

## Information leaflet for community clinicians

## Prophylactic Antibiotic Use in Patients with Bronchiectasis or COPD

Long term prophylactic antibiotics should only be initiated by specialist chest physicians or tertiary care centres such as The Brompton only, this document is aimed at supporting GPs with general advice. Several tests are needed before the antibiotics are initiated by secondary or tertiary care and patients need to be individually assessed for risk vs benefits. Patients considered are those with bronchiectasis or COPD who despite having their inhaled treatment optimised have had exacerbations requiring oral steroids and antibiotics 3 times or more in the last 12 months.

## Long term Azithromycin use

There is evidence for different Azithromycin regimes, the regime used in MK and Royal Brompton is **Azithromycin 250mg capsules three times a week** - (this use is off-license). The mechanisms of action include anti-inflammatory, anti-bacterial and immunomodulatory mechanisms.

# Who initiates this therapy and what tests should be carried out before it is commenced?

The respiratory team at MKHFT or respiratory specialists at other hospitals should initiate the patient on this therapy and provide initial supply. Before initiation, a number of tests and processes need to take place in order to ensure that the treatment will be both safe and effective; your patient will have had an ECG and LFTs.

## What if the patient has an exacerbation whilst on Azithromycin?

The antibiotic chosen to treat the exacerbation should be based on either recent sputum results for that patient or on local empirical guidelines. Local chest consultants advise to stop the Azithromycin whilst being treated for an exacerbation and to restart after the acute course of antibiotics. If in doubt please seek advice form the respiratory team and/or microbiologist.

### What are the ongoing monitoring requirements and who is responsible for these?

There are no official monitoring guidelines; however as with all medicines used off license, it is important to watch for signs of adverse effects.

If your patient suffers with any of the symptoms below, discontinue Azithromycin and refer back to the initiating specialist:

- Hearing loss
- Signs and symptoms of liver dysfunction, such as rapid developing asthenia associated with jaundice, dark urine, bleeding tendency or hepatic encephalopathy, perform liver function tests immediately
- Visual loss
- Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes
- Abnormal white blood cell counts
- As with all long term antibiotics, *C difficile* infection or fungal superinfections are possible, treat according to guidance.

If the patient history of exacerbations over previous 12 months requiring oral steroids and antibiotics does not improve, refer to respiratory team to review necessity of ongoing treatment. However as with all respiratory patients it is important to also:

- check for compliance with current medications
- maximise inhaler technique
- check stand-by antibiotics will still be effective and ask patient to return any that will no longer be useful.

## Which patients should not take Azithromycin?

- Patients with an allergy to azithromycin or any of the macrolide or ketolide antibiotics, erythromycin, or to any excipients thereof.
- Patients with significant hepatic disease
- Patients with congenital or documented QT prolongation
- Patients currently receiving treatment with other active substance known to prolong QT interval such as antiarrhythmics of class IA and class III, antipsychotic agents, antidepressants and fluoroquinolones. For further information
  - http://www.formularymk.nhs.uk/includes/documents/Stockley-QTc-prolongation-May14.pdf
- Patients with electrolyte disturbance, particularly in case of hypokalaemia and hypomagnesaemia
- Patients with clinically relevant bradycardia, cardiac arrhythmia or severe cardiac insufficiency.
- Patients with severe renal impairment (GFR <10 ml/min)</li>
- Patients with myasthenia gravis
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.
- Avoid use in pregnancy or breastfeeding

### What interactions are there with other medicines?

- Azithromycin and ergot derivatives should not be given concurrently.
- Azithromycin and medicines known to prolong QT interval should not be given concurrently.
- In patients receiving azithromycin and antacids, the drugs should not be taken simultaneously.
- Caution if given with anticoagulants e.g. warfarin as can enhance anticoagulant effect
- Caution if given with ciclosporin or digoxin
- Check latest BNF and SPC for up to date information.

### References:

- 1. BNF number 66 pages 373-374
- 2. Azithromycin SPC: <a href="https://www.medicines.org.uk/emc/medicine/1477/SPC/Zithromax+250+Capsules/accessed">https://www.medicines.org.uk/emc/medicine/1477/SPC/Zithromax+250+Capsules/accessed</a> February 2014
- 3. Clinical Guideline Care of adults with cystic fibrosis 2013 Royal Brompton and Harefield NHS foundation trust www.rbht.nhs.uk/cystic-fibrosis
- 4. Azithromycin for Prevention of Exacerbations of COPD Albert et al N ENG J Med 2011 365;8 689-98
- 5. Azithromycin for Prevention of exacerbations in non-cystic fibrosis bronchiectasis (EMBRACE): a randomised, double-blind, placebo-controlled trial Wong et al Lancet 2012; 380 660-667
- 6. Effect of Azithromycin Maintenance Treatment on Infectious Exacerbations Among Patients with Non-Cystic Fibrosis Bronchiectasis Attenburg et al JAMA 2013; 309(!") 1251-1259
- 7. Effects of prolonged use of Azithormycin in patients with cystic fibrosis: a meta-analysis Florescu et al The University of York Centre for Reviews and Dissemination National Institute for Health Research http://dx.doi.org/10.1016/j.pupt.2009.03.002
- 8. Azithromycin and the Risk of Cardiovascular Death Ray et al N ENG J Med 2102 366;20 1881-90
- 9. Azithromycin: Drug Safety Communication-Risk of Potentially Fatal Heart Rythms FDA <a href="http://www.fda.gov/Safety/MedWatch/SafetyInfomration/SafetyAlertsforhumanMedicinalProducts>Azithromycin">http://www.fda.gov/Safety/MedWatch/SafetyInfomration/SafetyAlertsforhumanMedicinalProducts>Azithromycin</a>
- NHRMC Internal Medicines Residency Online EBM Resource: Which of my COPD patients should I
  consider antibiotic prophylaxis for exacerbations http://seaecim.wordpress.com/2012/07/27/705-taken
  from Discussion N Eng J Med 2012 367 350-347
- 11. Cochrane review on macrolides and antibiotic prophylaxis for COPD 2013, issue 11