Macrolides for the prophylaxis of exacerbations of chronic lung disease

Prescribing Support Document

What is it?

Azithromycin and Clarithromycin are macrolide antibiotics which are recommended by the National Institute of Clinical Excellence (NICE) and British Thoracic Society (BTS) as an option in reducing exacerbation of chronic lung diseases.

This is an off-label use of azithromycin and clarithromycin, and clinicians should counsel and consent patients to this effect.

NICE and BTS Guidance

Between NICE and BTS azithromycin and clarithromycin for prophylaxis of exacerbations of chronic lung disease is recommended for:

Patients with COPD and:

- 3 or more exacerbations a year requiring oral corticosteroids
- Exacerbations resulting in hospital admissions
- Prolonged exacerbations with high levels of sputum production

Patients with asthma and:

- On high dose inhaled corticosteroids
- 1 or more exacerbations a year requiring oral corticosteroids

Patients with bronchiectasis and:

- 3 or more exacerbations a year

Formulary Status

The formulary status of azithromycin and clarithromycin locally can be found in the netFormulary monographs:
Azithromycin monograph
Clarithromycin monograph

Both treatments are considered suitable for prescribing in both primary and secondary care.

This prescribing support document has been provided as this is an off-label use of azithromycin and clarithromycin.

Which health professionals will prescribe?

Prophylactic azithromycin or clarithromycin will be initiated by a hospital specialist clinician for this indication and then can be continued by a primary care clinician.

Preparations and Dosage

Preparation

Azithromycin tablets 250 mg and 500 mg
Azithromycin capsules 250 mg and 500 mg
Azithromycin suspension 200 mg/5ml
Clarithromycin tablets 250 mg and 500 mg
Clarithromycin suspension 250 mg/5 ml

Dosage

Azithromycin 250 mg three times a week (Monday-Wednesday-Friday).
Increased as necessary to azithromycin 500 mg three times a week.

Or

Clarithromycin 250 mg daily.
Increased as necessary to clarithromycin 500 mg daily.

Initiation of treatment

A hospital specialist clinician will initiate azithromycin or clarithromycin and supply the first 3 months of medication.

Prior to initiation they will check the following:

- Spirometry
- Documented history of exacerbations and sputum
- Sputum culture and sensitivity
- Blood test including: Full Blood Count (FBCs), Liver Function Tests (LFTs), Ureas and Electrolytes (U&Es) and Creatinine Clearance (CrCl)
- Electrocardiogram (ECG)
- Assessment of drug-drug interactions. See BNF azithromycin interactions.
- Audiometry considerations

The hospital specialist will also repeat LFTs and the ECG at one month post initiation.

Counselling at initiation of treatment

The hospital specialist clinician will ensure the patient is counselled on the following:

- Risks and benefits of prophylactic macrolides
- Informed and consented to this off-label use of macrolides
- Side effects: GI upset, hearing and balance disturbances, cardiac events and microbiological resistance

- Give advice to stop prophylactic macrolides and seek advice if they notice hearing impairment or tinnitus
- Explain need to discuss holding prophylactic macrolides for the duration of other antibiotic treatment with other healthcare providers as appropriate:
    - Recommend hold while on any other macrolide.
    - Recommend hold while on any broad-spectrum antibiotic.

Continuation of treatment

A hospital specialist will review the effect of azithromycin or clarithromycin on the patient at 3 months.

If it has been beneficial, they will prescribe one further month or treatment and then handover repeat prescribing to the patient's primary care clinician. The primary care clinician will be asked to continue to monitor the ongoing effect of the macrolide i.e. the reduction in exacerbations of chronic lung disease, and to continue to check LFTs every 6 months. If the rate of exacerbations does not decline, LFTs rise by 2x the upper limit of normal or there are signs of hearing loss or tinnitus they should contact the hospital specialist clinician for advice.

If the prophylactic macrolide has not been beneficial at 3 months, the hospital specialist will discontinue azithromycin and inform the primary care clinician.

Contraindications and precautions for use

The advice in this document does not apply to the follow patient groups, or patient with the following conditions:

- Children
- Pregnant individuals
- Breastfeeding individuals
- Cystic fibrosis
- Mycobacterial infections
- Allergies to macrolide antibiotics
    - Abnormal QTc (Corrected QT Interval). QTc is >450ms for men and >470ms for women.
    - Severe liver disease, where LFTs are 2 times the upper limit of normal.

Special warnings and precautions for use

Please be aware the following conditions are cautions to using prophylactic macrolides.

- Severe renal disease where CrCl < 10 mL/minute
- Myasthenia gravis
- Electrolyte disturbance

Drug Interactions

The hospital specialist clinician will review drug-drug interactions with azithromycin at initiation as per BNF azithromycin interactions.

The hospital specialist clinician will review drug-drug interactions with azithromycin at initiation as per BNF clarithromycin interactions.

Adverse effects

See counselling at initiation of treatment.

For full details on contraindications, cautions, drug interactions and adverse effects, prescriber should consult the latest edition of the British National Formulary (BNF) or Summary of Product Characteristics (SPC).

References

- BTS Guideline for Long Term Macrolide Use (April 2020)
- NICE Guideline NG 115 Chronic obstructive pulmonary disease in over 16s
- NICE Guideline NG 117 Bronchiectasis
- Summary of product characteristics- Azithromycin 500 mg tablets
- BNF- Azithromycin
- BNF- Clarithromycin

Document ratification details

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