

Due to a potential for weak neuromuscular blockade, care should be taken in administering tetracyclines to patients with myasthenia gravis.
Systemic lupus erythematosus

Tetracyclines can cause exacerbation of systemic lupus erythematosus (SLE). Methoxyflurane
Caution is advised in administering tetracyclines with methoxyflurane.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of doxycycline may be impaired by concurrently administered antacids containing aluminium, calcium, magnesium or other drugs containing these cations; oral zinc, iron salts or bismuth preparations. Dosages should be maximally separated.

4.6 Fertility, Pregnancy and lactation

Doxycycline is contraindicated in pregnancy and lactation.
It has been shown to have no impact on fertility among men and women of childbearing age.

4.7 Effects on ability to drive and use machines

Visual disturbances such as blurring of vision may occur during treatment with doxycycline and in such cases; patients must be informed to refrain from driving or operating machinery.

4.8 Undesirable effects

The following adverse reactions have been observed in patients receiving tetracyclines, including doxycycline.
<u>Infections and infestations</u>

Superinfection: As with all antibiotics, overgrowth of non-susceptible organisms may cause candidiasis, glossitis, staphylococcal enterocolitis, pseudomembranous colitis (with Clostridium difficile overgrowth) and inflammatory lesions (with candidal overgrowth) in the anogenital region.

Blood and lymphatic system disorders
Haemolytic anaemia, thrombocytopenia, neutropenia, porphyria, and eosinophilia have been reported with tetracyclines.
Immune system disorders
Hypersensitivity reactions, including anaphylactic shock, anaphylaxis, anaphylactoid reaction, anaphylactoid purpura, hypotension, pericarditis, angioneurotic oedema, exacerbation of systemic lupus erythematosus, dyspnoea, serum sickness, peripheral oedema, tachycardia and urticaria.
Endocrine disorders
When given over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discolouration of thyroid tissue. No abnormalities of thyroid function are known to occur.
Nervous system disorders
Headache, bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults have been reported in individuals receiving full therapeutic dosages of tetracyclines. In relation to benign intracranial hypertension, symptoms included blurring of vision, scotomata diplopia and permanent visual loss has been reported.
Ear and labyrinth disorders Tinnitus Gastrointestinal disorders

Gastrointestinal symptoms are usually mild and seldom necessitate discontinuation of treatment. They include: abdominal pain, stomatitis, anorexia, nausea, vomiting, diarrhoea, dyspepsia and rarely dysphagia. Oesophagitis and oesophageal ulceration have been reported in patients receiving doxycycline. A significant proportion of these
occurred with the hydrochloride salt in the capsule form. Tetracyclines may cause discoloration of teeth and enamel hypoplasia, but usually only after long-term use.
Hepatobiliary disorders

There have been rare reports of hepatotoxicity with transient increases in liver function tests, hepatitis, jaundice, hepatic failure and pancreatitis.
Skin and subcutaneous tissue disorders

Rashes including maculopapular and erythematous rashes, exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported. Photosensitivity skin reactions and photo-onycholysis.

Musculoskeletal and connective tissue disorders

-Arthralgia and myalgia

Renal and urinary system disorders

-Increased blood urea.

Reproductive system and breast disorders

-Vaginitis

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals and the general public are advised to report any suspected adverse reactions to the relevant drug authority regulator, through the relevant platforms.

4.9 Overdose

Acute overdosage with antibiotics is rare. In the event of overdosage, discontinue medication. Gastric lavage plus appropriate supportive treatment is indicated.

Dialysis does not alter serum half-life and thus would not be of benefit in treating cases of overdosage.

5 Pharmacological Properties

5.1 Pharmacodynamic Properties

Therapeutic class: Tetracycline antibiotic ATC code: J01AA02

As an antibiotic, doxycycline exerts its antimicrobial effect by the inhibition of protein synthesis and is considered to be primarily bacteriostatic.

5.2 Pharmacokinetic Properties

Absorption

Absorption is rapid (effective concentrations are attained as from the first hour), and the peak serum concentration occurs after 2 to 4 hours.
Almost all of the product is absorbed in the upper part of the digestive tract. Absorption is not modified by administration with meals, and milk has little effect.

Distribution

In adults, an oral dose of 200 mg results in;

- A peak serum concentration of more than 3 µg/ml
- A residual concentration of more than 1 µg/ml after 24 hours
- A serum half-life of 16 to 22 hours.
- Protein binding varies between 82 and 93% (labile binding); intra- and extracellular diffusion is good.

With usual dosages, effective concentrations are found in the ovaries, uterine tubes, uterus, placenta, testicles, prostate, bladder, kidneys, lung tissue, skin, muscles, lymph glands, sinus secretions, maxillary sinus, nasal polyps, tonsils, liver, hepatic and gallbladder bile, gallbladder, stomach, appendix, intestine, omentum, saliva and gingival fluid. Doxycycline is transferred into breast milk. Only small amounts are diffused into the cerebrospinal fluid.

Excretion

The antibiotic is concentrated in the bile. About 40% of the administered dose is eliminated in 3 days in active form in the urine and about 32% in the faeces.
Urinary concentrations are roughly 10 times higher than plasma concentrations at the same time. In the presence of impaired renal function, urinary elimination decreases, faecal elimination increases and the half-life remains unchanged. The half-life is not affected by haemodialysis.

5.3 Preclinical Safety Data

Not applicable

6 Pharmaceutical Particulars

6.1 List of Excipients

Lactose BP, Microcrystalline Cellulose BP (Dried), Magnesium Stearate BP, Hard Gelatin

6.2 Incompatibilities

None

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25˚C. Protect from light and moisture.

6.5 Nature and contents of container

PVC film/ Aluminium foil in unit cartons with literature insert

Available in pack sizes of 10 X 10 Capsules, 1000 capsules, and 10 X 100 Capsules

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7 Marketing Authorization Holder

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8 Marketing Authorization Number

H1986/3877

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Date of First Registration: 10th July 1986

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10 Date of Revision of Text

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