161FM.7 MINOCYCLINE FOR USE IN DERMATOLOGY
Amber Initiation Guideline

This protocol provides prescribing and monitoring guidance for minocycline therapy. It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicinembers.org.uk/emc and the BNF.

Colour code:

- Antibiotics highlighted **red** and **bold** are **penicillin** based. They are contraindicated in patients with a history of penicillin allergy with life-threatening reaction e.g. anaphylaxis, angioedema and/or urticaria.
- Antibiotics highlighted *orange* and *italic* belong to either the cephalosporin or carbapenem groups of antibiotic and should be used with caution in patients a history of non-severe penicillin allergy e.g. delayed/minor rash. They are contraindicated if serious penicillin allergy e.g. anaphylaxis or angioedema.
- Antibiotics highlighted green are considered safe to use in patients allergic to penicillin.

BACKGROUND FOR USE

Minocycline has been used for many years in dermatology. It is an effective tetracycline but has a poorer side effect profile compared with other tetracyclines.[1,5] Occasionally the side effects are severe and deaths have been reported.[5,6] There is a lack of evidence that minocycline is better than other options for acne.[3,4,5] For these reasons, where another antibiotic can be used as an alternative, this is recommended.[1,3,5]

Tetracyclines (including minocycline) have a body of case reports and anecdotal evidence for use as a steroid sparing agent in some dermatological indications.[2]

Minocycline is therefore restricted in its indications for use in Buckinghamshire and the first month of treatment should always be prescribed by a secondary care specialist for all dermatological indications.

INDICATIONS FOR USE

For acne or rosacea: As a 3rd line choice in moderate to severe cases, after oxytetracycline, lymecycline, doxycycline and erythromycin have been tried.

For steroid sparing effects (*unlicensed*): e.g. pyoderma gangrenosum, pemphigus vulgaris, bullous pemphigoid, Behcet's disease. Initiation of treatment should be by a specialist.

If culture and sensitivity (C&S) suggests that it is the only suitable antibiotic choice: C&S results should be made available to the GP as part of the discharge information.

Minocycline is amber initiation for all formulary approved dermatology indications.

CONTRAINDICATIONS AND PRECAUTIONS[6]

Pregnancy and breastfeeding	1st trimester use has caused abnormal bone and skeletal development. If accidental exposure occurs, stop minocycline and seek an expert review. All tetracyclines may stain the primary dentition and cause enamel hypoplasia. If exposure occurs in utero - especially high risk if use is during the 3rd trimester. Consider using alternatives such as topical treatments while pregnant or breastfeeding.
Children <12 years	Tetracyclines are not recommended for children as they stain bones and teeth. Dental hypoplasia is also described in the literature.
Systemic lupus erythematosus (SLE)	Minocycline may cause or exacerbate SLE.
Myasthenia gravis	Minocycline may worsen muscle weakness.
Complete renal failure glomerular filtration rate (GFR) <10 ml/minute	Avoid use, drug accumulates and hepatic side effects more likely. The drug is **not** removed by haemo or peritoneal dialysis.
Hepatic impairment or with hepatotoxic drugs, including alcohol	Caution – side effects of hepatotoxicity may be more likely if less reserve of liver function. Seek specialist advice before use. Patient should be advised to keep alcohol intake within recommended limits (14 units per week for women; 21 units per week for men).
Elderly	Caution advocated by manufacturers due to greater possibility of hepatic, renal and cardiac problems. Assess the patient's overall risks and make a clinical judgement.
Known allergy to minocycline, other tetracyclines, gelatine, iron oxide, titanium dioxide, methanol, liquid paraffin, methylene chloride, hypromellose, croscarmellose or microcrystalline cellulose	Avoid use

DOSE AND ADMINISTRATION

Minocycline m/r 100 mg 24 hourly in acne or rosacea and as a steroid sparing agent.

Minocycline 100 mg immediate release 12 hourly may be prescribed on microbiological advice if C&S known and use is for an acute course of <2 weeks duration.

Give advice to swallow whole with plenty of fluid, upright (ideally standing). This aims to reduce the risk of oesophageal irritation/ulceration.

TIME TO RESPONSE

In acne, some response is usually seen after 6 weeks (summary product characteristics (SPC) Minocin®).

As a steroid sparing agent, give a 1 month course and then reassess value.

In any indication it is rare to exceed a course length of 12 - 18 months. If patients have had a course approaching 18 months duration, review and consider stopping or alternatives.

PRE-TREATMENT ASSESSMENT BY THE SPECIALIST

Full blood count (FBC), renal and hepatic assessment are only required if there is a history of abnormal results.

ONGOING MONITORING SCHEDULE BY THE GP

FBC, renal and hepatic function *every 3 months* if treatment is to continue for longer than 6 months	Patients being treated for more than 3 months should be warned to seek medical advice if pigmentation, hepatic side effects or if symptoms suggestive of SLE occur. See section on side effects. Abnormal effects on FBC are rare, but ask patient to seek medical advice if sore throat. If liver function tests (LFTs) >2 x upper limit of normal (ULN), stop the drug and seek specialist advice.

SIDE EFFECTS WITH ACTIONS TO BE TAKEN

Serious Side Effects	Action
Three serious syndromes have been reported:	Deaths from these syndromes have been described.
1) ***Hypersensitivity syndrome*** = Cutaneous reaction, eosinophilia and inflammation of a significant organ such as hepatitis, pneumonitis, nephritis, myocarditis, pericarditis. Fever and lymphadenopathy may be present.	Rare. Urgently stop the drug. Supportive care and seek specialist advice.
2) ***Lupus like syndrome*** = +ve antinuclear antibody, arthralgia or arthritis or joint stiffness or swelling and one or more of: fever, myalgia, hepatitis, rash, vasculitis.	Rare. Urgently stop the drug. Supportive care and seek specialist advice.
3) ***Serum sickness-like syndrome*** = Fever, urticaria or rash, and arthralgia, arthritis or joint swelling. Eosinophilia may be present.	Rare. Urgently stop the drug. Supportive care and seek specialist advice.
Other Serious Side Effects	
Raised LFTs, hepatitis and autoimmune hepatitis, hepatic failure, cholestatic jaundice.	If abnormal LFTs suspected, stop the drug and check LFTs. Seek expert advice once LFTs known. Deaths have been described.
SLE or Stevens-Johnson syndrome	May cause or worsen SLE, stop the drug and seek expert advice.
Photosensitivity	Stop treatment and avoid direct exposure to natural or artificial light. If severe seek specialist advice.
Hyperpigmentation (blue/black/grey/brown). May affect skin, nails, teeth, oral mucosa, bones, thyroid, eyes, breast milk, lacrimal secretions, sweat.	Stop the drug. Avoid sunlight if possible as the staining in combination with sunlight becomes less reversible. Seek specialist advice.
Bulging fontanelles – a sign of benign intracranial hypertension (BIH).	BIH is described with tetracyclines. Stop the drug and seek specialist advice.
Neutropenia, agranulocytosis, haemolytic anaemia and pancytopenia.	Rare but have been described. If suspected, check FBC - if abnormal stop treatment and seek expert advice.
Severe hypersensitivity reactions are described including anaphylaxis, shock, pulmonary infiltrates, anaphylactic purpura, asthma and bronchospasm.	Rare. Stop the drug. Supportive care and seek specialist advice.
Pneumonitis	Rare. Stop the drug. Supportive care and seek specialist advice.
Myocarditis, pericarditis	Rare. Stop the drug. Supportive care and seek specialist advice.
Oesophagitis/oesophageal ulceration	Follow administration instructions to prevent. If occurs stop the drug and seek expert advice.
Common Side Effects >1%	
Dizziness (lightheaded)	Usually not severe and may resolve spontaneously. If severe or associated with other signs such as fits or sedation, seek specialist advice.
Gastrointestinal (GI) upset – nausea, vomiting, diarrhoea	Usually resolves with time.
For other less common side effects see SPC[7]	

NOTABLE DRUG INTERACTIONS (REFER TO BNF AND SPC)

- **Antacids, calcium salts and iron salts:** Adjust timing so that minocycline is not taken at the same time as an antacid (given at least 2 - 3 hours apart). If given together, minocycline may have reduced absorption leading to subtherapeutic levels.
- Oral **anticoagulants:** Minocycline enhances the effects of warfarin and phenidione. Monitor international normalised ratio (INR) and consider reducing the warfarin dose.
- **Combined oral contraceptives (COC):** Minocycline, like all broad spectrum antibiotics, has been thought to reduce the effectiveness of the COC, but the magnitude of this effect is thought to be less than previously believed. If diarrhoea occurs take other contraceptive precautions for the duration of symptoms plus 7 days.
- **Ergot alkaloids:** Avoid combination increased risk of ergotism.
- Avoid **penicillin** use with minocycline, as the bacterostatic action of minocycline reduces the effectiveness of the penicillin.
- Administration with systemic **retinoids** increases the risk of BIH. Therefore a wash-out period after stopping minocycline and before starting a systemic retinoid is recommended. Use of this combination should be avoided.

BACK-UP INFORMATION AND ADVICE

Contact Details	Amersham and Wycombe	Stoke Mandeville
Dermatology	09:00 – 17:00 contact on-call registrar or consultant via switchboard. 01494 526161	09:00 – 17:00 contact on-call registrar or consultant via switchboard. 01296 315000
Medicines Resource Centre	01494 425355	
Switchboard	Amersham 01494 434411 Wycombe 01494 526161	01296 315000

PHARMACY INFORMATION

For all dermatology indications: Hospital pharmacy to supply first four weeks of treatment.

REFERENCES

1. BNF 76. September 2018 - March 2019
2. Harmann KE et al. Guidelines for the management of pemphigus vulgaris – on behalf of the British Association of Dermatology. Brit J Derm 2017; 177; 1170-1201937.
3. PrescQIPP (2014) *Minocycline use in acne vulgaris. PrescQIPP*. www.prescqipp.info
4. Gardner SE et al. Minocycline for acne vulgaris: efficacy and safety. The Cochrane Database of Systematic Reviews. 2012; issue 8, Art no: CD002086. Available https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002086.pub2/epdf/full
5. Ochsendorf F. Minocycline in acne vulgaris: benefits and risks. Am J Clin Derm 2010;11:327-341.
6. Minocin® MR 100 mg capsule SPC dated 9th July 2018. Accessed via www.medicines.org.uk/emc on 21st April 2020.

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