

**DOXYCYCLINE 100 MG CAPSULES**

**PL 20395/0011**

**UKPAR**

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## **DOXYCYCLINE 100 MG CAPSULES**

**PL 20395/0011**

### **LAY SUMMARY**

The Medicines and Healthcare products Regulatory Agency (MHRA) granted RelonChem Ltd a Marketing Authorisation (licence) for the medicinal product Doxycycline 100 mg Capsules (Product Licence number: 20395/0011). This antibiotic is only available with a prescription.

Doxycycline 100 mg Capsules contain the active ingredient doxycycline hyclate. Doxycycline works by preventing the microorganisms responsible for infection from making the proteins that they need to grow.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Doxycycline 100 mg Capsules outweigh the risks, hence a Marketing Authorisation has been granted.

# **DOXYCYCLINE 100 MG CAPSULES**

**PL 20395/0011**

## **SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

The UK granted a marketing authorisation for the medicinal product Doxycycline 100 mg Capsules (PL 20395/0011) to RelonChem Ltd on 24 October 2006. This product is a Prescription Only Medicine (POM).

The application was submitted as an abridged informed consent application according to Article 10.1 (a)(i) of EC Directive 2001/83. The cross reference product is Ethypharm Doxycycline 100mg Capsules (PL 12365/0004), held by Ethypharm Labs and granted 11 August 1994.

No new data were submitted, nor was it necessary for this simple application as the data is identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) was generated for it.

## **PHARMACEUTICAL ASSESSMENT REPORT**

### **INTRODUCTION & BACKGROUND**

This is a simple, 'piggy-back' application for Doxycycline 100mg Capsules, submitted under Article 10.1 (a)(i) of Directive 2001/83/EC, as amended, from RelonChem Ltd. The marketing authorisation to which this application cross-refers is PL 12365/0004 for Ethypharm Doxycycline 100mg Capsules, held by Ethypharm Labs, France. This MA was initially granted on 11 August 1994. A letter of informed consent is present. A letter confirming that RelonChem has a copy of the Part II preclinical and clinical data is also provided.

Doxycycline is a broad spectrum antibacterial agent indicated for the treatment of infections caused by chlamydia, rickettsia, brucella and the spirochaete, *Borrelia burgdorferi*. It is also used to treat respiratory and genital mycoplasma infections, acne, destructive periodontal disease, exacerbations of chronic bronchitis and leptospirosis in penicillin hypersensitive patients (BNF, No. 51, March 2006). In particular, doxycycline is used for the treatment of chronic prostatitis, sinusitis, syphilis, pelvic inflammatory disease, oral ulcers, oral herpes simplex infections and for acne vulgaris. It is also used for the treatment and prophylaxis of malaria.

### **EXPERT REPORT**

The CV of the medical expert indicates that she is a physician with suitable qualifications and experience to assume the role of clinical expert. The CV of the pharmaceutical expert indicates that he is a pharmacist with nearly twenty years' experience in quality control, production and pharmaceutical development. The CV indicates that he is suitably qualified for the role of pharmaceutical expert.

### **MARKETING AUTHORISATION APPLICATION (MAA)**

The MAA form submitted with this application is satisfactory.

### **ACTIVE INGREDIENT SOURCE**

The source of active ingredient is also listed on the licence of the cross-reference product. A copy of the EDQM Certificate of Suitability (R2-CEP 1992-018-Rev 00) for the supplier is provided, which is current and satisfactory.

A drug substance specification for doxycycline hyclate has been provided by the applicant that complies with the BP monograph. This is acceptable.

### **MANUFACTURER**

The two sites of manufacture stated in the MAA form are identical to those on the licence of the cross-reference product. Appropriate manufacturing authorisations are provided.

A statement of willingness to manufacture the product is provided from the manufacturer.

A flow chart detailing the sites involved in the manufacturing process has been supplied. Other sites have been specified as storage, distribution and batch release sites. Appropriate manufacturing authorisations are provided. Batch release is carried out by Klocke Verpackungs Service GmbH.

### **MANUFACTURING PROCESS**

The qualitative and quantitative composition of the product is the same as that of the cross-reference product.

The manufacturing process for the maximum batch size has been outlined and is identical to that of the cross-reference product.

### **PRODUCT SPECIFICATIONS**

The finished product specifications at release and shelf life are provided. All tests and limits are satisfactory.

### **STORAGE DETAILS**

The shelf lives and storage conditions for the applicant's product are identical to those of the cross-reference product and are 36 months (3 years) with no special precautions for storage. These are in agreement with the SPCs.

### **PACKAGING**

The packaging is identical to that described for the cross-reference product (blister).

### **PACK SIZES**

The proposed blister pack sizes are 8, 10 and 50 capsules. These are the same as the cross-reference product.

### **TSE COMPLIANCE**

Compliance with TSE requirements for gelatin for the capsule shells has been demonstrated by the provision of Ph.Eur. Certificates of Suitability, copies of which have been provided. The certificates from the three specified suppliers of capsule shells are up-to-date and satisfactory.

### **OTHER INFORMATION**

The qualified person nominated to be responsible for pharmacovigilance matters is suitably qualified.

### **SUMMARY OF PRODUCT CHARACTERISTICS**

The SPC is based on that of the cross-reference product. This is in line with current guidelines.

### **LEAFLET AND LABELLING**

Leaflet mock-ups have been provided, which are consistent with the SPC and are satisfactory in terms of content and readability.

Full colour, actual size mock-ups of the carton and blister are provided.

### **CONCLUSION**

A product licence may be granted.

## **PRECLINICAL ASSESSMENT**

No new preclinical data have been supplied with this application and none is required for an application of this type.

## **CLINICAL ASSESSMENT**

No new clinical data have been supplied with this application and none is required for an application of this type.



## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

The data for this application is consistent with that previously assessed for the cross-reference product and as such has been judged to be satisfactory.

### **PRECLINICAL**

No new preclinical data were submitted and none are required for an application of this type.

### **EFFICACY AND SAFETY**

The efficacy of doxycycline has been well documented in the past. No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory.

### **RISK BENEFIT ASSESSMENT**

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. The risk benefit ratio is considered to be positive.

## DOXYCYCLINE 100 MG CAPSULES

PL 20395/0011

### STEPS TAKEN FOR ASSESSMENT

<b>1</b>	The MHRA received the marketing authorisation application on 20 August 2003
<b>2</b>	Following assessment of the application the MHRA requested further information relating to the quality dossier on 3 March 2004
<b>3</b>	The applicant responded to the MHRA's requests, providing further information on 6 August 2004
<b>4</b>	Following assessment of the response the MHRA requested further information relating to the quality dossier on 15 December 2004
<b>5</b>	The applicant responded to the MHRA's requests, providing further information on 16 February 2006
<b>6</b>	Following assessment of the response the MHRA requested further information relating to the quality dossier on 19 June 2006
<b>7</b>	The applicant responded to the MHRA's requests, providing further information on 20 September 2006
<b>8</b>	Following assessment of the response the MHRA requested further information relating to the quality dossier on 20 September 2006
<b>9</b>	The applicant responded to the MHRA's requests, providing further information on 19 October 2006
<b>10</b>	The application was determined on 24 October 2006

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

Doxycycline 100mg Capsules

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

One capsule contains 100 mg doxycycline base  
(as doxycycline hyclate)

For a full list of excipients, see Section 6.1

### **3 PHARMACEUTICAL FORM**

Capsules

Hard gelatin capsules, containing spherical yellow to yellowish microgranules, intended for oral administration.

### **4 CLINICAL PARTICULARS**

#### **4.1 Therapeutic indications**

Doxycycline 100 mg 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). Doxycycline 100 mg is also indicated in chancroid, granuloma inguinale and lymphogranuloma venereum. Doxycycline 100 mg is an alternative drug in the treatment of gonorrhoea and syphilis.

Skin infections: *Acne vulgaris*, when antibiotic therapy is considered necessary. Since Doxycycline 100 mg 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 Doxycycline 100 mg 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, tularaemia glanders, melioidosis, chloroquine-resistant falciparum malaria and acute intestinal amoebiasis (as an adjunct to amoebicides).

Doxycycline 100 mg is an alternative drug in the treatment of leptospirosis, gas gangrene and tetanus.

Doxycycline 100 mg 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**

### **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, 200 mg daily should be given throughout treatment.

Capsules are for oral administration only.

Doxycycline 100 mg capsules should be administered with adequate amounts 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 100 mg be given with food or milk. Studies indicate that the absorption of Doxycycline 100 mg 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.

Dosage recommendations in 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 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 gonorrhoea*  
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: doxycycline 200 mg orally twice daily for two weeks, as an alternative to penicillin therapy.

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

Treatment of chloroquine-resistant falciparum malaria: 200 mg 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 100 mg; 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 1-2 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: 200 mg as a single dose.

For the prevention of travellers' diarrhoea in adults: 200 mg on the first day of travel (administered as a single dose or as 100mg every 12 hours) followed by 100 mg 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: 200 mg 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 for children: see under “contra-indications”.

Use in the elderly: Doxycycline 100 mg 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 under “special warnings and precautions for use”.

Use in patients with renal impairment: Studies to date have indicated that administration of Doxycycline 100 mg at the usual recommended doses does not lead to accumulation of the antibiotic in patients with renal impairment see under “special warnings and precautions for use”.

### **4.3 Contraindications**

Persons who have shown hypersensitivity to doxycycline, any of its inert ingredients or to any of the tetracyclines.

This product also contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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 100 mg is therefore contra-indicated in these groups of patients.

**Pregnancy:** Doxycycline 100 mg 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 100 mg is contra-indicated in children under the age of 12 years. As with other tetracyclines, Doxycycline 100 mg 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 25mg/kg every 6 hours. This reaction was shown to be reversible when the drug was discontinued. (See above about use during tooth development).

#### **4.4 Special warnings and precautions for use**

**Use in patients with impaired hepatic function:** Doxycycline 100 mg 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 100 mg 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.

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 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 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 erythematosus: Tetracyclines can cause exacerbation of SLE.

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**

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.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving Doxycycline 100 mg 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 100 mg should be considered.

Alcohol may decrease the half-life of doxycycline.

A few cases of pregnancy or breakthrough bleeding have been attributed to the

concurrent use of tetracycline antibiotics with oral contraceptives.  
Doxycycline may increase the plasma concentration of cyclosporin. 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

Laboratory test interactions

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

#### **4.6 Pregnancy and lactation**

See “Contra-indications”

#### **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**

The following adverse reactions have been observed in patients receiving tetracyclines, including doxycycline.

Autonomic nervous system: Flushing.

Body as a whole: 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.

Central and Peripheral nervous system: 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 and diplopia. Permanent visual loss has been reported.

Gastro-intestinal: Gastro-intestinal symptoms are usually mild and seldom necessitate discontinuation of treatment. Abdominal pain, anorexia, nausea, vomiting, diarrhoea, dyspepsia and rarely dysphagia. Oesophagitis and oesophageal ulceration have been reported in patients receiving Doxycycline 100 mg. A significant proportion of these occurred with the hyclate salt in the capsule form. (see 'special warnings and precautions for use' section).

Hearing/Vestibular: Tinnitus.

Haemopoietic: Haemolytic anaemia, thrombocytopenia, neutropenia, porphyria, and eosinophilia have been reported with tetracyclines.

Liver/Biliary: Transient increases in liver function tests, hepatitis, jaundice, hepatic failure and pancreatitis have been reported rarely.



Musculo-Skeletal: Arthralgia and myalgia.

Skin: Rashes including maculopapular and erythematous rashes, exfoliative dermatitis, erythema multiforme, Steven-Johnson syndrome and toxic epidermal necrolysis. Photosensitivity skin reactions (see 'special warnings and precautions for use' section).

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.

Urinary system: Increased blood urea. (see 'special warnings and precautions for use' section.)

Other: 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.

Tetracyclines may cause discoloration of teeth and enamel hypoplasia, but usually only after long-term use.

#### **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**

Doxycycline 100 mg is primarily bacteriostatic and is believed to exert its antimicrobial effect by the inhibition of protein synthesis. Doxycycline 100 mg is active against a wide range of Gram-positive and Gram-negative bacteria and certain other micro-organisms.

#### **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 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.

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 Pre-clinical safety data**

Not applicable.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Sucrose and maize starch microgranules,  
Crospovidone,  
Polymethacrylate,  
Talc.

### **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf Life**

3 years

### **6.4 Special precautions for storage**

None stated

### **6.5 Nature and contents of container**

Doxycycline capsules are packed in blister packs made of one sheet of 200 micron rigid,

opaque white polyvinyl chloride and a second sheet of 20 micron aluminium.  
Pack sizes are: 8, 10 and 50 capsules. Not all pack sizes may be marketed.

**6.6 Special precautions for disposal**

No special requirements.

**7 MARKETING AUTHORISATION HOLDER**

Relonchem Ltd  
27 Old Gloucester Street  
London WC1 3XX

**8 MARKETING AUTHORISATION NUMBER(S)**

PL 20395 / 0011

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

24/10/2006

**10 DATE OF REVISION OF THE TEXT**

24/10/2006

**PATIENT INFORMATION LEAFLET**

# Doxycycline 100mg Capsules

Doxycycline hydrate

RelonChem

## Patient Information Leaflet

Please read this leaflet carefully before you start to take your capsules. It contains important information. If you are not sure about anything, or you want to know more, ask your doctor or a pharmacist. Keep this leaflet safe, as you may want to read it again.

### ABOUT YOUR MEDICINE

The name of this medicine is Doxycycline 100 mg Capsules. Doxycycline 100 mg Capsules is one of a group of medicines called tetracycline antibiotics.

### WHAT IS YOUR MEDICINE:

Each capsule contains 100mg of the active ingredient doxycycline (as doxycycline hydrate).

The capsule shell contains indigocarmine (E132), yellow and black iron oxide (E172), gelatin, titanium dioxide (E171), shellac and potassium hydroxide.

Doxycycline 100 mg Capsules have opaque green caps and bodies and are printed in white with <<100 mg>>.

- Doxycycline 100mg Capsules come in pack sizes of 8, 10 and 50 capsules.

### WHO MAKES YOUR MEDICINE:

The manufacturer is Nocke Verpackungs Service GmbH, Max Becker Strasse 6, Weingarten, Germany.

The product licence holder is Relonchem Limite d, 27 Old Gloucester Street, London WC1 3XX.

### WHAT IS YOUR MEDICINE FOR

You may be given Doxycycline 100 mg Capsules by your doctor to treat infections such as:

- Chest, lung or nasal infections e.g. bronchitis, pneumonia, sinusitis.
- Urinary tract infections e.g. cystitis, urethritis.
- Acne which is a skin infection.
- Eye infections.
- Sexually transmitted diseases e.g. gonorrhoea, syphilis, chlamydia.
- Infections caused by parasites (associated with louse or tick bites).
- Malaria, when chloroquine is not effective.

Doxycycline 100 mg Capsules is also used to prevent certain infections developing, these are scrub typhus, travellers' diarrhoea, malaria and leptospirosis.

Your doctor may want you to take Doxycycline 100 mg Capsules to treat another infection not listed above. You may also be prescribed an additional medicine to take with Doxycycline 100 mg Capsules to treat your infection. If in doubt talk to your doctor.

### BEFORE YOU TAKE YOUR MEDICINE

If the answer is **YES** to any of the questions below **DO NOT TAKE Doxycycline 100 mg Capsules**.

- Have you been told you are allergic to Doxycycline 100 mg Capsules or any other tetracycline antibiotic?
- Are you allergic to any of the other ingredients in Doxycycline 100 mg Capsules listed above?
- Are you pregnant or trying to become pregnant?
- Are you breast feeding?
- Is this medicine prescribed for a child under the age of 12 years?

Tetracyclines should not be used during tooth development (during pregnancy, infancy and children below 12 years old) as such use may lead to permanent discolouration or underdevelopment of the teeth (yellow-grey-brown).

Avoid exposure to strong sunlight while taking this medicine. Your skin may be more sensitive to sunburn than normal. If you get a skin rash, itching, redness or severe sunburn when out in strong sunlight or under ultraviolet light (e.g. on a sun bed) stop taking the medicine and check with your doctor.

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

If the answer is **YES** to any of the following questions tell your doctor before you start Doxycycline 100 mg capsules.

- Are you likely to be exposed to strong sunlight or ultraviolet light (e.g. on a sun bed)?
- Do you have liver problems?

- Do you have myasthenia gravis (a disease which causes unusual tiredness and weakness of certain muscles, particularly in the eyelids)?
- Do you have porphyria (a rare disease of blood pigments)?
- Do you have (or have you ever had) systemic lupus erythematosus? This condition may be worsened by taking Doxycycline 100 mg Capsules.

If you are suspected as having syphilis, your doctor will continue to monitor you after your treatment has stopped.

### Can Doxycycline 100 mg Capsules be taken with other medicines?

Some medicines may interfere with Doxycycline 100 mg Capsules. You should tell your doctor if you are taking any of the medicines listed below. Also check with your doctor if you are taking any other medicines:

- Antacids (indigestion remedies), iron preparations, oral zinc or bismuth. If you take these at the same time of day as Doxycycline it may stop this medicine from working properly.
- Warfarin or coumarins (used to prevent blood clots). A reduced dose of these medicines may be required when taking doxycycline.
- Oral contraceptives (birth control pills). Use of birth control pills with tetracyclines may impair the effect of the birth control pill and increase the chance of unwanted pregnancy.
- Penicillin antibiotics (used to treat infections). Doxycycline may reduce the effect of these antibiotics.
- Alcohol. Alcohol may reduce the effect of Doxycycline.
- Carbamazepine, phenytoin (medicines used to control epilepsy) and barbiturates (used to control epilepsy or as a sedative).
- Cyclosporin (used to affect the body's immune response).
- Methoxyflurane (an anaesthetic). If you are going to have a general anaesthetic for an operation or dental surgery you must tell your anaesthetist or dentist that you are taking Doxycycline 100 mg Capsules.

### Can you drive whilst taking this medicine?

There is no evidence to suggest that this medicine will affect your ability to drive.

### HOW TO TAKE YOUR MEDICINE

Usual Dose (Respiratory, Urinary tract, Ophthalmic and other infections):	200mg on the first day then 100mg daily. The duration of treatment is dependent on the infection being treated.
Acne:	50mg daily for 6-12 weeks, with food or fluid.
Sexually Transmitted Diseases:	100mg twice daily for 7-10 days.
Primary and Secondary Syphilis:	200mg twice daily for 2 weeks.
Fevers associated with louse or tick bites:	Single dose of 100mg or 200mg depending on severity.
Treatment of malaria, when chloroquine is not effective:	200mg daily for at least 7 days.
Prevention of malaria:	100mg daily from 1-2 days before travelling until 4 weeks after returning.
Prevention of scrub typhus:	Single dose of 200mg.
Prevention of travellers' diarrhoea:	100mg twice daily on the first day of travel, followed by 100mg daily throughout the stay in the area. If you are planning to take these capsules for more than 21 days, please consult your doctor.
Prevention of leptospirosis:	200mg once each week during the stay in the area; 200mg on completion of the trip. If you are planning to take these capsules for more than 21 days, please consult your doctor.

Doctors may prescribe different doses to these depending on the infection being treated. Check with your doctor if you are not sure why you have been prescribed the medicine.

The label on the pack will tell you what dose **YOU** should take, how often and for how long to take it. If you are still not sure, ask your doctor or pharmacist.

- Take Doxycycline 100 mg Capsules with a full glass of water.
- It is best to take your capsules at the same time(s) each day, when standing or while sitting.
- It is important not to lie down for at least thirty minutes after taking Doxycycline 100 mg Capsules, so that the capsule can move as swiftly as possible into the stomach and prevent irritation of the throat or oesophagus (canal taking food from the mouth to the stomach).
- If your stomach is upset, Doxycycline 100 mg Capsules can be taken with milk or a meal.
- Take the capsules for the full time of treatment, even when you begin to feel better. If you stop taking the capsules too soon, the infection may return.

### **What to do if you take too many capsules?**

An occasional extra dose taken by accident is unlikely to be a problem, but if a large overdose has been taken contact your doctor or your nearest hospital Casualty Department immediately.

### **What to do if you miss a dose?**

Do not worry. If you forget to take a capsule take it as soon as you can. Take your next capsule at the right time.

### **How quickly will the treatment start to work?**

You should start to feel better within a few days. If you have been given Doxycycline 100 mg Capsules for acne it may be a few weeks before you start to see an improvement.

### **What if you do not feel better?**

If your infection gets worse or you do not start to feel better within a few days (except for acne), or a new infection develops, go back and see your doctor.

### **AFTER TAKING YOUR MEDICINE**

Like many medicines, doxycycline may occasionally cause side-effects in some patients, particularly when you first start taking it. These effects may include:

**Allergic reactions:** All medicines can cause allergic reactions. Serious allergic reactions are very rare. Any sudden wheeziness, difficulty in breathing, chest pain, fever, sudden swellings, rash or itching (especially affecting the whole body) should be reported to a doctor immediately.

**Particular effects of antibiotics in general:** Sore or swollen tongue and diarrhoea may occur. A diarrhoeal disease (pseudomembranous colitis) has been reported which may show as watery diarrhoea, fever and cramps. You should contact a doctor immediately if this occurs. Soreness and itching around the back passage and/or genital areas, inflammation around the vagina, or thrush of the vagina or mouth may also occur.

**Effects on the blood:** Doxycycline may alter the numbers of certain types of blood cells. If you notice that you are bruising easily, have more nose bleeds, or suffer from an increased number of infections and sore throats, you should contact your doctor. Porphyria has been reported and may appear as sensitivity of the skin to sunlight, inflammation of nerves and stomach pains.

**Effects on glands and hormones:** When taken for a long time, discolouration of thyroid tissue has been reported. However, this medicine does not impair thyroid function.

**Effects on the central nervous system (CNS):** Headache. Increased pressure in the skull resulting in severe headaches together with blurred and/or double vision and blind spots have been reported. These effects usually disappear upon stopping the medicine, however, permanent loss of vision has been reported. Bulging fontanelles (soft spot on head) of infants has been reported and usually disappears rapidly on stopping the capsules.

**Effects on the ears:** Tinnitus (ringing or buzzing in the ears) has been reported.

**Effects on the heart:** Pericarditis (inflammation of the membrane surrounding the heart which may produce fever or chest pain), and an increased heart rate. Flushing and hypotension (low blood pressure) have also been reported.

**Effects on the gastrointestinal tract:** inflammation and/or ulcers of the gullet have been reported causing stomach pain, loss of appetite, feeling or being sick, heartburn, diarrhea, difficulty swallowing and a sore or painful tongue or mouth. These symptoms are very unlikely if you take the capsules with water while standing or sitting (see "how to take your medicine"). Discolouration and underdevelopment of teeth has been reported after long term use.

**Effects on the liver:** Changes in liver function tests, hepatitis and jaundice (yellowing of the skin or white of the eyes) has been reported rarely. Liver failure and pancreatitis has been reported rarely. If you suffer from severe stomach pains, you should contact your doctor.

**Effects on the skin:** Severe skin reactions that make you feel unwell, which may be red, and flaking or peeling of skin. You may notice that your skin is very sensitive to light. If you get a skin rash, itching, redness or severe sunburn when out in sunlight or after using a sun bed stop taking the medicine and seek immediate medical advice from your doctor. If you suffer from systemic lupus erythematosus (SLE) you may notice that your condition gets worse.

**Effects on the muscles and bones:** Aching muscles or joints have been reported.

**Effects on the kidneys:** an increase in the amount of urea in the blood has been reported. This is detected by a blood test.

If these effects are troublesome or you have any other unusual effects, seek advice from your doctor or pharmacist.

### **LOOKING AFTER YOUR MEDICINE**

Keep your capsules in a safe place where children cannot see or reach them.

Keep your medicine in the original package.

Do not put them into another container.

Do not take the capsules after the use by ('expiry') date marked on the packaging.

You should take any capsules that are out of date or which you no longer need back to your pharmacist.

These capsules are only for you. Only a doctor can prescribe them for you. Never give them to anyone else.

PL 20395/0011.

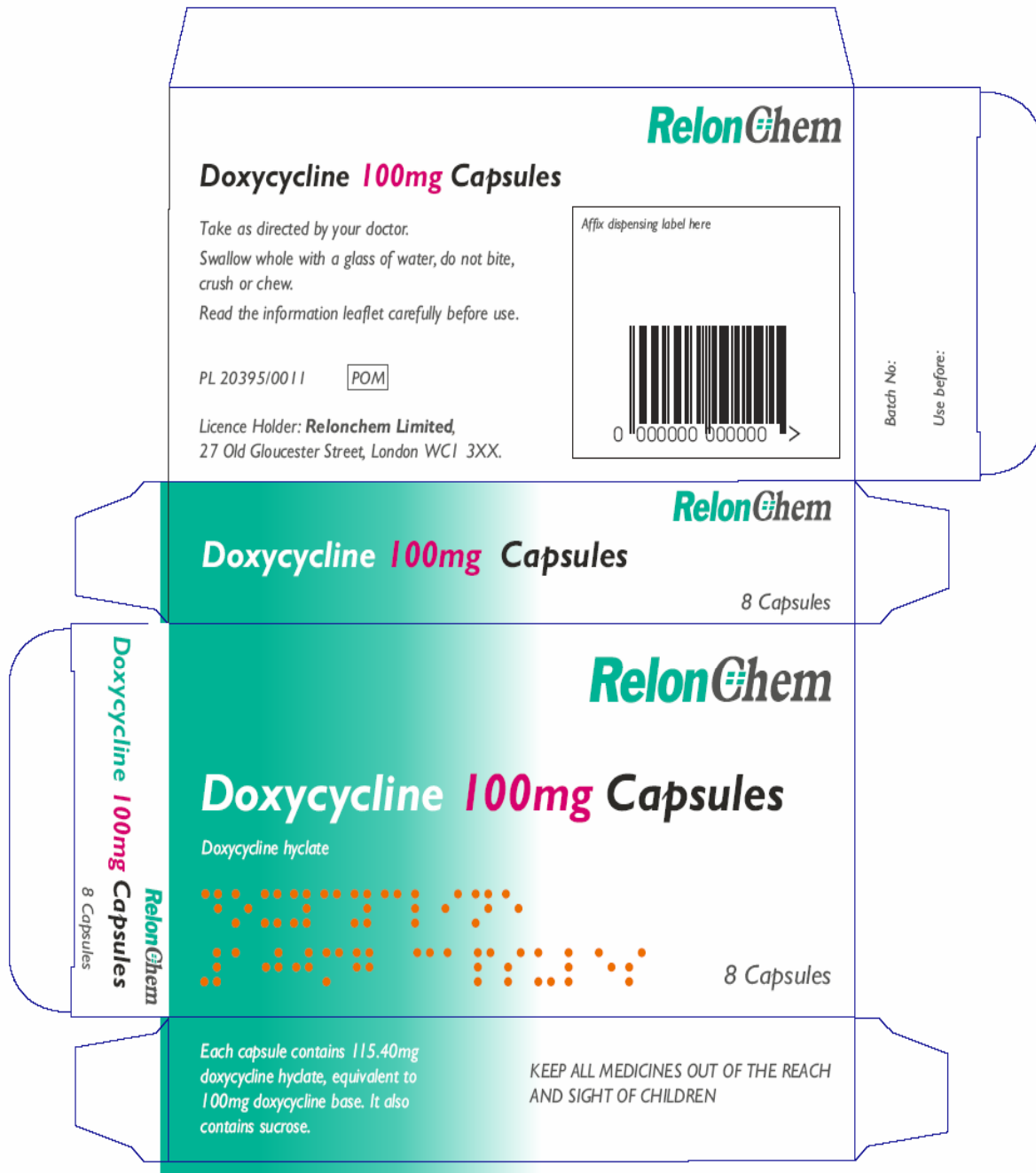
This leaflet was approved in XXXX 2006.

## LABELLING

### Blister foil:



**Carton:**



**Doxycycline  
#100mg Capsules**