Rationale for Initiation, Continuation and Discontinuation (RICaD)

Azithromycin Tablets- Off-label Use

For COPD or bronchiectasis patients who have ≥3 exacerbations per year

This document supports the use and transfer of an agent which is classified as **AMBER**.
It is intended for completion by specialists in order to give Primary Care prescribers a clear indication of the reason for recommending an **AMBER** medication together with suggested criteria for its subsequent continuation or discontinuation. This RICaD should be provided as a supplement to the specialist's clinical letter.

Patient details		**GP details**		**Specialist details**	
Name		**GP Name**	**Dr**	**Specialist Name**	
NHS Number		**GP address**		**I confirm that this patient is eligible to receive azithromycin tablets under the restrictions listed below**	
DOB				**Signature**	
Patient address				**Date**	
				Contact details	

Rationale for Choice

Relevant Diagnosis and Agreed Indication(s) for inclusion in the BSSE APC Formulary:	Inclusion criteria: COPD or bronchiectasis patients who have ≥3 exacerbations* per year. *Exacerbation is defined as sustained episode (>48 hours) in which the patient's symptoms exceed the normal daily variability, including sputum purulence and requires a new intervention. Exclusion criteria: children, cystic fibrosis, asthma without bronchiectasis, mycobacterial infections, abnormal QTc, pregnancy, breast feeding.
Reason why azithromycin has been chosen in preference to drugs without Formulary restrictions:	Two randomised controlled trials [2,3] found that, compared with placebo, azithromycin reduced the rate of pulmonary exacerbations needing antibiotics in adults with non-cystic fibrosis bronchiectasis over 6 to 12 months. However, the improvement in exacerbations must be balanced against the risk of experiencing adverse events and the development of antibiotic resistance. In both trials azithromycin was generally well tolerated and few people discontinued treatment due to adverse events[4].
Baseline evaluation:	Document the nature & frequency of exacerbations including: • increased breathlessness • new sputum production or increased volume • the purulent nature of the sputum • Chest x-ray, (check CT chest has been done to confirm bronchiectasis diagnosis) Investigations: • FBC, LFT and U+E. Avoid azithromycin in severe liver disease and renal disease (eGFR <10mL/min) • Sputum sample for MC&S and viral nasopharyngeal swab during exacerbation • 3 sputum samples to exclude non-tuberculous mycobacterium infection • Assess for azithromycin interactions with concomitant medications. See: BNF[5] • ECG (record QTc interval). Avoid azithromycin if QTc >480 ms and consider referral to electrophysiology/cardiology (Caution if patient has low serum potassium or is on concomitant medications that prolong the QTc interval) See: CredibleMeds-Drugs that prolong QT / cause TDP[6] • Consider audiometry referral especially if baseline hearing impairment or tinnitus

Based on HeFT RICaD template
Prepared by Satnaam Singh Nandra
Interface Lead Pharmacist
Birmingham CrossCity CCG

Guidance on initiation

Initiation dose:	**Document informed patient consent (this is an off-label use).** Dose: Depending on patient compliance, use either • Azithromycin 500mg **tablets** (not capsules) three times a week (Monday, Wednesday, Friday). or • Azithromycin **tablets** (not capsules) 250mg each day.
Specialist recommendations	**Specialist to**: • Encourage patient to record a symptom diary: to have a hand held record to document exacerbations, antibiotic courses, hospital admissions e.g. BronkoTest • Give advice to patients to stop medication and seek advice if they notice hearing impairment or signs of tinnitus • Give advice to GP to undertake liver function tests 2- 4 weeks post initiation of azithromycin • Patients requiring IV or second line oral antibiotics while on long-term azithromycin should normally have the prophylaxis stopped and recommenced once the exacerbation has been treated
Monitoring:	**GP** to undertake liver function tests 2- 4 weeks post initiation of azithromycin. **Specialist to review**: symptoms, exacerbations, LFTs, U+Es, sputum culture results, compliance with therapy, ECG (record QTc). **If patient shows no benefit**: this should be reassessed at each clinic appointment and treatment stopped if no benefit identified.

Suggested Criteria for Continuation or Discontinuation

Assessment of Efficacy	
Frequency	6 months, then review to assess efficacy. If continuing treatment, this will require annual specialist review. Consider trial off antibiotics in summer months, and some patients may only require in winter months due to seasonal variations.
Location	Outpatients clinic
Method	Please refer to Respiratory use of long term azithromycin in adults' guidelines that support this RICaD.
Continuation Criteria	Patient has improved from previous baseline assessment, breathlessness, sputum production and purulence. Duration of treatment is 6 months, then review to assess efficacy; if continuing treatment, this will require annual specialist review.
Discontinuation Criteria	• If patient shows no benefit: this should be reassessed at each clinic appointment and treatment stopped if no benefit identified • New hearing impairment / tinnitus • Deranged LFT profile • Sputum samples from new exacerbations show evidence of mycobacterial infection • eGFR <10mL/min • Raised QTc interval (>480 ms) • Clostridium difficile associated diarrhoea (CDAD)

Follow up action	**GP to seek specialist advice in the following situations**: • Patient has a recurrent or non-resolving exacerbation whilst on azithromycin, except where there is a clear reason e.g. acute viral infection. • Patient not compliant with optimal therapy (e.g. inhalers, oral medication). • Patient has not been reviewed at 6 months after initiation of azithromycin, or at regular intervals not exceeding12 month intervals thereafter. • Significant drug interaction with essential therapy.
Shared Care Read Code	In the patients notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement/ RICaD

GP Prescribing System	Read Code	Description
EMIS and Vision	8BM5.00	Shared care prescribing
SystmOne	XaB58	Shared care

References

1. Pomares et al. (2011) International Journal of COPD. 6:449-456
2. BAT Altenburg et al. (2013) JAMA 27:309(12):1251-9
3. EMBRACE Wong et al. (2012) Lancet. 18:380(9842):660-7
4. NICE ESUOM38 Non-cystic fibrosis bronchiectasis: long-term azithromycin (November 2014)
5. https://www.evidence.nhs.uk/formulary/bnf/current/a1-interactions/list-of-drug-interactions/antibacterials/macrolides/azithromycin
6. https://crediblemeds.org/pdftemp/pdf/CombinedList.pdf

Please note the information included in this document is correct at the time of writing. The manufacturer's Summary of Product Characteristics (SPC) and the most current edition of the British National Formulary should be consulted for up to date and more detailed prescribing information.