Respiratory use of long term azithromycin in adults

Initiation by respiratory consultant only

- **Inclusion criteria:** COPD or bronchiectasis patients who have ≥3 exacerbations* per year
- **Exclusion criteria:** children, cystic fibrosis, asthma without bronchiectasis, mycobacterial infections, abnormal QTc, pregnancy, breast feeding.

*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.

All patients should have had their pharmacological and non-pharmacological therapy optimised prior to initiating treatment with azithromycin:

- Smoking cessation
- Correct inhaler choice and dose
- Correct inhaler technique
- Chest clearance advice, consider mucolytic therapy

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)
- **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 Azithromycin[a]
- **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[b])
- **Consider audiometry** referral especially if baseline hearing impairment or tinnitus.

Treatment:

- **Document informed patient consent** (this is an off-label use)
- **Dose:** Depending on patient compliance, use either 500mg azithromycin **tablets** (not capsules) three times a week (Monday, Wednesday, Friday) **or** azithromycin **tablets** (not capsules) 250mg each day.
- **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**
- **Action 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

6 month review:

- **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.
- **Duration:** 6 months, then review to assess efficacy, if continuing treatment 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.

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

References: Pomares et al. (2011) International Journal of COPD. 6:449-456; BAT Altenburg et al. (2013) JAMA 27:309(12):1251-9; EMBRACE Wong et al. (2012) Lancet. 18:380(9842):660-7.

a https://www.evidence.nhs.uk/formulary/bnf/current/a1-interactions/list-of-drug-interactions/antibacterials/macrolides/azithromycin

b https://crediblemeds.org/pdftemp/pdf/CombinedList.pdf

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