PrescQIPP Community Interest Company

Minocycline prescribing

Nationally £15.1 million is spent annually on tetracyclines for acne, of which approximately £457,000 is spent on minocycline (ePACT July to September 2019).

QIPP projects in this area are aimed at reviewing the continued need for oral antibiotics and switching to an alternative with better safety and efficacy and a lower acquisition cost. This bulletin reviews the place in therapy of minocycline and offers guidance and support material for organisations considering reviewing their prescribing as a QIPP project.

Recommendations

- Do not commence new patients requiring oral antibiotic acne treatment on minocycline.
- Commence new patients requiring oral acne treatment on a once daily tetracycline antibiotic with a better safety profile than minocycline (doxycycline or lymecycline). Once daily treatments may provide better adherence.
- Review all patients on oral antibiotic treatment for acne for continued need after 3 months.
- Do not prescribe oral acne treatment for patients with mild acne.
- Review all patients on minocycline for continued need and discontinue treatment if no longer indicated.
- For patients on minocycline where treatment for acne is still indicated, review for suitability of switching to an alternative treatment. Switch all suitable patients to an alternative treatment. As with all switches, these should be tailored to the individual patient.

National guidance

NICE published a Key Therapeutic Topic bulletin entitled Minocycline in January 2015.[1] The recommendation arising from the bulletin is to review and, where appropriate, revise prescribing of minocycline in light of its potential harms.[1]

The Primary Care Dermatology Society (PCDS) has produced a primary care treatment pathway for acne also highlighting that minocycline should not normally be used in view of the higher risks associated with this treatment.[2]

Oral antibiotics are not recommended for patients with mild acne.[3] Oral antibiotics are generally used for moderate to severe acne or where topical preparations are not tolerated or are ineffective or where application to the site is difficult.[4]

Oral antibiotics should not be used as a sole treatment for acne but should be prescribed with a topical retinoid (tretinoin, isotretinoin or adapalene) and/or topical benzoyl peroxide, due to concerns around growing bacterial resistance.[2] For the same reason, topical and oral antibiotics should not be prescribed together.[2,4]

A tetracycline antibiotic is considered to be the first line oral antibiotic for acne, where an oral antibiotic is indicated.[2,4] All tetracyclines show similar efficacy although lymecycline and doxycycline are likely to have better adherence due to their once daily dosage.[1,2,5]

An adequate dose should be given and treatment reviewed after 8 to 12 weeks.[3,4] If there has been a good response to oral antibiotic therapy and treatment goals have been reached, the antibiotic should be stopped.[2,3] Evidence suggests that there is little additional benefit in using antibiotics for more than three months, and in addition, prolonged use increases the resistance of Propionibacterium acnes. Antibiotic courses can be repeated in the future if required.[3] If treatment goals are not reached after three months, adherence to treatment should be checked and alternatives should be considered.[2] Change to an alternative antibiotic if there is no improvement to the skin condition, the person is unable to tolerate side effects or acne worsens while on treatment. If the person does not respond to two different courses of antibiotics, or if they are starting to scar, refer to a dermatologist.[3]

Erythromycin is a second line alternative (first line in pregnancy) due to high bacterial resistance which may explain poor response rates to erythromycin.[2,4]

NHS England have published guidance on items which should not be routinely prescribed in primary care, advising that prescribers in primary care should not initiate minocycline for any new patient and deprescribing of minocycline should be undertaken in all patients.[5]

Clinical effectiveness

A Cochrane systematic review evaluating the safety and efficacy of minocycline for acne vulgaris concluded that there is no evidence that it is superior to other commonly-used therapies.[6]

NICE also concluded that there is no clear evidence that minocycline is more effective or better tolerated than other tetracycline antibiotics and once daily tetracycline antibiotics are available.[1]

Safety

Minocycline can cause serious adverse reactions including:

1. Early-onset dose-related toxicity reactions resulting in single organ dysfunction (such as potentially fatal liver failure),
2. Autoimmune disorders (such as systemic lupus erythematosus-like syndrome, which has a strong relationship with duration of exposure, and autoimmune hepatitis)
3. Hypersensitivity reactions including eosinophilia, pneumonitis and nephritis.[6]

In addition, minocycline can cause slate-grey hyperpigmentation of the skin, which may be irreversible.[7]

Consequently, there is no reliable evidence to justify recommending minocycline as treatment for acne and concerns remain about its safety compared to other tetracycline antibiotics.[3]

Patient factors

Oxytetracycline and tetracycline both have a twice daily dosage regime.[4] Lymecycline or doxycycline are indicated where adherence to treatment is a concern, due to their once daily dosage.[2]

Oxytetracycline and tetracycline are recommended to be taken at least one hour before, or two hours after food (including any dairy containing drinks) as food and dairy can impair their absorption.[8] Doxycyline capsules should be taken at least one hour before going to bed to reduce the likelihood of oesophageal irritation and ulceration. They can be taken with food or milk as absorption of doxycycline is not notably influenced by simultaneous ingestion.[9] The absorption of lymecycline is not significantly impaired by moderate amounts of milk. The capsules should be taken with a glass of water in order to reduce the risk of oesophageal irritation and ulceration.[10] Lymecycline can be taken with or without food.

Costs

There is a significant difference in cost between different oral antibiotic treatments for acne. Table 1 illustrates the cost differences.

Table 1: Oral antibiotics for acne product and price comparison – Drug Tariff November 2019[11]

Product	Dose	Cost per 28 days
Doxycycline 100mg capsules	One capsule once daily	£3.89
Lymecycline 408mg capsules	Once capsule once daily	£4.33
Oxytetracycline 250mg tablets	Two tablets twice daily	£4.36
Erythromycin 250mg gastro-resistant tablets (second line)	Two tablets twice daily	£6.68
Tetracycline 250mg tablets	Two tablets twice daily	£7.60
Minocycline 100mg MR capsules	Once capsule once daily	£10.04
Minocycline 100mg capsules or tablets	Once capsule/ tablet once daily	£13.09 to £14.18
Minocycline 50mg capsules or tablets	One capsule/ tablet twice daily	£12.38 to £15.27

Switching options

There are several potential options to switch from minocycline to alternative antibiotics depending on which other treatments have already been tried (although clinicians may choose other options according to the clinical need of the patient).

These include:

1. If the patient still requires an oral tetracycline antibiotic, then doxycycline 100 mg capsules represent the most cost effective option with a once daily dosage regimen.
2. If the patient has been taking a tetracycline antibiotic treatment for acne for more than six months AND it has been more than three months since any additional improvement was seen, then antibiotic treatment should be stopped and topical maintenance therapy should be used instead.
3. If the patient has been taking a tetracycline antibiotic treatment for acne for at least three months with no improvement seen, then a second line antibiotic such as erythromycin 500 mg BD should be considered.
4. If the patient has mild acne, the patient should be switched to a suitable topical treatment instead of an oral antibiotic. This can be purchased over the counter.

Switch savings

There is a significant difference in cost between minocycline and alternative oral antibiotics for acne. In England and Wales, around £15.1 million is spent on tetracycline acne treatments per year. Discontinuing treatment that is no longer indicated is recommended. If 50% of treatment was discontinued then this would equate to savings of £7.6 million nationally or £12,022 per 100,000 patients nationally.

Switching from minocycline to a less costly and safer alternative could release savings of up to £230,000 nationally. This equates to savings of £362 per 100,000 patients nationally.

Summary

There is no clear evidence that minocycline is more effective or better tolerated than other tetracycline antibiotics. Minocycline is also associated with serious adverse reactions including organ dysfunction such as potentially fatal liver failure, autoimmune disorders including systemic lupus erythematosus-like syndrome and autoimmune hepatitis, hypersensitivity reactions including eosinophilia, pneumonitis and nephritis and potentially irreversible grey hyperpigmentation of the skin.[6,7]

In view of these concerns about the safety of minocycline compared to other tetracycline antibiotics, there is no reliable evidence to justify recommending that it is used for the treatment of acne, when other suitable alternative treatment options exist within the same class of antibiotic.

All treatments should be reviewed after 3 months and discontinued if no longer indicated.

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Additional PrescQIPP resources

	Bulletin	https://www.prescqipp.info/our-resources/bulletins/bulletin-246-minocycline-prescribing/
	Implementation tools	

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