NEW ZEALAND DATA SHEET

DOXINE

1. Product Name

Doxine, 100 mg, film-coated tablet.

2. Qualitative and Quantitative Composition

Each film-coated tablet contains doxycycline hyclate 115 mg, equivalent to 100 mg doxycycline.

Excipient(s) with known effect: Microcrystalline Cellulose, Pregelatinised Maize Starch and Opadry II Yellow.

Allergen Declaration: Lactose and sulfites.

Each Doxine film coated tablet contain 1 mg of lactose and trace amounts of sulfites.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Yellow, film-coated, normal convex tablets, 8.5 mm diameter, debossed 'DE' over '100' on one side, 'G' on the reverse.

4. Clinical Particulars

4.1 Therapeutic indications

Doxycycline is indicated in the treatment of uncomplicated chest, urethral, endocervical or rectal infections in adults caused by susceptible organisms (see section 5.1) as shown by culture and sensitivity testing. It may also be a useful adjunct to amoebicides in acute intestinal amoebiasis and has a place as adjunctive therapy in severe acne.

4.2 Dose and method of administration

The usual dose in adults is 200 mg on the first day of treatment followed by a maintenance dose of 100 mg/day. This may be given as either a single dose or divided doses administered every 12 hours.

In the management of more severe infections, 200 mg daily should be given throughout the treatment period. Therapy should be continued at least 24 - 48 hours after symptoms and fever has subsided. If used in streptococcal infections, therapy should be continued for 10 days to prevent the development of rheumatic fever or glomerulonephritis.

For children over 12 years of age, the recommended dosage schedule for those under 50 kg is 4 mg/kg on the first day and 2 mg/kg daily subsequently. For children over 50 kg the usual adult dose is used.

In the treatment of acute gonococcal anterior urethreitus in males, administer either: 200 mg stat and 100 mg at bedtime on the first day followed by 100 mg twice daily for 3-7 days, or 300 mg stat followed by 300 mg one hour later. For acute gonococcal infections in females use 200 mg twice daily until cure is effected. When treating uncomplicated urethral, endocervical or rectal infection in adults caused by chlamydia trachomatis, give 100 mg twice daily for at least 7 days. The treatment of primary or secondary syphilis requires 300 mg daily in divided doses for at least 10 days.

In all cases doxycycline should be administered with adequate amounts of fluid or food and the patient should remain sitting or standing for up to 2 hours afterwards to prevent the possible development of oesophageal irritation.

Method of administration

To reduce the possibility of gastric irritation, it is recommended that doxycycline be given with food or milk. The absorption of doxycycline is not markedly influenced by simultaneous ingestion of food or milk.

4.3 Contraindications

- Hypersensitivity to doxycycline, any of the excipients in Doxine, or to any of the tetracyclines.
- Concomitant treatment with oral retinoids, such as isotretinoin or etretinate, and vitamin A (see section 4.8)
- Children under 12 years of age
- Pregnancy (see section 4.6)
- Breastfeeding (see section 4.6)
- Concurrent use of tetracycline and methoxyflurane (see section 4.5)

4.4 Special warnings and precautions for use

Photosensitivity

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients likely to be exposed to direct sunlight or ultra-violet light should be advised that this reaction can occur with tetracycline medicines and treatment should be discontinued at the first evidence of skin erythema.

Severe Skin Reactions

Severe 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 doxycycline. Fixed drug eruptions have occurred with doxycycline and have been associated with worsening severity upon subsequent administrations, including generalized bullous fixed drug eruption (see section 4.8). If severe skin reactions occur, discontinue doxycycline immediately and institute appropriate therapy.

Increased serum urea

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

Intracranial hypertension

Intracranial hypertension (IH) has been associated with the use of tetracyclines including doxycycline (see sections 4.3 and 4.8). The use of tetracyclines in infants, even in the usual therapeutic doses, may cause increased intracranial pressure and bulging of the fontanelles. Women of childbearing age who are overweight or have a history of IH are at greater risk for developing tetracycline associated IH. Clinical manifestations include headache, blurred vision, diplopia and vision loss. Although intracranial hypertension typically resolves after discontinuation of treatment, the possibility for permanent visual loss exists. If visual disturbance occurs during treatment, prompt ophthalmologic evaluation is warranted. Discontinuation of therapy results in prompt return of the pressure to normal. However, since intracranial pressure

can remain elevated for weeks after medicine cessation patients should be monitored until they stabilise.

Antibiotic associated pseudomembranous colitis

The use of antibiotics may occasionally result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, the antibiotic should be discontinued, and appropriate therapy instituted.

Clostridium difficile associated diarrhoea (CDAD) and antibiotic associated pseudomembranous colitis have been reported with 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* and *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. Mild cases usually respond to medicine discontinuation alone. However, in moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated. Medicines which delay peristalsis, e.g. opiates and diphenoxylate with atropine may prolong and/or worsen the condition and should not be used.

Treatment of venereal disease with coexistent syphilis

In venereal disease when co-existent syphilis is suspected, proper diagnostic measures including a dark field examination should be done before treatment is started and the blood serology repeated monthly for at least four months.

Long term therapy

In long term therapy, periodic laboratory evaluation of organ systems, including haematopoietic, renal and hepatic studies should be performed.

Oesophagitis/oesophageal ulceration

If doxycycline is ingested in an incorrect manner there is a risk of adhesion of the tablet to the oesophagus. If this happens, oesophageal injury may occur. Dysphagia, retrosternal pain, new or worsening heartburn are possible symptoms of such injury. In order to avoid oesophageal injury, doxycycline must be ingested with at least 100 mL of fluid (half a glass) and the patient must remain upright for at least 30 minutes. Administration in the morning is recommended rather than in the evening.

Rarely, oesophagitis and oesophageal ulceration have been reported in patients receiving doxycycline tablets. Most of these patients took medication immediately before going to bed. Administration of adequate amounts of fluid with the tablets is recommended to reduce the risk of oesophageal irritation and ulceration, and late evening ingestion of the dose should be avoided.

Treatment of Group A beta-haemolytic streptococci infections

Tetracyclines are not the medicines of choice for the treatment of streptococcal infections. However, when used, therapy should be continued for 10 days. All infections due to group A beta-haemolytic streptococci should be treated for at least 10 days.

Hepatic effects

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

Paediatric Use

(See section 4.3)

Doxycycline is contraindicated in children under 12 years of age.

The use of medicines of the tetracycline class, including doxycycline, during tooth development may cause permanent discolouration of the teeth (yellow grey-brown). This adverse reaction is more common during long term use of the medicine but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported.

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 premature infants given oral tetracycline in doses of 25 mg/kg every six hours. This reaction was shown to be reversible when the medicine was discontinued.

The use of tetracyclines in infants, even in the usual therapeutic doses, may cause increased intracranial pressure and bulging of the fontanelles.

Interference with laboratory tests

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

Excipient(s) with known effect

Doxine film coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Retinoids

Rare cases of benign intracranial hypertension have been reported after taking tetracyclines and oral retinoids, such as isotretinoin or etretinate, and vitamin A. Concomitant treatment is therefore contraindicated (see section 4.3).

Anticoagulants

There have been reports of prolonged prothrombin time in patients taking warfarin and doxycycline. Because the tetracyclines have been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

Penicillin

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

Antacids

Antacids containing aluminium, calcium or magnesium, or other medications containing these cations; bismuth salts; and preparations containing iron impair absorption and should not be given to patients taking doxycycline.

Medicines that reduce plasma levels of doxycycline

Plasma levels of doxycycline are reduced by the ingestion of alcohol or the administration of barbiturates, anticonvulsants (phenytoin, carbamazepine), disodium hydrogen citrate, sodium bicarbonate, sodium lactate, acetazolamide and ethoxzolamide.

Methoxyflurane

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

Oral contraceptives

There have been anecdotal reports that concurrent use of tetracyclines may render oral contraceptives less effective and breakthrough bleeding may occur. Unplanned pregnancy may occur with this combination. A barrier method of contraception should be used while taking Doxine and for seven days following completion of the course of Doxine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category D (See section 4.3).

During the period of mineralisation of a child's teeth (the last half of pregnancy, the neonatal period and the first 12 years of life) tetracyclines may induce hypoplasia of the enamel and discolouration of the teeth. Tetracyclines also accumulate in the growing skeleton.

There are no adequate and well-controlled studies on the use of doxycycline in pregnant women. The vast majority of reported experience with doxycycline during human pregnancy is short-term, first trimester exposure. An expert review of published data on experiences with doxycycline use during pregnancy by TERIS (the Teratogen Information System) concluded that therapeutic doses during pregnancy are unlikely to pose a substantial teratogenic risk (the quantity and quality of data were assessed as limited to fair), but the data are insufficient to state that there is no risk. A case control study (18,515 mothers of infants with congenital anomalies and 32,804 mothers of infants with no congenital anomalies) shows a weak but marginally statistically significant association with total malformations and use of doxycycline anytime during pregnancy. Sixty-three (0.19%) of the controls and fifty-six (0.30%) of the cases were treated with doxycycline. This association was not seen when the analysis was confined to maternal treatment during the period organogenesis (i.e. in the second and third months of gestation) with the exception of a marginal relationship with neural tube defect based on only two exposed cases.

A small prospective study of 81 pregnancies describes 43 pregnant women treated for ten days with doxycycline during early first trimester. All mothers reported their exposed infants were normal at 1 year of age.

Results of animal studies indicate that tetracyclines cross the placenta, are found in foetal tissues and can have toxic effects on the developing foetus (often related to retardation of skeletal development). Evidence of embrytoxicity has also been noted in animals treated early in pregnancy.

Large doses of tetracyclines have caused acute fatty necrosis of the liver in pregnant women, especially those with pyelonephritis.

Breastfeeding

(See sections 4.3 and 4.4)

Doxycycline is present in the milk of lactating women. It forms a stable calcium complex in bone-forming tissue and a decrease in the fibula growth has been observed in prematures. The use of medicines of the tetracycline class during tooth development may also cause permanent discolouration of the teeth. Because of the potential for serious adverse reactions in breastfeeding infants, doxycycline is contraindicated in nursing mothers.

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

Doxycycline is generally well tolerated.

Cases of benign intracranial hypertension have been reported with tetracyclines. It has also occurred with concomitant vitamin A or retinoids such as isotretinoin and etretinate.

Due to doxycycline's virtually complete absorption, side effects of the lower bowel, particularly diarrhoea, have been infrequent. The following adverse reactions have been observed in patients receiving doxycycline.

More common reactions

Dermatological: Photosensitive dermatitis (see section 4.4), erythematous rash, maculopapular rash, morbilliform rash, pustular rash, urticaria, photo-onycholysis and discolouration of the nails.

Gastrointestinal: Nausea, anorexia, vomiting, dysphagia, diarrhoea, oesophagitis, oesophageal ulceration, abdominal pain, glossitis, black hairy tongue.

Hypersensitivity reactions: Urticaria, exacerbation of systemic lupus erythematosus and Jarisch-Herxheimer reaction has been reported in the setting of spirochete infections treated with doxycycline.

Hepatic: Cholestatic hepatitis, fatty liver degeneration.

Renal: Dose related increase in serum urea (see section 4.4).

Musculoskeletal: Tooth discolouration, enamel hypoplasia.

Nervous system disorders: Dizziness.

Others: Bulging fontanelles have been reported in young infants following full therapeutic dosage. The sign disappeared rapidly when the medicine was discontinued.

When given over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discolouration of thyroid glands. No abnormalities of thyroid function studies are known to occur.

Less common reactions

Gastrointestinal: Enterocolitis (see section 4.4), inflammatory lesions (with monilial overgrowth) in the anogenital region; dyspepsia and pseudomembranous colitis (see section 4.4); *C. difficile* diarrhoea, pancreatitis.

Hepatic: Hepatotoxicity and hepatitis.

Skin: Exfoliative dermatitis; Stevens-Johnson syndrome, Toxic Epidermal Necrolysis (TEN) and fixed drug eruption.

Musculoskeletal: Arthralgia; myalgia.

Genitourinary: Acute renal failure.

Hypersensitivity reactions: Angioneurotic oedema, anaphylaxis, anaphylactic shock, anaphylactic reaction, anaphylactoid purpura, serum sickness, pericarditis, hypotension, dyspnoea, peripheral oedema, tachycardia, erythema multiforme.

Haematological and reticuloendothelial: Phlebitis associated with intravenous administration leucopenia, thrombocytopenia purpura, increase in prothrombin time, haemolytic anaemia, eosinophilia.

Nervous system: Flushing, malaise, headache, confusion, taste loss, stupor, hypoaesthesia, paraesthesia, somnolence, benign intracranial hypertension in adults, increased intracranial pressure in infants. In relation to benign intracranial hypertension, symptoms included blurring of vision, scotomata and diplopia. Permanent visual loss has been reported.

Ocular: Conjunctivitis, periorbital oedema.

Hearing/vestibular: Tinnitus.

Psychiatric: Depression, anxiety, hallucination.

Respiratory: Bronchospasm.

Rare reactions

Retrosternal pain

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Signs and symptoms

Tetracyclines, including doxycycline, generally have low toxicity. Severe toxicity following acute overdosage is unlikely, with nausea and vomiting being the most common effects after ingestion of therapeutic and overdose amounts.

Treatment

Treatment may include immediate discontinuation of medication, dilution with water or milk and general supportive care. Antacids may be useful in managing gastric irritation. In most cases, gastrointestinal decontamination is not required. Plasma levels are not clinically useful and specific laboratory monitoring is not needed unless otherwise indicated.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Tetracyclines, ATC code: J01AA02

Mechanism of action

Doxycycline is a broad spectrum antibiotic that is primarily bacteriostatic. It is thought to exert its antimicrobial effect by inhibition of protein synthesis. It prevents the binding of amino-acyl-tRNA to the messenger RNA-30S ribosomal subunit. The binding of fMet-tRNA is especially sensitive. As a result, initiation and therefore polyribosome formation are blocked. Doxycycline inhibits only rapidly multiplying organisms.

Doxycycline is active against the following organisms:

- Rickettsiae: rocky mountain spotted fever, typhus fever and the typhus group, Q fever, rickettsial pox, and tick fevers
- *Mycoplasma pneumoniae*

- Agents of lymphogranuloma venereum and granuloma inguinale
- The spirochetal agent of relapsing fever (*Borrelia recurrentis*)
- *Chlamydia trachomatis*
- *Haemophilus ducreyi* (chancroid)
- *Pasteurella pestis*, and *Pasteurella tularensis*, *Bartonella bacilliformis*, Bacteroids species, Vibriocomma and *Vibrio fetus* and Brucella species (in conjunction with an aminoglycoside).

Doxycycline may be active against the following organisms although this should be confirmed by culture and sensitivity testing since many strains are resistant.

- *Neisseria gonorrhoeae*
- *Escherichia coli*
- *Enterobacter aerogenes*
- Shigella species
- Mima species and Herellea species
- *Haemophilis influenzae*
- Klebsiella species
- Streptococcus species
- *Streptococcus pneumoniae*
- *Staphylococcus aureus* in respiratory, skin or soft tissue infection.

When penicillin is contraindicated, doxycycline is an alternative medicine in the treatment of infections due to:

- *Treponema pallidum* and *Treponema pertenue* (syphilus and yaws)
- *Listeria monocytogenes*
- Clostridium species
- *Bacillus anthracis*
- *Fusobacterium fusiforme* (Vincent's infection)
- Actinomyces species.

Microbiology

Doxycycline is primarily bacteriostatic and is thought to exert its antimicrobial effect by the inhibition of protein synthesis. Doxycycline is active against a wide range of Gram-positive and Gram-negative organisms.

Susceptibility testing

Dilution or Diffusion Techniques. Either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. CLSI, formerly NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable.

A report of "Intermediate" indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative, clinically feasible medicines, the test should be repeated. This category implies possible clinical applicability in body sites where the medicine is physiologically concentrated or in situations where high dosage of medicine can be used. This category also provides a buffer zone, which prevents small-uncontrolled technical factors from causing major discrepancies in interpretation.

A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

5.2 Pharmacokinetic properties

Tetracyclines are readily absorbed, but to varying extents. 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. Its absorption is not significantly affected by the presence of food or milk.

Normal adult volunteers averaged peak serum levels of approximately 2.6 µg/mL of doxycycline at 2 hours, decreasing to 1.45 µg/mL at 24 hours, following a 200 mg dose. Excretion of doxycycline by the kidney is about 40% in 72 hours in individuals with normal renal function (creatinine clearance above 75 mL/min). This percentage excretion may fall as low as 1 to 5% in 72 hours in individuals with severe renal insufficiency (creatinine clearance below 10 mL/min). The serum half-life of doxycycline ranges from 18-22 hours. No significant difference in serum half-life has been seen in individuals with normal and severely impaired renal function. Haemodialysis does not alter serum half-life.

The fraction of drug that is not eliminated with urine is mainly excreted in the faeces. More than 90% of an oral dose of doxycycline is eliminated from the body within 72 hours of drug administration.

The metabolism of doxycycline in the human body has not been investigated. *In vitro* serum protein binding of doxycycline varies from 23 to 93%.

6. Pharmaceutical Particulars

6.1 List of excipients

Doxine film-coated tablets also contains:

- microcrystalline cellulose
- pregelatinised maize starch
- colloidal silicon dioxide
- magnesium stearate

The tablet Opadry II Yellow film-coat contains:

- lactose monohydrate
- titanium dioxide (E171)
- hypromellose (E464)
- macrogol (E1521)
- quinoline yellow lake (E104)
- sunset yellow lake (E110)
- indigo carmine lake (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

HDPE bottle with PP cap. Pack-sizes of 250 and 500 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Viatris Ltd
PO Box 11-183
Ellerslie
AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

17 December 1982

10. Date of Revision of the Text

5 May 2026

Section	Summary of changes
Throughout	Update ‘DOXINE’ to ‘Doxine’
2	Updated Excipient(s) with Known Effect section.
4.3	Updated list for clarification
4.4	Addition of Severe Skin Reactions. Addition of Excipient(s) with Known Effect section. Additional information for use in children under 12 years of age from section 4.3.
4.5	Addition of Retinoid section to align with section 4.3
4.8	Addition of ‘erythema multiforme and fixed drug eruption’.
4.9	Update to overdose statement in line with template.
All	Minor editorial changes.