SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Doxycycline 100mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 100 mg doxycycline as doxycycline hyclate.  
Excipient with known effect:

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard gelatin capsules for oral administration.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Doxycycline is clinically effective in the treatment of a variety of infections caused by a wide range of gram-negative and gram-positive bacteria, as well as certain other micro-organisms.

Respiratory tract infections

Urinary tract infections

Sexually transmitted diseases
Infections due to *Chlamydia trachomatis* including uncomplicated urethral, endocervical or rectal infections. Non-gonococcal urethritis caused by *Ureaplasma urealyticum* (T- mycoplasma). Doxycycline is also indicated in chancroid, granuloma inguinale and lymphogranuloma venereum. Doxycycline is an alternative drug in the treatment of gonorrhoea and syphilis.
**Skin infections**

Acne vulgaris, when antibiotic therapy is considered necessary.

As doxycycline is one of the tetracycline group of antibiotics, it may be expected to be useful in the treatment of infections which respond to other tetracyclines such as:

**Ophthalmic infections**

Due to susceptible strains of staphylococci, gonococci and *Haemophilus influenzae*. Trachoma, although the infectious agent, as judged by immunofluorescence, is not always eliminated. Inclusion conjunctivitis may be treated with oral doxycycline alone or in combination with topical agents.

**Rickettsial infections**

Rocky Mountain spotted fever, typhus group, Q fever, Coxiella endocarditis and tick fevers.

**Other infections**

Psittacosis, brucellosis (in combination with streptomycin), cholera, bubonic plague, louse and tick-borne relapsing fever, tularemia, glanders, melioidosis, chloroquine-resistant falciparum malaria and acute intestinal amoebiasis (as an adjunct to amoebicides).

Doxycycline is an alternative drug in the treatment of leptospirosis, gas gangrene and tetanus.

Doxycycline is indicated for prophylaxis in the following conditions: Scrub typhus, travellers’ diarrhoea (enterotoxigenic *Escherichia coli*), leptospirosis and malaria. Prophylaxis of malaria should be used in accordance to current guidelines, as resistance is an ever changing problem.

### 4.2 Posology and method of administration

**Posology**

**Adults:**

The recommended adult dose for doxycycline is 200 mg on the first day of treatment - which can be given as a single dose or it can be divided into two 100 mg doses with a 12 hour interval - followed by a 100 mg/day maintenance dose. For more severe infections, especially chronic urinary tract infections, a daily dose of 200 mg should be administered during the period of treatment.

Doxycycline capsules should be administered with an adequate amount of fluid. This should be done in the sitting or standing position and well before retiring at night to reduce the risk of oesophageal irritation and ulceration. If gastric irritation occurs, it is recommended that doxycycline be given with food or milk. Studies indicate that the absorption of doxycycline is not notably influenced by simultaneous ingestion of food or milk.

Exceeding the recommended dosage may result in an increased incidence of side effects. Therapy should be continued for 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.

**Specific Infections**

**Acne vulgaris**
50 mg daily with food or fluid for 6 to 12 weeks.

**Sexually transmitted diseases**
100 mg twice daily for 7 days is recommended in the following infections:
Uncomplicated gonococcal infections (except anorectal infections for men); uncomplicated urethral, endocervical, or rectal infection caused by *Chlamydia trachomatis*; non-gonococcal urethritis caused by *Ureaplasma urealyticum*. Acute epididymo-orchitis caused by *Chlamydia trachomatis* or *Neisseria gonorrhoea* 100 mg twice daily for 10 days. Primary and secondary syphilis: Non-pregnant penicillin-allergic patients who have primary or secondary syphilis can be treated with the following regimen: doxycycline 200 mg orally twice daily for two weeks as an alternative to penicillin.

**Louse and tick-borne relapsing fevers**
A single dose of 100 mg or 200 mg depending on the severity of the infection.

**Treatment of chloroquine-resistant falciparum malaria**
200 mg per day for at least 7 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.

**Prophylaxis of malaria**
100 mg daily in adults and children over the age of 12 years. Prophylaxis can begin 1 to 2 days before travel to areas where malaria is present. It should be continued daily during travel in malarial areas and for 4 weeks after the traveller leaves the malarial area. For current advice on geographical resistance patterns and appropriate chemoprophylaxis, current guidelines or the Malaria Reference Laboratory should be consulted, details of which can be found in the British National Formulary (BNF).

**Prevention of scrub typhus**
200 mg as a single dose.

**Prevention of travellers’ diarrhoea 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 during the visit. Data on the use of the drug prophylactically are not available beyond 21 days.

**Prevention of leptospirosis**
200 mg once each week during the stay in the area and 200 mg on completion of the visit. Data on the use of the drug prophylactically are not available beyond 21 days.

**Paediatric population**
Use in children
Doxycycline is contra-indicated in children under 8 years of age (see section 4.3).

Use in Older people
Doxycycline may be prescribed in the older in the usual dosages with no special precautions. No dosage adjustment is necessary in the presence of renal impairment.

Use in patients with impaired hepatic function
See section 4.4.

Use in patients with renal impairment
Studies to date have indicated that administration of doxycycline at the usual recommended doses does not lead to accumulation of the antibiotic in patients with renal impairment see section 4.4.

4.3 Contraindications

Hypersensitivity to the active substance or other tetracyclines, or to any of the excipients listed in section 6.1.

The use of drugs of the tetracycline class during tooth development (pregnancy, infancy and childhood to the age of 12 years) may cause permanent discolouration of the teeth (yellow-grey-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. Doxycycline is therefore contra-indicated in these groups of patients.

Pregnancy
Doxycycline is contra-indicated 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 (see above about use during tooth development).

Nursing mothers
Tetracyclines are excreted into milk and are therefore contra-indicated in nursing mothers (see above about use during tooth development).

Children
Doxycycline is contraindicated in children under the age of 12 years. 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 tetracyclines in doses of 25 mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued. (See notes above about use during tooth development).
**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.

Abnormal hepatic function has been reported rarely and has been caused by both the oral and parenteral administration of tetracyclines, including doxycycline.

**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). Studies have shown no significant difference in the serum half-life of doxycycline in individuals with normal and severely impaired renal function. Haemodialysis does not alter the serum half-life of doxycycline. The anti-anabolic action of the tetracyclines may cause an increase in blood urea. Studies to date indicate that this anti-anabolic effect does not occur with the use of doxycycline in patients with impaired renal function.

**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 the overgrowth of non-susceptible organisms including Candida. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including doxycycline, and has ranged in severity from mild to life-threatening. It is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

*Clostridium difficile* associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including doxycycline, and may range in severity from mild diarrhoea 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 diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

**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.

**Benign intracranial hypertension**
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 coexistent syphilis is suspected, proper diagnostic procedures including dark-field examinations should be utilised. In all such cases monthly serological tests should be made 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**
Tetracyclines can cause weak neuromuscular blockade therefore doxycycline should be used with caution in patients with myasthenia gravis.

**Systemic lupus erythematosus**
Tetracyclines can cause exacerbation of SLE.

**Methoxyflurane**
Caution is advised in administering tetracyclines with methoxyflurane (see section 4.5).

**Jarisch-Herxheimer reaction**
Some patients with spirochaete infections may experience a Jarisch-Herxheimer reaction shortly after doxycycline treatment is started.

**Lactose intolerance**
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
4.5 Interaction with other medicinal products and other forms of interaction

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

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving Doxycycline in conjunction with penicillin.

There have been reports of prolonged prothrombin time in patients taking warfarin and doxycycline. Tetracyclines depress plasma prothrombin activity and reduced doses of concomitant anticoagulants may be necessary.

The serum half-life of doxycycline may be shortened when patients are concurrently receiving barbiturates, carbamazepine or phenytoin. An increase in the daily dosage of doxycycline should be considered.

Alcohol may decrease the half-life of doxycycline.

Doxycycline may increase the plasma concentration of ciclosporin. Co-administration should only be undertaken with appropriate monitoring.

The concurrent use of tetracyclines and methoxyflurane has been reported to result in renal failure. See section 4.4

Laboratory test interactions
False elevations of urinary catecholamine levels may occur due to interference with the fluorescence test.

4.6 Fertility, pregnancy and lactation

Doxycycline is contra-indicated in pregnancy and lactation (see section 4.3).

4.7 Effects on ability to drive and use machines

The effect of doxycycline on the ability to drive or operate heavy machinery has not been studied. There is no evidence to suggest that doxycycline may affect these abilities.

4.8 Undesirable effects

List of adverse reactions
The frequencies of adverse events are ranked according to the following: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

**Autonomic nervous system:** Flushing.

**Oral formulations**

**Infections and infestations**

Not known: 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. Similarly there have been reports for products in the tetracycline class of stomatitis and vaginitis.

**Blood and lymphatic system disorders**

Not known: Haemolytic anaemia, thrombocytopenia, neutropenia, porphyria and eosinophilia have been reported with tetracyclines.

**Immune system disorders**

Not known: Hypersensitivity reactions, including anaphylactic shock, anaphylaxis, anaphylactoid reactions, anaphylactoid purpura, hypotension, pericarditis, angioneurotic oedema, exacerbation of systemic lupus erythematous, dyspnoea, serum sickness, peripheral oedema, tachycardia and urticaria, Jarisch-Herxheimer reaction (see section 4.4).

**Nervous system disorders**

Rare: Headache.

Not known: 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 and diplopia. Permanent visual loss has also been reported.

**Gastrointestinal disorders**

Rare: Gastro-intestinal symptoms are usually mild and seldom necessitate discontinuation of treatment. Nausea, diarrhoea, dyspepsia

Very rare: Abdominal pain, discolouration of teeth
Not known: Anorexia, vomiting and rarely dysphagia, enamel hypoplasia, black hairy tongue. Oesophagitis and oesophageal ulceration have been reported in patients receiving doxycycline.

A significant proportion of these occurred with the hyclate salt in the capsule form. See section 4.4.

Hepatobiliary disorders

Not known: Transient increases in liver function tests, hepatitis, jaundice and pancreatitis.

Skin and subcutaneous tissue disorders

Rare: Rashes including maculopapular and erythematous rashes occur

Very rare: Photosensitivity skin reactions (see section 4.4.)

Not known: Exfoliative dermatitis, erythema multiforme, Steven-Johnson syndrome and toxic epidermal necrolysis, photo-onycholysis, Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)

Musculoskeletal and connective tissue disorders

Very rare: Arthralgia

Not known: Myalgia.

Renal and urinary disorders

Not known: Increased blood urea. See section 4.4.

Hearing/vestibular: Tinnitus

Other: When given over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid tissue. No abnormalities of thyroid function are known to occur.

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 are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard
4.9 Overdose

Acute overdose with antibiotics is rare.

**Treatment**: In the event of overdosage discontinue medication. Gastric lavage and appropriate supportive measures are 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

Doxycycline is primarily bacteriostatic and is believed to exert its antimicrobial effect by the inhibition of protein synthesis. Doxycycline is active against a wide range of Gram-positive and Gram-negative bacteria and certain other microorganisms.

5.2 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 faeces at high concentrations and in a biologically active form. Doxycycline is virtually completely absorbed after oral administration. Studies reported to date indicate that the absorption of doxycycline, unlike certain other tetracyclines, is not notably influenced by the ingestion of food or milk. Following a 200mg dose, normal adult volunteers averaged peak serum levels of 2.6 micrograms/ml of doxycycline at 2 hours decreasing to 1.45 micrograms/ml at 24 hours. Doxycycline has a high degree of lipid solubility and a low affinity for calcium. It is highly stable in normal human serum. Doxycycline will not degrade into an epianhydro form.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate BP
Starch BP
Lactose BP
Capsule shell ingredients:
Gelatin EP
Patent blue V E131
Quinoline yellow E104
Erythrosine E127
Titanium dioxide E171

Printing ink ingredients:
Shellac
Iron Oxide (E172)
Propylene Glycol (E1520)

6.2 Incompatibilities
May interfere with the bactericidal action of penicillin, and therefore should not be administered concurrently with penicillins. Cross resistance between tetracyclines may develop in micro-organisms and cross sensitisation in patients.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store in a cool dry place below 25°C and protect from light.

6.5 Nature and contents of container
Each container consists of a polypropylene tubular container with an open end equipped to accept a polyethylene closure, with a tamper-evident tear strip or tampertainers or PVC/Aluminium blister packs or PVC/PVdC/Aluminium blister packs, and is of the appropriate size to accommodate 8, 10, 14, 20, 28, 30, 50, 100, 250, 500, 1,000 or 100,000 capsules.

6.6 Special precautions for disposal
No special instructions.
7  MARKETING AUTHORIZATION HOLDER
Teva UK Limited
Brampton Road
Hampden Park
Eastbourne
East Sussex
BN22 9AG

8  MARKETING AUTHORIZATION NUMBER(S)
PL 00289/1425

9  DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
26/02/91 and 12.03.96.

10  DATE OF REVISION OF THE TEXT
13/06/2017