

## Minocycline for acne vulgaris: efficacy and safety

NICE has developed the Cochrane Quality and Productivity (QP) topics to help the NHS identify practices which could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care. Each topic has been derived from a Cochrane systematic review that has concluded that the evidence shows that the practice is harmful or ineffective and should not be used, or that there is insufficient evidence to support widespread use of the practice

### Summary

#### **NICE summary of review conclusions**

Minocycline is an effective treatment for moderate acne vulgaris, but this review found no reliable randomised control trial evidence to justify its continued first-line use, especially given the price differential and the concerns that still remain about its safety. Its efficacy relative to other acne therapies could not be reliably determined because of the poor methodological quality of the trials and lack of consistent outcome measures. Similarly the relative risk of adverse drug reactions could not be ascertained reliably and no recommendations can be made concerning the appropriate dose that should be used. It is hoped that this review will highlight the inadequacy of acne trials in general and encourage improvements in methodological quality and standards of reporting.

Stopping the use of minocycline as the first-line systemic antibiotic for management of acne vulgaris, outside of well designed clinical trials, is likely to improve the quality of patient care and savings of approximately £2.2m may be generated by replacing its use with a safe, effective and less costly alternative.

#### **The 'Implications for practice' section of the Cochrane review stated:**

'The 27 studies included in this review do not provide any clear and unbiased evidence to support the first-line use of minocycline in the treatment of acne. Although it has been shown to be an effective treatment for moderate acne vulgaris at a dose of 100 mg per day, no study has conclusively shown any important clinical difference between the tetracycline antibiotics or other commonly used therapies. Given that it is 2.9 to 4.8 times more expensive than (oxy)tetracycline in the UK (Drug Tariff Jan 2000) depending on the formulation, the additional cost of minocycline is not justified on the basis of clinical efficacy alone.

Similarly, there is no evidence that it is more effective in acne resistant to other therapies or that it has a faster onset of action or a more prolonged effect. Insufficient information was located to make any recommendations concerning the appropriate dose that should be used. The relative safeties of the tetracyclines have still not been adequately determined and little further information could be derived from the studies due to their inherent inability to detect rare events. Recent reviews of case reports and case series suggest that minocycline therapy for acne may be associated with a broader spectrum and a higher incidence of severe adverse drug reactions than other tetracyclines.

The lack of a denominator in nearly all of the studies means that the risks for minocycline compared to other tetracyclines cannot be compared. Only in the case of lupus-like syndrome has it been conclusively shown that acne patients treated with minocycline are at a significantly greater risk than those given tetracycline or no treatment. Doctors should be aware that the risk of lupus-like syndrome and pigmentation increases with cumulative dose.'

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## Details of Cochrane review

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### Cochrane review title

Minocycline for acne vulgaris: efficacy and safety

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### Citation

[Garner SE, Eady A, Popescu CM, Newton J, Li Wan Po A. Minocycline for acne vulgaris: efficacy and safety. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD002086. DOI: 10.1002/14651858.CD002086](#)

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### When the review content was assessed as up to date

19 November 2002

Edited (no change to conclusions) and published in 2009.

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### QIPP category

Medicines use and procurement

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### Relevant codes

OPCS	ICD10	HRG
Not relevant –relates to community prescribing	Not relevant –relates to community prescribing	Not relevant –relates to community prescribing

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### Programme budget

Problems of the skin

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## Evidence

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### Relevance to the NHS

The Cochrane review included 27 randomised controlled trials, involving a total of 3031 patients with mild to severe acne. Minocycline was compared with placebo and other anti-acne treatments (oxytetracycline, tetracycline, doxycycline, lymecycline, topical clindamycin, topical erythromycin with zinc, cyproterone acetate with ethinyloestradiol, oral isotretinoin and topical fusidic acid).

Of the seven trials that compared minocycline with a first-generation tetracycline, five did not find any difference in efficacy and two suggested that minocycline was superior. Both trials were open-label multicentre studies sponsored by the developers of minocycline. Large numbers of patients were recruited in these studies; however, the results remain unclear because they had major design faults including use of inappropriate outcome measures and failure to account for large numbers of participants. It does not appear that any single-blind or double-blind study has been undertaken to compare the commonly used daily doses of 1 g tetracycline to 100 mg minocycline.

Although minocycline was shown to be an effective treatment for acne vulgaris, only two out of seven trials found it superior to other tetracyclines. In all trials comparing minocycline to tetracycline (or oxytetracycline) the initial response to minocycline was faster, but the magnitude of the reduction in acne severity produced by the drugs at the end of the treatment period was similar. A third trial showed minocycline to be more effective than 2% fusidic acid against inflammatory lesions in mild to moderate acne. Although, in this study the

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# Cochrane Quality and Productivity topics

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mean lesion counts did not change in the minocycline group after the second week. No evidence was found to support the benefits of minocycline in acne resistant to other therapies.

The dose-response study, suggested that maintaining patients on 100 mg minocycline confers no additional benefit to reducing the dose to 50 mg/day after two weeks, although these conclusions are only valid for the eight-week period of the study and assumptions cannot be made about the relative efficacies beyond this period. No overall evaluation of the relative risk of adverse effects of minocycline versus other tetracyclines could be made.

The objective of this Cochrane review was to evaluate the efficacy and safety of minocycline in acne vulgaris by systematic review of the evidence from randomised control trials. The intention was to pool the results of individual trials to produce an overall summary measure of effect. This was not however possible, because the internal validity of most of the studies was severely compromised due to inadequate design. As well as the use of many disparate outcome measures, numerous methodological differences between the retrieved studies could not be reconciled, which meant that pooling was not appropriate. Additionally, many of the trial reports were deficient and as a result the legitimacy of their conclusions could not be properly evaluated.

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## Relevant NICE guidance

No relevant NICE guidance was available at the time of publication (December 2011).

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## Other accredited guidance

### [Clinical knowledge summary – acne vulgaris](#)

[http://www.cks.nhs.uk/acne\\_vulgaris](http://www.cks.nhs.uk/acne_vulgaris)

### **How should I treat moderate acne?**

In moderate acne, inflammatory lesions (papules and pustules) predominate. The acne may be widespread, there may be a risk of scarring, and there may be considerable psychosocial morbidity, all of which are indications for aggressive treatment. Treatment options are a single topical drug, a combination of topical drugs, or oral antibiotics. Consider a single topical drug in people with limited acne which is unlikely to scar.

Prescribe benzoyl peroxide or a topical retinoid first-line as they are most effective against inflammatory acne. However, topical retinoids are also effective, and azelaic acid may be an option if other drugs are poorly tolerated. Combined treatment should be considered in all people with moderate acne. Benzoyl peroxide combined with a topical antibiotic is the usual preferred regimen, as it is proven to be effective and may limit the development of bacterial resistance.

Other options include a topical retinoid combined with benzoyl peroxide (but this may be poorly tolerated) or a topical retinoid combined with a topical antibiotic (but this may promote bacterial resistance). Consider prescribing an oral antibiotic (tetracycline, oxytetracycline, doxycycline, lymecycline, or erythromycin) if topical treatment cannot be tolerated, if there is moderate acne on the back or shoulders (where it may be particularly extensive or difficult to reach), or if there is a significant risk of scarring or substantial pigment change.

### **Treatment of severe acne**

In severe acne, there are nodules and cysts (nodulocystic acne), as well as a preponderance of inflammatory papules and pustules. There is a high risk of scarring (or scarring may already be evident), and there is likely to be considerable psychosocial morbidity. Refer all people with severe acne for specialist assessment and treatment (for example with oral isotretinoin), and consider prescribing an oral antibiotic in combination with a topical drug

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# Cochrane Quality and Productivity topics

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whilst waiting for an appointment.

Oral tetracycline, oxytetracycline, doxycycline, or lymecycline are first-line options. Erythromycin is an alternative if tetracyclines are poorly tolerated or contraindicated (such as in pregnancy). Minocycline is not recommended. Benzoyl peroxide or a topical retinoid are recommended as adjunctive treatment for most people. Azelaic acid is an alternative, but avoid the use of topical antibiotics with oral antibiotics.

Consider prescribing a combined oral contraceptive in women who require contraception. Standard combined oral contraceptives or co-cyprindiol (Dianette) are options.

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## Potential productivity savings

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### Estimate of current NHS use

An estimated 1.2 million people in England currently seek medical advice for acne. Prescribing data from 2008 show just over 260,000 prescriptions issued for minocycline.

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### Level of productivity savings anticipated

Using the October 2010 BNF prices (which exclude VAT), the estimated savings of substituting minocycline for an alternative tetracycline is approximately £2.2 million

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### Type of saving

The savings are likely to be cash-releasing efficiency savings

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### Any costs required to achieve the savings

There is not likely to be a cost barrier to change

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### Other information

The savings are likely to impact on community prescribing.

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## Potential impact on quality of NHS care

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### Impact on clinical quality

Clinical quality will be improved resulting in better outcomes anticipated for patients

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### Impact on patient safety

Given the uncertainty regarding minocycline's side effect and safety profile there may be potential improvements in patients' safety

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### Impact on patient and carer experience

Not anticipated to have any impact on patient and carer experience

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## Likely ease of implementation

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### Time taken to implement

Can be achieved in the short term: 0–3 months

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## Healthcare sectors affected

Affects several departments or teams across organisations

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## Stakeholder support

Likely to achieve good buy-in from all key influencers

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