South East London Area Prescribing Committee
Formulary recommendation

Reference	**074**
Intervention:	**Tioguanine for the treatment of adults with inflammatory bowel disease – Crohn's disease and ulcerative colitis** (Tioguanine is an immunosuppressive cytotoxic medicine)
Date of Decision:	**August 2017**
Date of Issue:	**September 2017**
Recommendation:	**Red – suitable for prescribing and supply by the hospital only**
Further Information:	• Tioguanine is accepted as a **3rd line** oral immunosuppressive agent for maintaining remission in adult patients with Crohn's disease and ulcerative colitis. • Tioguanine may be considered for patients who are intolerant or unresponsive to **both** azathioprine and mercaptopurine and, for patients with Crohn's disease, who are unsuitable for treatment with methotrexate. Tioguanine will be a 3rd line oral option before progressing to biologic therapy. • Tioguanine is licensed in the UK for the treatment of acute leukaemias especially acute myelogenous leukaemia and acute lymphoblastic leukaemia. The use of tioguanine in IBD is off-label. This should be communicated to the patient in line with the organisation's usual consent processes. • The dose of tioguanine in IBD will be 20mg to 40mg daily. • Tioguanine is a cytotoxic and is only available in a 40mg formulation. Tablets will need to be halved for the 20mg dose. Cytotoxics should be handled in accordance with Trust procedures. If halving of the tablet is required, patients should be advised that care should be taken not to contaminate the hands or inhale the drug. • There is a risk of hepatic toxicity associated with tioguanine. Clinicians should ensure that appropriate monitoring is in place to minimise, identify and manage this risk. Tioguanine therapy should be discontinued in patients with evidence of liver toxicity • The South East London IBD pathway will be updated to incorporate tioguanine in line with this recommendation. • Funding will need to be confirmed at individual Trust level as tioguanine will be prescribed and supplied by the hospital.
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	• The cost of treatment with tioguanine 20mg to 40mg daily is between £800-£1,600 per patient per year (excluding VAT). • In the formulary submission, GSTfT estimated 35 patients eligible for treatment of which 50% will be from SEL (~18 patients). KCH and LGT estimate 5 patients per Trust per year. • Assuming ~50 patients will be eligible for treatment, this will result in a total drug cost impact of up to £80,000 per year. Based on information in the formulary submission, an estimated 50% of this spend will be for SEL based patients. • A significant proportion of this spend represents patients that are maintained on immunosuppression that would have otherwise required biologics, therefore tioguanine may be cost-delaying. • No increased service activity is expected from the addition of tioguanine for this indication; activity is likely to be comparable to standard immunosupressants.

Usage Monitoring & Impact Assessment	**Acute Trusts:** • Monitor usage and report back to the APC when requested. • Audit use as required by commissioners to ensure use is in line with this recommendation, this includes auditing against the IBD monitoring framework for submission to the APC when requested.
	CCGs: • Monitor ePACT data • Monitor exception reports from GPs if inappropriate transfer of prescribing to primary care is requested.
Evidence reviewed	**References (from evidence review)** 1. Clinical Knowledge Summaries (CKS): Crohn's disease. Available online here (accessed 18/07/2017) 2. Crohn's disease: management. National Institute for Health and Clinical Excellence Clinical Guideline 152 May 2016. Available online at: https://www.nice.org.uk/guidance/cg152 (accessed 18/07/2017) 3. Clinical Knowledge Summaries (CKS): Ulcerative colitis. Available online at: https://cks.nice.org.uk/ulcerative-colitis (accessed 18/07/2017) 4. Ulcerative colitis: management. National Institute for Health and Clinical Excellence Clinical Guideline 166 June 2013. Available online at: https://www.nice.org.uk/guidance/cg166 (accessed 18/07/2017) 5. Azathioprine tablets, Summary of Product Characteristics. Available online at: http://www.medicines.org.uk/emc/medicine/33245 (accessed 20/07/2017) 6. Tioguanine tablets, Summary of Product Characteristics. Available online at: http://www.medicines.org.uk/emc/medicine/24687 (accessed 20/07/2017) 7. Meijer B, Mulder C, Peters C et al. Efficacy of thioguanine treatment in inflammatory bowel disease: A systematic review. World Journal of Gastroenterology 2016 22 (40) p9012-9021 8. Pavlidis P, Ansari A, Duley J et al. Splitting a therapeutic dose of thioguanine may avoid liver toxicity and be an efficacious treatment for severe inflammatory bowel disease: a 2-center observational cohort study. Inflammatory Bowel Disease 2014 20 (12) p2239 to 2246 9. Ward M, Patel K, Kraiyawasam V et al. Thioguanine in inflammatory bowel disease: long term efficacy and safety. United European Gastroenterology Journal 2016 DOI:10.1177/205064061663438 10. Omer O, Salehi S, Loganayagam A et al. 6-Thioguanine as an alternative therapy in inflammatory bowel disease? – Experience in a London District General Hospital. Gut 2016 65 1 A1-A310 (PTH-079). 11. Dubinsky M, Vasiliauskas E, Sing H et al. 6-Thioguanine can cause serious liver injury in inflammatory bowel disease patients. Gastroenterology 2003 125 p298-303 12. Teml A, Schwab M, Hommes D et al. A systematic survey evaluating 6-thioguanine-related hepatotoxicity in patients with inflammatory bowel disease. Wiener Klinische Wochenschrift 2007 119/17-18 p519-527 13. BNF Online: Tioguanine medicinal forms, available online here (accessed 24.08.17)

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.**