NHS
Fylde and Wyre
Clinical Commissioning Group

Colistimethate sodium/Colistin sulfomethate sodium (Colomycin®) For non-Cystic Fibrosis in Patients with Bronchiectasis Colonised with Pseudomonas Aeruginosa

Commissioning Statement

NHS Fylde and Wyre Clinical Commissioning Group has agreed to fund Colistimethate sodium (Colomycin®) as an option for patients with non-cystic fibrosis bronchiectasis, colonised with *Pseudomonas aeruginosa* if:

- Patients have had three or more exacerbations per year requiring antibiotics or fewer exacerbations that are causing significant morbidity, in whom long term nebulised antibiotic therapy is being considered.

This medicine is classified as AMBER 0 for this indication

Summary of supporting evidence:

- The BTS guidelines for bronchiectasis in non-cystic fibrosis patients recommend nebulised antibiotics for patients who have three or more exacerbations per year requiring antibiotics, or fewer exacerbations that are causing significant morbidity.
- These guidelines also recommend that patients with *P.aeruginosa* should have regular follow up in secondary care if they are receiving prophylactic oral or nebulised antibiotic therapy.
- A systematic review (n=1264) evaluating the efficacy and safety of inhaled antibiotics in patients with stable non-CF bronchiectasis concluded that inhaled antibiotics reduce sputum load, eradication of bacteria from sputum and reduce the risk of acute exacerbation compared to placebo or symptomatic treatment. However, the paper found there was no significant benefit in reducing unscheduled hospitalisations or improving health related quality of life.
- Of the twelve trials included in the systematic review, two assessed the use of inhaled colistimethate; one of which was a RCT comparing colomycin to placebo, the other an unpublished open label trial which has not been discussed further in this assessment.
- The RCT (n=144) did not meet the primary endpoint of time to exacerbation. A total of 36 out of 73 (49%) vs. 42 out of 71 (59%) experienced an exacerbation during the 6 months for colomycin and placebo respectively. Median time (25% quartile) to exacerbation was 165 days (42 days) in the colistin group vs. 111 days (52 days) for placebo (p=0.11).
- A subgroup analysis of those patients who complied with therapy (≥ 81%) demonstrated a significant reduction in exacerbations compared to placebo; 27 out of 54 (505) vs. 37 out of 52 (71%) (p=0.038) respectively. However, the study was not powered to show this and therefore we cannot reliably conclude whether this was as a result of treatment difference or chance.
- Quality of life measured using the SGRQ showed an estimated mean treatment difference in change in total SGRQ score for inhaled colistin of -10.51 (95% CI, -17.87 to -3.14) (p=0.006) at week 26. A reduction of 4 units or more is considered clinically significant.

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- The mean treatment difference in weight of sputum from baseline to week 4 was not statistically significant.
- Three retrospective and one prospective observational study in patients with non-cystic fibrosis bronchiectasis and *P. aeruginosa* colonisation (n=148) evaluated the effect of nebulised colistimethate sodium. However, one of the studies used a different dosing schedule to that which is recommended and the individual studies had small numbers of patients.
- Two of case series found no significant effect on hospital admissions, the other found a reduction in the mean number of hospital admissions before and after treatment from 3.0 to 0.95 per year (p=0.002). Two of the case series found a statistically significant reduction in the number of exacerbations needing antibiotics compared to before treatment.
- One study found a statistically significant reduction in the number of positive *pseudomonas* samples from 4.2 per year to 0.5 per year, the other found initial eradication of *pseudomonas* but after a median of 6 months nearly 50% experienced a recurrence. All three case series found no significant effect on FEV_1.
- The prospective case series found no significant differences in the mean number of hospital admissions (1.6 admissions compared with 1.9 per person per year), duration of hospital stay (19.7 days compared with 22.5 days per person per year), or duration of antibiotic use (15.4 days per person per year compared with 14.8 days per person per year) between colistimethate sodium and tobramycin.
- The systematic review found the only statistically significant difference in reported AEs compared to control group was for bronchospasm, which occurred in 10% of patients. However, it was found that for the colomycin subgroup this difference was not statistically significantly different compared to placebo; five (7%) patients in the colistin group of the RCT developed bronchoconstriction that led to treatment discontinuation.
- No colistimethate-resistant strains of *P. aeruginosa* were identified during the study and there were no significant differences in treatment-emergent pathogens between treatment groups.
- 143 AEs were reported in the RCT in 47 patients (64%) in the colistin group vs. 108 AEs in 38 patients (54%) for the placebo group (p=0.25). The incidence of adverse events leading to discontinuation of the study drug was low; 9.6% and 8.5% patients in colistin group and placebo group, respectively.
- The NRLS identified incidents of errors with colistimethate sodium preparations. Of particular concern were incidents when the wrong strength was prescribed, dispensed or administered.
- The UKMI assessment found that there are some risks with prescribing, product selection and administration of colistimethate sodium products.
- Colomycin 1 million unit vials twice daily, cost £1314 annually; colomycin 2 million unit vials twice daily, cost £2365 annually. In addition, Saline Steripoules required for dilution currently cost £493 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/