Doxycycline Capsules BP 100mg

Summary of Product Characteristics Updated 12-Sep-2018 | Accord-UK Ltd

1. Name of the medicinal product

DOXYCYCLINE CAPSULES BP 100mg

2. Qualitative and quantitative composition

Each capsule contains Doxycycline hyclate equivalent to 100mg of Doxycycline base.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Green hard gelatin capsules printed “C” and “DW” in black.

4. Clinical particulars

4.1 Therapeutic indications

Doxycycline Capsules are used in the treatment of a variety of infections caused by susceptible strains of Gram-positive and Gram-negative bacteria and certain other micro-organisms.

1) Respiratory tract infections: Pneumonia and other lower tract respiratory tract infections due to susceptible strains of *Streptococcus pneumoniae, Haemophilia influenzae, Klebsiella pneumoniae* and other organisms. *Mycoplasma pneumoniae* pneumonia. Treatment of chronic bronchitis. Sinusitis.

2) Urinary tract infections: Infections caused by susceptible strains of Klebsiella species, Enterobacter species. *Escherichia coli, Streptococcus faecalis* and other organisms.

3) Sexually transmitted diseases: Infections due to *Chlamydia trachomatis* including uncomplicated urethral, endocervical or rectal infections. Non-gonococcal, urethritis caused by *Ureaplasma urealyticum*. Chancroid infections due to *alymmatobacterium granulomatis.* Alternative drug in the treatment of gonorrhoea and syphilis.

4) Dermatological infections: Acne vulgaris when antibiotic therapy is considered necessary.

Since 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, such as:

1) Ophthalmic infections: Due to susceptible strains of gonococci, staphylococci and *Haemophilus influenzae*. Doxycycline Capsules are indicated in the treatment of trachoma, although the infectious agent is not always eliminated, as judged by immunofluorescence.

2) Rickettsial infections: Rocky Mountain spotted fever, typhus group, Q fever and *Coxiella endocarditis* and tick fevers.

3) Miscellaneous: Psittacosis, cholera, meliodosis, leptospirosis, other infections due to susceptible strains of Yersinia species, Brucella species (in combination with Streptomycin), Clostridium species, *Francisella tularensis* and chloroquine-resistant falciparum malaria.

4) Doxycycline Capsules are indicated for prophylaxis in the following conditions: Scrub typhus, travellers diarrhoea (enterotoxigenic *Escherichia coli*), leptospirosis.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

Adults and children aged 12 years to less than 18 years

The usual dose of Doxycycline Capsules for the treatment of acute infections in adults and children aged 12 years to less than 18 years is 200mg on the first day (administered as a single dose or divided into two equal doses with a twelve hour interval), 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 period.

Children aged 8 years to less than 12 years. (Section 4.4)

The use of doxycycline for the treatment of acute infections in children aged 8 years to less than 12 years should be carefully justified in situations where other drugs are not available, are not likely to be effective or are contraindicated.

In such circumstance, the doses for the treatment of acute infections are:

For children 45 kg or less- Initial dose: 4.4 mg/kg (in single or 2 divided doses) with maintenance dose: 2.2 mg/kg (in single or 2 divided doses). In the management of more severe infections, up to 4.4 mg/kg should be given throughout treatment.

For children, over 45 kg - Dose administered for adults should be used.

Children aged from birth to less than 8 years.

Doxycycline should not be used in children aged younger than 8 years due to the risk of teeth discolouration. (Section 4.4 and 4.8)

Exceeding the recommended dosage may result in an increased incidence of side effects.

Therapy should be continued at least 24-48 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: 50mg daily with food or fluid for 6-12 weeks.

Sexually transmitted diseases: 100mg twice daily for 7 days is recommended in the following infections: uncomplicated gonococcal infections (except anorectal infections in 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 gonorrhoeae 100mg twice daily for 10 days.

Primary and secondary syphilis: 300mg a day in divided doses for at least 10 days.

Louse-borne and tick-borne relapsing fevers: A single dose of 100mg or 200mg according to severity.

Chloroquine-resistant falciparum malaria: 200mg daily 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: 100mg daily in adults and children over the age of 12 years. Prophylaxis can begin 1-2 days before travel to malarial areas. It should be continued daily during travel in the 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).

For the prevention of scrub typhus: 200mg as a single dose.

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

For the prevention of leptospirosis: 200mg once each week throughout the stay in the area and 200mg at the completion of the trip. Data on the use of the drug prophylactically are not available beyond 21 days.

Paediatric population: Not recommended.

Elderly: Doxycycline may be prescribed in the usual dose with no special precautions. No dosage adjustment is necessary in the presence of renal impairment.

Renal impairment: 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.

The anti-anabolic action of the tetracyclines may cause an increase in blood urea. Studies to date indicate that this does not occur with the use of doxycycline in patients with impaired renal function.

Haemodialysis does not alter the serum half-life of doxycycline.

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. Studies indicate that the absorption of doxycycline is not notably influenced by simultaneous ingestion of food or milk.

4.3 Contraindications

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

• *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 section 4.4 regarding use during tooth development).

• *Nursing mothers:* Tetracylines are excreted into milk and are therefore contra-indicated in nursing mothers. (See section 4.4 regarding use during tooth development).

4.4 Special warnings and precautions for use

Paediatric population

The use of drugs of the tetracycline class during tooth development (last half of pregnancy; infancy and childhood to the age of 8 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. Use doxycycline in paediatric patients aged younger than 8 years only when the potential benefits are expected to outweigh the risks in severe or life-threatening conditions (e.g. Rocky Mountain spotted fever), only when there are no adequate alternative therapies.

Although the risk of permanent teeth staining is rare in children aged 8 years to less than 12 years, the use of doxycycline should be carefully justified in situations where other drugs are not available, are not likely to be effective or are contraindicated.

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.

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.

Microbiological overgrowth: The use of antibiotics may occasionally result in over-growth 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 antibiotics, including doxycycline, and has ranged 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 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 should be considered in all patients who present with diarrhoea after antibiotic treatment. 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.

Bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults have been reported in individuals receiving full therapeutic drugs. 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 diseases, 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: Due to a potential for weak neuromuscular blockade, care should be taken in administering tetracyclines to patients with myasthenia gravis.

Systemic lupus erythematous: Tetracyclines can cause exacerbation of systemic lupus erythematosus (SLE).

Jarisch-Herxheimer reaction: 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.

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

4.5 Interaction with other medicinal products and other forms of interaction

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.

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

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.

Barbiturates, carbamazepine, primidone and phenytoin may increase the metabolism of doxycycline (reduced half-life). An increase in the daily dosage of doxycycline should be considered.

Alcohol may decrease the half-life of doxycycline.

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

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

Drugs that induce hepatic enzymes such as rifampicin may accelerate the decomposition of doxycycline, thereby decreasing its half-life. Sub-therapeutic doxycycline concentrations may result. Monitoring concurrent use is advised and an increase in doxycycline dose may be required.

Ergotamine and methysergide

There is an increased risk of ergotism when doxycycline is co-administered with ergotamine and methysergide.

Methotrexate

Doxycycline increases the risk of methotrexate toxicity; prescribe with caution to patients on methotrexate.

Kaolin and sucralfate may reduce the absorption of doxycycline.

Quinapril contains magnesium carbonate and may interfere with the absorption of doxycycline.

A few cases of pregnancy or breakthrough bleeding have been attributed to the concurrent use of tetracycline antibiotics with oral contraceptives.

There is a possible increased risk of benign intra-cranial hypertension when doxycycline given with retinoids. Concomitant use should be avoided.

Antibacterials inactivate oral typhoid vaccines. Avoid administration of vaccine during treatment with doxycycline.

Laboratory test interactions

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

4.6 Fertility, pregnancy and lactation

See “Contra-indications”, section 4.3.

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.

Hypersensitivity reactions, including anaphylactic shock, anaphylaxis, anaphylactoid reactions, anaphylactoid purpura, hypotension, pericarditis, angioneurotic oedema, exacerbation of systemic lupus erythematosus, dyspnoea, serum sickness, peripheral oedema, tachycardia and urticaria.

Infections and infestations: 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 diosorders: Jarisch-Herxheimer reaction (frequency not known) (see section 4.4).

Endocrine disorders: 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.

Nervous system disorders: Headache. Bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults have been reported in some individuals receiving full therapeutic dosages of tetracyclines. These are reversible on stopping the drug. Symptoms include blurring of vision, scotomata and diplopia. Permanent visual loss has been reported.

Ear and labyrinth disorders: Tinnitus.

Gastrointestinal disorders: Gastro-intestinal symptoms are usually mild and seldom necessitate discontinuation of treatment. 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 cases has occurred with the hydrochloride salt in the capsule form. (See section 4.4). Tooth discolouration[a]. Black hairy tongue (frequency not known).

Hepato-biliary disorders: Transient increases in liver function tests, hepatitis, jaundice, hepatic failure and pancreatitis have been reported rarely.

Skin and subcutaneous tissue disorders: Rashes including maculopapular and erythematous rashes occur, exfoliative dermatitis, erythema multiforme, Stevens- Johnson syndrome and toxic epidermal necrolysis, photo-onycholysis. Photosensitivity (see section 4.4). Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) (frequency not known).

Musculo-skeletal, connective tissue and bone disorders: Arthralgia and myalgia.

Renal and urinary disorders: Increased blood urea. (See section 4.4).

Reproductive system and breast disorders: vaginitis.

[a] Reversible and superficial discolouration of permanent teeth has been reported with the use of doxycycline but frequency cannot be estimated from available data

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; website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Acute overdosage with antibiotics is rare. In the event of overdosage, 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

Pharmacotherapeutic group: tetracyclines, ATC code: J01AA02

Doxycycline is primarily a bacteriostatic antibiotic.

Mechanism of action

The main mechanism of action of doxycycline is on protein synthesis. Doxycycline passes directly through the lipid bilayer of the bacterial cell wall and an energy dependent active transport system pumps the drug through the inner cytoplasmic membrane. Once inside the cell doxycycline inhibits protein synthesis by binding to 30S ribosomes and prevents the addition of amino acids to the growing peptide chain. Doxycycline will impair protein synthesis in mammalian cells at very high concentrations but these cells lack the active transport system found in bacteria.

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.

5.2 Pharmacokinetic properties

Absorption

Doxycycline is almost completely absorbed and is not subject to presystemic metabolism 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 varying 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.

Biotransformation

No significant metabolism occurs.

Elimination

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

Also contains:

Gelatin

Magnesium stearate

Shellac glaze

Sodium lauryl sulfate

Starch

Quinoline Yellow (E104)

Erythrosine (E127)

Patent Blue V (E131)

Titanium Dioxide (E171)

Iron oxide black (E172)

Propylene glycol

6.2 Incompatibilities

None known.

6.3 Shelf life

PVC Blister packs

Five years.

All other containers

Four years.

6.4 Special precautions for storage

Store below 25°C in a dry place.

6.5 Nature and contents of container

The product containers are rigid injection moulded polypropylene or injection blow-moulded polyethylene containers with polyfoam wad or polyethylene ullage filler and snap-on polyethylene lids; in case any supply difficulties should arise the alternative is amber glass containers with screw caps and polyfoam wad or cotton wool.

The product may also be supplied in blister packs in cartons:

a) Carton: Printed carton manufactured from white folding box board.

b) Blister pack: (i) 250µm white rigid PVC. (ii) Surface printed 20µm hard temper aluminium foil with 5-7g/M² PVC and PVdC compatible heat seal lacquer on the reverse side.

Pack sizes: 7s, 8s, 10s, 14s, 16s, 28s, 30s, 50s, 56s, 60s, 84s, 90s, 100s, 112s, 120s, 168s, 180s

6.6 Special precautions for disposal and other handling

Not applicable.

Administrative Data

7. Marketing authorisation holder

Name or style and permanent address of registered place of business of the holder of the Marketing Authorisation:

Actavis UK Limited

(Trading style: Actavis)

Whiddon Valley

BARNSTAPLE

N Devon EX32 8NS

8. Marketing authorisation number(s)

PL 0142/0407

9. Date of first authorisation/renewal of the authorisation

02.04.97, 02.04.03

10. Date of revision of the text

30th August 2018

Company Contact Details

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