

DOXYCYCLINE & MINOCYCLINE – SAFE PRESCRIBING – DON'T GET BURNT

- ▶ WARN ABOUT RISK OF OESOPHAGITIS
- ▶ ADVISE ABOUT SUN PROTECTION - PHOTSENSITIVITY IS COMMON
- ▶ BEWARE OF HYPERSENSITIVITY REACTIONS
- ▶ DO NOT PRESCRIBE WITH ISOTRETINOIN
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- ▶ MONITOR ANTICOAGULANT THERAPY CLOSELY

Tetracyclines are broad spectrum antibiotics often used for skin, chest, sinus, ophthalmic and pelvic infections. They are bacteriostatic^{1,2} and depending on the condition may need to be continued for weeks or months. Tetracyclines also have indirect anti-inflammatory effects, which makes them useful for acne, rosacea and perioral dermatitis.³

Note: Doxycycline is also used for the prophylaxis of malaria, but this is an unapproved indication.⁴

WARN ABOUT RISK OF OESOPHAGITIS

If doses are taken immediately before bedtime, or without fluids, there is a high risk of oesophagitis; this is especially problematic with doxycycline.⁵ Symptoms include a sudden onset of pain on swallowing and severe chest pain. In some cases, recovery may take several weeks.⁵

Advise to take these medicines with a meal, or large glass of water, and remain upright (standing or sitting) for at least 30 minutes afterwards.⁶ It is advisable to encourage morning dosing, late evening doses should be avoided.²

Doxycycline and minocycline are not affected by food,^{1,2,3,6} but antacids and supplements with aluminium, calcium, iron, magnesium and zinc should not be taken within 2-3 hours of dosing because they decrease the absorption of the tetracycline.⁴

ADVISE ABOUT SUN PROTECTION – PHOTSENSITIVITY IS COMMON

Doxycycline is one of the most commonly reported medicines associated with photosensitivity reactions in New Zealand.⁷ Exposure to excessive sunlight or sun lamps should be avoided.⁴ Inform patients that it is possible for photosensitivity reactions to occur during winter.

Photosensitivity reactions typically appear as unexpected or exaggerated sunburn or as a dry, blistering rash on sun-exposed skin, which may or may not be itchy. The reaction may occur immediately, or as long as 72 hours after exposure to ultraviolet light.⁷

Photosensitivity is more likely to occur with doxycycline than minocycline, and is dose-related.³ Treatment with tetracyclines should be discontinued at the first evidence of skin erythema.^{1,2}

Minocycline can cause prolonged greyish discolouration of teeth in about 5% of people, especially with doses over 100mg per day. Bluish discolouration of the skin (especially scars) may also occur with prolonged courses, at high doses, and particularly with older people.³ Irreversible skin pigmentation has been reported with minocycline, it is advisable to discontinue treatment if symptoms occur.⁴ Minocycline and doxycycline can both cause nail discolouration.^{1,2}

BEWARE OF HYPERSENSITIVITY REACTIONS

Tetracyclines, especially minocycline, may cause hypersensitivity reactions which can be serious. Reported reactions include rash, exfoliative dermatitis, Stevens-Johnson syndrome, urticaria, angioedema, anaphylaxis and pericarditis.⁴ Minocycline is associated with Drug Hypersensitivity Syndrome (DHE). This is a rare but severe multi-system reaction defined by a triad of fever, rash and internal organ involvement (hepatitis, myocarditis, nephritis or pneumonitis) and typically occurs between 1-8 weeks after exposure. It is strongly advised to avoid re-exposure and to inform first degree relatives because genetic factors are suspected.⁸

▶ continued

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Tetracyclines may increase symptoms of muscle weakness if patients have myasthenia gravis, and they can exacerbate systemic lupus erythematosus (SLE).⁴ Pre-existing SLE is a contraindication to therapy with minocycline¹ which is associated with a greater risk of lupus-erythematosus-like syndrome than other tetracyclines.³ If SLE occurs while taking tetracyclines, discontinue treatment.⁴

DO NOT PRESCRIBE WITH ISOTRETINOIN

Isotretinoin and tetracyclines are both associated with benign intracranial hypertension (BIH), so the combination of tetracyclines with oral vitamin A or retinoids is contraindicated.^{1,2} BIH is a very rare but potentially serious condition and minocycline is the most frequently reported medicine associated with BIH in the literature (approximately 9% of all cases).⁹

The presenting complaint is usually a pulsatile headache; visual disturbance and pulsatile tinnitus have also been reported. Symptoms generally occur within the first 4 weeks of treatment.⁹ Actively ask about headaches and visual disturbance at each visit. If BIH is suspected, discontinue treatment immediately⁴ and seek neurological advice.⁹ The condition may completely resolve, but a delay in diagnosis can lead to lasting visual defects, and even blindness.⁹ Dizziness, light-headedness, vertigo and reduced hearing have also been associated with tetracyclines, especially minocycline. Advise caution with driving if these symptoms occur.¹

AVOID DURING PREGNANCY, BREASTFEEDING AND IN CHILDREN UNDER 12 YEARS

Tetracyclines bind to calcium and deposit in growing bone and teeth. During the period of mineralisation of a child's teeth (from 2nd trimester of pregnancy up to 12 years of age) tetracyclines can cause discolouration of the child's teeth, hypoplasia of the enamel, and can accumulate in the growing skeleton.²

Tetracyclines are considered pregnancy category D,² and should be used with extreme caution, if at all, during pregnancy.

Tetracyclines are excreted at very low concentrations into breastmilk, so they may be used during breastfeeding, but

preferably for no more than 10 days.⁴ It is advisable to monitor for gastrointestinal effects in the infant.

Due to the potential effect on growing bones and teeth, tetracyclines are contraindicated in children less than 12 years of age.²

MONITOR ANTICOAGULANT THERAPY CLOSELY

If patients are receiving anticoagulant therapy, and are unwell enough to require an antibacterial, it is advisable to monitor them closely. Monitor coagulation status ideally within 3 days of starting the antibacterial.⁴

There is some evidence to suggest that tetracyclines depress plasma prothrombin activity,^{1,2} but a pre-emptive dose reduction of anticoagulants is not required.

How long to treat for acne?

Oral antibiotics are generally appropriate for **moderate** acne that has not responded to 2 months of topical therapy.^{10,11,12}

Improvement is expected to occur steadily but slowly, typically over 4-6 months. Start with doxycycline 50-100mg daily for 4-6 months. If effective after 4 months, taper the dose down to alternate day treatment. If this dose is ineffective, the dose may be increased to 200mg per day provided this is tolerated.¹¹

Review during the course to encourage compliance and discuss any adverse effects. After the course, continue with topical therapy as maintenance.¹³ If acne relapses, treat with the same antibiotic as previously used.¹⁰

Combination therapy with a topical benzoyl peroxide or retinoid may enhance response. It is recommended that topical antibiotic acne treatments are not used at the same time as oral antibiotics due to the increased risk of resistance.¹⁴ To reduce the risk, limit the duration of oral antibiotic therapy.¹⁵ Short term courses are preferred over traditional longer term therapy.¹⁶ If minocycline is used for longer than six months, liver function tests will be required every three months.⁴

Note: The patient expectation is usually for complete clearance;¹³ inform them from the first visit that this may not be realistic.

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