1. Name of the medicinal product

Emzor Doxcycline Capsule BP 100mg

2. Qualitative and quantitative composition

Each capsule contains EMZOR DOXCYCLINE hyclate equivalent to 100mg of EMZOR DOXCYCLINE CAPSULE 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
EMZOR DOXCYCLINE CAPSULE 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.

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

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

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

Skin infections: Acne vulgaris when antibiotic therapy is considered necessary.

Since EMZOR DOXCYCLINE CAPSULE 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:

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

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

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

EMZOR DOXCYCLINE CAPSULE is an alternative drug in the treatment of leptospirosis, gas gangrene and tetanus.

EMZOR DOXCYCLINE CAPSULE Capsules are 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.

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 EMZOR DOXCYCLINE CAPSULE 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 (as a single dose or divided doses), followed by a maintenance dose of 100mg/day. In the management of more severe infections, 200mg daily should be given throughout treatment.

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

The use of EMZOR DOXCYCLINE CAPSULE 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.

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

Dosage recommendations in 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: Non-pregnant penicillin-allergic patients who have primary or secondary syphilis can be treated with the following regimen: EMZOR DOXCYCLINE CAPSULE 200 mg orally twice daily for two weeks, as an alternative to penicillin therapy.

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

Treatment of 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 EMZOR DOXCYCLINE CAPSULE; 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.

Use in the elderly: EMZOR DOXCYCLINE CAPSULE may be prescribed in the elderly 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 EMZOR DOXCYCLINE CAPSULE at the usual recommended doses does not lead to accumulation of the antibiotic in patients with renal impairment see section 4.4.

Rocky Mountain spotted fever

Adults: 100 mg every 12 hours.

Children: weighing less than 45 kg: 2.2 mg/kg body weight given twice a day. Children weighing 45 kg or more should receive the adult dose (see section 4.4 paediatric population).

Patients should be treated for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Minimum course of treatment is 5-7 days.

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 EMZOR DOXCYCLINE CAPSULE Capsules be given with food or milk. Studies indicate that the absorption of EMZOR DOXCYCLINE CAPSULE 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.

4.3 Contraindications

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

• **Pregnancy:** EMZOR DOXCYCLINE CAPSULE 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 EMZOR DOXCYCLINE CAPSULE 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 EMZOR DOXCYCLINE CAPSULE should be carefully justified in situations where other drugs are not available, are not likely to be effective or are contraindicated.

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Use in patients with impaired hepatic function: EMZOR DOXCYCLINE CAPSULE 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 EMZOR DOXCYCLINE CAPSULE.

Use in patients with renal impairment: Excretion of EMZOR DOXCYCLINE CAPSULE 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 EMZOR DOXCYCLINE CAPSULE in individuals with normal and severely impaired renal function. Haemodialysis does not alter the serum half-life of EMZOR DOXCYCLINE CAPSULE. 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 EMZOR DOXCYCLINE CAPSULE in patients with impaired renal function.

Serious skin reactions: Serious skin reactions, such as exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in patients receiving EMZOR DOXCYCLINE CAPSULE (see section 4.8). If serious skin reactions occur, EMZOR DOXCYCLINE CAPSULE should be discontinued immediately and appropriate therapy should be instituted.

Photosensitivity: Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines, including EMZOR DOXCYCLINE CAPSULE. 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

Photoonycholysis has also been reported in patients receiving EMZOR DOXCYCLINE CAPSULE (see section 4.8).

Benign intracranial hypertension: Bulging fontanelles in infants have been reported in individuals receiving tetracyclines. Benign intracranial hypertension (pseudotumor cerebri) has been associated with the use of tetracyclines including EMZOR DOXCYCLINE CAPSULE. Benign intracranial hypertension (pseudotumor cerebri) is usually transient, however cases of permanent visual loss secondary to benign intracranial hypertension (pseudotumor cerebri) have been reported with tetracyclines including EMZOR DOXCYCLINE CAPSULE. If visual disturbance occurs during treatment, prompt ophthalmologic evaluation is warranted. Since intracranial pressure can remain elevated for weeks after drug cessation patients should be monitored until they stabilize. Concomitant use of isotretinoin or other systemic retinoids and EMZOR DOXCYCLINE CAPSULE should be avoided because isotretinoin is also known to cause benign intracranial hypertension (pseudotumor cerebri). (See section 4.5).

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 EMZOR DOXCYCLINE CAPSULE, 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 EMZOR DOXCYCLINE CAPSULE, 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 must be considered in all patients who present with diarrhoea following 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 EMZOR DOXCYCLINE CAPSULE. Most of these patients took medications immediately before going to bed or with inadequate amounts of fluid.

Porphyria: There have been rare reports of porphyria in patients receiving tetracyclines.

Venereal disease: When treating venereal diseases, where co-existent 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).

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

Jarisch-Herxheimer reaction: Some patients with spirochete infections may experience a Jarisch-Herxheimer reaction shortly after EMZOR DOXCYCLINE CAPSULE treatment is started. Patients should be reassured that this is a usually self-limiting consequence of antibiotic treatment of spirochete infections.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of EMZOR DOXCYCLINE CAPSULE 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.

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

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

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

Alcohol may decrease the half-life of EMZOR DOXCYCLINE CAPSULE.

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

EMZOR DOXCYCLINE CAPSULE 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 fatal renal toxicity. See section 4.4.

Concomitant use of isotretinoin or other systemic retinoids and EMZOR DOXCYCLINE CAPSULE should be avoided. Each of these agents used alone has been associated with benign intracranial hypertension (pseudotumor cerebri). (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

See section 4.3.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The following adverse reactions have been observed in patients receiving tetracyclines, including EMZOR DOXCYCLINE CAPSULE.

System Organ Class	Common ≥1/100 to <1/10	Uncommon ≥1/1000 to <1/100	Rare ≥1/10,000 to <1/1000	Not known

				Cannot be estimated from the available data.
Infections and infestations		Vaginal infection	Candida Infection	
Blood and lymphatic system disorders			Haemolytic anaemia, neutropenia, thrombocytopenia, eosinophilia	
Immune system disorders	Hypersensitivity (including anaphylactic shock, anaphylactic reaction, anaphylactoid reaction, angioedema, exacerbation of systemic lupus erythematosus, pericarditis, serum sickness, Henoch-Schonlein purpura, hypotension, dyspnoea, tachycardia, peripheral oedema and urticaria)		Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Jarisch-Herxheimer reaction[b] (see section 4.4)	
Endocrine disorders			Brown-black microscopic discolouration of thyroid glands	
Metabolism and nutrition disorders			Porphyria, decreased appetite	
Nervous system disorders	Headache		Anxiety, benign intracranial hypertension (pseudotumor cerebri)[a], fontanelle bulging	
Ear and labyrinth disorders			Tinnitus	
Eye disorders			Visual disturbance[d]	
Vascular disorders			Flushing	
Gastrointestinal disorders	Nausea/vomiting	Dyspepsia (Heartburn/gastritis)	Pancreatitis, pseudomembranous colitis, *Clostridium difficile* colitis, oesophageal ulcer, oesophagitis, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region, dysphagia,	tooth discolouration[e]

			abdominal pain, diarrhoea, glossitis, stomatitis	
Hepatobiliary disorders			Hepatic failure, hepatitis, hepatotoxicity, jaundice, hepatic function abnormal	
Skin and subcutaneous tissue disorders	Photosensitivity reaction, rash including maculopapular and erythematous rashes		Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, dermatitis exfoliative, photoonycholysis, skin hyperpigmentation[e]	
Musculoskeletal, connective tissue and bone disorders			Arthralgia, myalgia	
Renal and urinary disorders			Blood urea increased	

[a] In association with tetracyclines, including EMZOR DOXCYCLINE CAPSULE, benign intracranial hypertension has been reported with possible symptoms of headache, vomiting, visual disturbances including blurred vision, scotoma, diplopia or permanent loss of vision. The manifestation of clinical symptoms, including headache or visual disturbances, should suggest a possible diagnosis of intracranial hypertension. If an increase in intracranial pressure is suspected during treatment with tetracyclines, administration should be discontinued.

[b] in the setting of spirochete infections treated with EMZOR DOXCYCLINE CAPSULE.

[c] with chronic use of EMZOR DOXCYCLINE CAPSULE.

[d] Associated with Benign intracranial hypertension (pseudotumor cerebri).

[e] Reversible and superficial discolouration of permanent teeth has been reported with the use of EMZOR DOXCYCLINE CAPSULE 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 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

Pharmacotherapeutic group: tetracyclines,

ATC code: J01AA02

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

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. EMZOR DOXCYCLINE CAPSULE is virtually completely absorbed after oral administration. Studies reported to date indicate that the absorption of EMZOR DOXCYCLINE CAPSULE, unlike certain other tetracyclines, is not notably influenced by the ingestion of food or milk.

Following a 200 mg dose, normal adult volunteers averaged peak serum levels of 2.6 micrograms/ml of EMZOR DOXCYCLINE CAPSULE at 2 hours decreasing to 1.45 micrograms/ml at 24 hours. EMZOR DOXCYCLINE CAPSULE has a high degree of lipid solubility and a low affinity for calcium. It is highly stable in normal human serum. EMZOR DOXCYCLINE CAPSULE will not degrade into an epianhydro form.

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

Emzor Pharmaceutical Industries Limited

Plot 3c,Blk A,Aswani Market Road,Oshodi-Apapa Expressway, Lagos

8. Marketing authorisation number(s)

N/A

9. Date of first authorisation/renewal of the authorisation

N/A

10. Date of revision of the text

N/A