

Co-trimoxazole Prophylaxis of Primary and Secondary Spontaneous Bacterial Peritonitis (SBP)

Commissioning Statement

NHS Fylde and Wyre Clinical Commissioning Group has agreed to fund co-trimoxazole for the treatment of Prophylaxis of Primary and Secondary Spontaneous Bacterial Peritonitis (SBP) as:

- a second-line option for primary and secondary SBP prophylaxis
- an alternative first-line option for primary and secondary SBP prophylaxis in place of ciprofloxacin if there is known sensitivity

In the absence of Shared Care Guidelines this is a RED medicine and prescribing must stay in secondary care.

This medicine is classified as RED for this indication

Summary of supporting evidence:

- American and European Guidelines recommend antibiotic prophylaxis to reduce the incidence of SBP. Both guidelines currently recommend norfloxacin, however this is not currently available as a licensed product in the UK. Co-trimoxazole and ciprofloxacin are also listed as possible alternative options, which are currently available in the UK, but neither are licensed for the prophylaxis of SBP.
- There have been several trials assessing antibiotic prophylaxis in SBP, however they are of low quality and the majority focus on the use of norfloxacin.
- Evidence for co-trimoxazole use consists of three studies with small numbers of patients; one retrospective (n=69) in 2008, comparing co-trimoxazole with norfloxacin, a RCT (n=60) from 1995, comparing co-trimoxazole against no prophylaxis and a randomised non-blinded trial (n=80) in 2014, comparing co-trimoxazole to norfloxacin.
- The 2014 paper showed no statistically significant difference in the incidence of SBP, bacteraemia or overall infection between co-trimoxazole and norfloxacin. The retrospective review conducted by the same authors also showed no statistically significant difference in rates of SBP, spontaneous bacteraemia or extraperitoneal infections between norfloxacin and co-trimoxazole.
- The RCT (1995) found SBP developed in 8 patients (27%) receiving no prophylaxis and in 1 patient (3%) receiving co-trimoxazole (p=0.025). It should be noted that the RCT used a dosing schedule of 960mg for 5 days per week and the proposed use is 960 mg daily. The guidance recommending co-trimoxazole for prophylaxis of SBP is based on this 1995 RCT and a Cochrane review rated the quality of this trial as low.
- The incidence of AEs in the trials were found to be similar between co-trimoxazole and norfloxacin groups. However, it was noted that the number of AEs related to the treatment drug was increased for the co-trimoxazole group compared to norfloxacin group (22.5% vs. 0% p=0.01) and included; gastrointestinal, renal and skin related reactions, which resolved on discontinuation of the drug.
- The 1995 paper which compared co-trimoxazole to no treatment stated that no patients experienced AEs. It was noted that one patient developed diarrhoea, with no *C. difficile* present, which resolved despite continuation of the study drug.

Policy date: Sept 2016

Review date: Sept 2019

- It should be borne in mind that there is an increased incidence of *C. difficile* infection with co-trimoxazole treatment; OR 1.81 (95% CI 1.34 to 2.43). The conclusion of a review of 3 meta-analyses did state however, that the association is greater with quinolones, clindamycin and cephalosporins.
- Co-trimoxazole includes amongst other undesirable effects blood and lymphatic system disorders, which patients with hepatic failure are more susceptible to.
- Patients on prolonged treatment should have blood counts at monthly intervals due to the possibility of blood dyscrasias, more especially in elderly patients.
- The annual cost per patient of co-trimoxazole at 960 mg daily for the prophylaxis of SBP is £86. The alternative, ciprofloxacin 500 mg daily, has an annual per patient cost of £40. The request states the expected use to be 1-2 patients per month, equating to 24 a year. Using co-trimoxazole over ciprofloxacin would equate to an additional £1197 annually.

For further details around the evidence, cost effectiveness and for an explanation of the colour classification system please refer to the website of the Lancashire Medicines Management Group at: <http://www.lancsmmg.nhs.uk/>