

**South East London Area Prescribing Committee
Formulary recommendation**

Reference:	066
Intervention:	Clofazimine in combination with clarithromycin and rifabutin as anti-MAP (<i>Mycobacterium avium subspecies paratuberculosis</i>) therapy for the treatment of Crohn's disease in adults (Clofazimine, clarithromycin and rifabutin are antimicrobial agents)
Date of Decision	April 2017
Date of Issue:	May 2017
Recommendation:	RED – suitable for prescribing and supply by hospital only
Further Information	<ul style="list-style-type: none"> • Clofazimine in combination with clarithromycin and rifabutin is accepted for use in South East London as an anti-MAP therapy regimen for the treatment of patients with Crohn's disease. • The anti-MAP regimen may be considered as a last line option in patients: <ul style="list-style-type: none"> – Who have not responded to/have been intolerant of or have a contraindication to treatment options and strategies for Crohn's disease outlined within the SEL IBD Pathways AND do not wish to have surgery. • Treatment is delivered in the following regimen: <ul style="list-style-type: none"> – Clarithromycin 250mg in the morning and 500mg at night – Rifabutin titrated up to a maximum total daily dose of 450mg daily – Clofazimine 100mg once a day • Clinical response will be assessed at 3-4 months and will be measured on a case by case basis determined by patient specific factors. These include the type of Crohn's disease the patient has, inflammatory markers, and patient symptoms using the Harvey Bradshaw index (HBI). • In patients with ongoing clinical response, the maximum treatment duration is 2 years. • Patients prescribed the anti-MAP regimen will require routine monitoring, including disease activity, full blood counts and liver function tests. This will be undertaken in the specialist clinic • Funding will need to be confirmed at individual Trust level as the anti-MAP regimen will be prescribed and supplied by the hospital. • It should be noted that clofazimine is not licensed in the UK and the use of clarithromycin and rifabutin in this indication is off-label. This should be communicated to the patient in line with the organisation's usual consent processes. • The gastroenterology teams in SEL should work collaboratively to develop a registry for these patients. Outcome data (effectiveness, safety and impact on service activity) on the use of the anti-MAP regimen should be collected
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	<ul style="list-style-type: none"> • Based on assumptions from the applicant, it is estimated that up to 10 patients per year might be suitable for treatment. • If it is assumed that 50% are from SEL (5 patients), based on a cost of the regimen of £4,660 per patient per year, this would result in a total cost of £23,300 across SEL.

Usage Monitoring & Impact Assessment	<p>Acute Trusts:</p> <ul style="list-style-type: none"> • Develop patient registry • Monitor and audit use. • Submit usage data and audit reports upon request to the APC. <hr/> <p>CCGs:</p> <ul style="list-style-type: none"> • Monitor ePACT data • Monitor exception reports from GPs if inappropriate transfer of prescribing to primary care is requested.
Evidence reviewed	<p>References (extracted from evidence evaluation)</p> <ol style="list-style-type: none"> 1. Clinical Knowledge Summaries: Crohn's Disease. Available online at: https://cks.nice.org.uk/crohns-disease#!topicsummary (accessed 28/12/2016) 2. National Institute for Health and Care Excellence CG152, October 2012: Crohn's Disease: management. Available online at: https://www.nice.org.uk/guidance/cg152 (accessed on 28/12/2016) 3. National Institute for Health and Care Excellence TA187: Infliximab and adalimumab for Crohn's Disease: https://www.nice.org.uk/guidance/ta187 (accessed on 28/12/2016) 4. National Institute for Health and Care Excellence TA352: Vedolizumab for treating moderately to severely active Crohn's Disease after prior therapy. Available online at: https://www.nice.org.uk/guidance/ta352 (accessed on 28/12/2016) 5. Mycobacterium avium paratuberculosis and the etiology of Crohn's Disease: A review of the controversy from the clinician's perspective. Canadian Journal of Gastroenterology 2010 24 (10) p619-624. 6. Patton P, Parker C, MacDonald J et al. Anti-tuberculosis therapy for maintenance of remission in Crohn's disease (Review). The Cochrane Database of Systematic Reviews July 2016 7. Afdhal N, Long A, Lennon J et al. Controlled trial of anti-mycobacterial therapy in Crohn's disease. Clofazimine versus placebo. Digestive Diseases and Sciences 1991 36 (4) p449-453 8. Kelleher D, O'Brien S, Weir D. Preliminary trial of clofazimine in chronic inflammatory bowel disease. Gut 1982 23 A449 9. Kohn A, Prantera C, Mangiarotti R et al. Antimycobacterial therapy and Crohn's disease: results of a controlled double blind trial with a multiple antibiotic regimen. American Journal of Gastroenterology 1994 89 p513-518 10. Selby W, Pavli P, Crotty B et al. Two year combination antibiotic therapy with clarithromycin, rifabutin and clofazimine for Crohn's disease. Gastroenterology 2007 132 (7) p2313-2319 11. Summary of Product Characteristics, Klaricid tablets. Available online at: http://www.medicines.org.uk/emc/medicine/16945 (accessed 30/12/2016) 12. Summary of Product Characteristics, Mycobutin. Available online at: http://www.medicines.org.uk/emc/medicine/1545 (accessed 30/12/2016) 13. Lamprene SPC (translated), Novartis. 14. Vedolizumab for moderately to severely active Crohn's disease after prior therapy – costing report. Available online at: https://www.nice.org.uk/guidance/ta352/resources/costing-report-495822349 (accessed 30.12.2016)

NOTES:

- a) Area Prescribing Committee recommendations and minutes are available publicly on member CCG websites.
- b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
- c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS.**