This policy statement is approved by Halton, Knowsley, Liverpool, Southport and Formby, South Sefton, St Helens, Warrington and West Lancashire CCGs

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PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
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NHS Pan Mersey Area Prescribing Committee

AZITHROMYCIN tablets for prevention of exacerbations of COPD and bronchiectasis in selected high-risk patients

AMBER

The Pan Mersey Area Prescribing Committee recommends the prescribing of azithromycin tablets in selected high risk patients, when recommended by a respiratory specialist, for the prevention of exacerbations in COPD and bronchiectasis.

RECOMMENDED

The Pan Mersey Area Prescribing Committee recommends azithromycin tablets for the prevention of exacerbations in COPD and bronchiectasis in selected high risk patients, when recommended by a respiratory specialist. This is an off-label use and informed patient consent should be sought before prescribing. The specialist should clearly communicate that this discussion has taken place and the daily dose in the letter to the GP. Azithromycin has anti-inflammatory, immunomodulatory and lung remodelling properties in chronic airways disease.

The CHEST/CTS 2015[1] Acute Exacerbation of COPD Guidelines recommend macrolide prophylaxis for patients with moderate to severe COPD, who have a history of one or more moderate or severe COPD exacerbations in the previous year despite optimal maintenance inhaler therapy to prevent acute exacerbations of COPD.

Conversely, the GOLD Guidelines 2015[2] state that although recent trials of daily azithromycin showed efficacy on exacerbation rates, they did not recommend treatment due to an unfavourable balance between benefits and side-effects.

NICE CG101 (2010) has not issued any recommendations on the use of azithromycin in COPD for its immunomodulatory and lung remodelling properties,

Azithromycin capsules are significantly more expensive than tablets; therefore tablets should be prescribed where possible.

All patients should be reviewed by a respiratory specialist after a 6 month trial to consider stopping therapy if no reduction in exacerbations is seen and establishing overall risk/benefit

Azithromycin does not significantly affect the hepatic cytochrome P450 system. It is not believed to undergo the pharmacokinetic drug interactions as seen with erythromycin and other macrolides. Hepatic cytochrome P450 induction or inactivation via cytochrome-metabolite complex does not occur with azithromycin.[3]

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Version: 3.1
Review date: November 2017
(or earlier if there is significant new evidence relating to this recommendation)

AZITHROMYCIN tablets for prevention of exacerbations of COPD and bronchiectasis in selected high-risk patients.

EFFECTIVENESS

Two randomised controlled trials BAT[4] and EMBRACE[5] found that, compared with placebo, azithromycin reduced the rate of pulmonary exacerbations needing antibiotics in adults with non-cystic fibrosis bronchiectasis over 6-12 months. The trials showed that azithromycin reduces exacerbations in the short term compared with placebo, but the evidence for other outcomes was unclear

A recent Cochrane review (2013)[6] concluded that the use of continuous prophylactic macrolide antibiotics in COPD for a period of up to 12 months was likely to reduce the number of patients with exacerbations, exacerbation frequency, the median time to first exacerbation and possibly health-related quality of life. There were, however, some concerns regarding potentially serious adverse effects such as hearing loss and prolongation of the QT interval and the potential for macrolide resistance.

SAFETY

Long term safety has not been established as published trial data does not extend to greater than 1 year.

Clinicians should consider the arrhythmogenic potential (due to QT-interval prolongation) of azithromycin, particularly in those patients already taking medications that could prolong the QT interval and perform a baseline ECG prior to initiation. The largest trial to date excluded patients with tachycardia, prolonged QT interval and patients taking medications that could prolong the QT interval[7]

Nausea, vomiting, abdominal discomfort and diarrhoea are common side-effects. Hepatotoxicity and rash occur less frequently. Hearing loss occurs commonly after long-term therapy with azithromycin, which is usually reversible[8].

Azithromycin is contraindicated if there is hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic, or to any excipients listed in the SPC.

Microbiologists across the locality have been consulted and the general consensus of opinion is that azithromycin for prevention of exacerbation should not lead to bacterial resistance; however, consideration should be paid to the possibility of macrolide resistance.

COST

Azithromycin capsules are significantly more expensive than tablets; therefore tablets should be prescribed where possible.

It is not possible to estimate patient numbers for this indication, however, this intervention is likely to be cost neutral due to the reduction in non-elective hospital attendance.

Annual Costs[9] (if tablets prescribed)

250mg 3 times per week = £70.20

250mg daily = £164.25

500mg 3 times per week = £90.48 (using 500mg tablets)

(Capsules 250mg 3 times/week = £393.12, 250mg daily = £919.80, 500mg 3 times/week = £786.24)

PATIENT FACTORS

No dose adjustment necessary in patients with mild to moderate renal impairment but caution is advised in patients with severe renal impairment (**eGFR**< 10mL/min) as systemic exposure to azithromycin may be increased.

Use with caution in patients with significant hepatic disease. and those taking medication which may prolong the QT interval.

LFTs and ECG should be performed at baseline.

Although full information on the risk this poses is not available patients should be advised of the potential for hearing loss after long term use.

PRESCRIBING INFORMATION

Opinion on dosing in this condition is varied, with a dose range of between 250mg to 500mg three times per week to to 250mg daily, as per consultant recommendation.

Azithromycin does not significantly affect the hepatic cytochrome P450 system and is not believed to undergo the pharmacokinetic drug interactions as seen with erythromycin and other macrolides. Please refer to the Summary of Product Characteristics (SPC)[3] for further information.

All patients should be reviewed by a respiratory specialist after a 6 month trial to consider stopping therapy if no reduction in exacerbations is seen and establishing overall risk/benefit.

IMPLEMENTATION NOTES

Azithromycin can be prescribed in primary care following recommendation by a respiratory specialist. The specialist should advise the GP of the daily dose and communicate that patient consent has been obtained.

REFERENCES

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5. Wong C, et al. (2012) Azithromycin for prevention of exacerbations in non-cystic fibrosis bronchiectasis (EMBRACE): a randomised, double-blind, placebo-controlled trial. Lancet 380:660−7
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9. National Health Service England and Wales. Drug Tariff. August 2015: accessed 14/8/15