

HISTORICALLY ACCEPTED USE

Tertiary and Quaternary Committee

Executive Summary

Date: June 2023

Medicine (INN): Mercaptopurine

Medicine (ATC): L01BB02

Indication (ICD10 code): Crohn's disease (K50.9)

Patient population: Patients diagnosed with Crohn's disease

Prevalence of condition: the prevalence of Crohn's disease for medical aid beneficiaries over the age of 20 years was reported at about 0.2 per 1000.¹ Incidence reported to be 2.6/100 000 per year.²

Level of Care: Tertiary and Quaternary

Prescriber Level: Specialist

Current standard of Care: *Mercaptopurine forms part of standard regimen for management of Crohn's in the public sector, and has been for the past three decades.*

Efficacy estimates:

Mercaptopurine has been shown to be effective in Crohn's disease since the early 1980's.

- Mercaptopurine:
 - » In a 1980 randomised double-blind study, 6-mercaptopurine was evaluated compared to placebo over 2 years for the treatment of Crohn's disease in 83 patients. Improvement was shown in 67% of patients on 6-mercaptopurine compared to 8% in the placebo group ($p < 0.001$). Additionally 6-mercaptopurine was more effective in closing fistulas, 31% versus 6%; and in permitting discontinuation of reduction of steroid dosage, 75% versus 36%.³

Evidence based guideline recommendations:

| Guideline | Recommendations |
|---|--|
| American College of Gastroenterology, 2018 ⁴ | <p><u>Moderate to severe disease/moderate/high risk</u></p> <ul style="list-style-type: none"> • Thiopurines (azathioprine, 6-mercaptopurine) effective and steroid sparing (strong recommendation, low level of evidence). • Thiopurines for maintenance of remission (strong recommendation, moderate level of evidence). |
| British Society of gastroenterology, 2019 ⁵ | <p><u>Induction of remission in mild to moderate disease ileocolonic disease:</u></p> <ul style="list-style-type: none"> • Azathioprine or mercaptopurine can be used as monotherapy in the maintenance of remission in Crohn's disease (GRADE: strong recommendation, low-quality evidence. Agreement: 100%). • Recommend that for patients with moderate to severe Crohn's disease responding to prednisolone, early introduction of maintenance therapy with thiopurines (GRADE: strong recommendation, low-quality evidence) or methotrexate (GRADE: strong recommendation, moderate-quality evidence) should be considered to minimise risk of flare as prednisolone is withdrawn (Agreement: 93.3%). |
| European Crohn's and Colitis organization (ECCO), 2020 ⁶ | <ul style="list-style-type: none"> • Suggest thiopurines as monotherapy for the induction of remission of moderate-to severe luminal Crohn's disease [weak recommendation, very low-quality evidence]. • Thiopurines are recommended for the maintenance of remission in patients with steroid-dependent Crohn's disease [strong recommendation, moderate-quality evidence]. |

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| American Gastroenterological Association, 2021 ⁷ | <ul style="list-style-type: none"> In adult outpatients with quiescent moderate to severe CD (or patients in corticosteroid-induced remission), suggest the use of thiopurines over no treatment for the maintenance of remission. (Conditional low). |
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Historically accepted use Criteria

| Criteria | | Comment | |
|----------|--|---|---|
| 1 | The medicine is included in the WHO Model Essential Medicines List, either as a core or complementary item, for the indication requested. | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| | | <i>Included but not for this specific indication.</i> | |
| 2 | The medicine is currently registered by SAHPRA for the indication. | YES <input checked="" type="checkbox"/> | NO <input type="checkbox"/> |
| | | Approved by FDA in 1953 | |
| 3 | There is evidence of long-established (prior to 1996*) safe and effective use of the medicine for the recognised indication in the public health sector. | YES <input checked="" type="checkbox"/> | NO <input type="checkbox"/> |
| | | Comment: | |
| 4 | New safety or efficacy concerns. | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| | | Comment: | |
| 5 | Is budget impact expected to have an incremental increase, that a de novo review is justified? | YES <input type="checkbox"/> | NO <input checked="" type="checkbox"/> |
| | | <i>MHPL – May 2023</i> <i>Mercaptopurine 50 mg tablets, 25 tablets: R1118.86</i> | |
| 6 | Equitable access across the country is essential and is limited only by the availability of adequately trained staff and availability of equipment. | YES <input checked="" type="checkbox"/> | NO <input type="checkbox"/> |
| | | Comment: | |

* The Essential Drugs Programme (EDP) of South Africa was established in terms of the National Drug Policy (NDP), which was implemented in 1996

Recommendation

It is recommended mercaptopurine be included on the Tertiary Essential Medicines List for use in patients with Crohn's disease.

REFERENCES

- ¹ Council for Medical Schemes. Trends in chronic disease prevalence in SA medical aid schemes: 2006-2011. November 2013. https://www.medicalschemes.com/files/Research%20Briefs/CD2006_2011_20131115.pdf
- ² Wright JP, et al. The epidemiology of inflammatory bowel disease in Cape Town 1980-1984. *S Afr Med J*, 1986;70(1):10-5.
- ³ Present DH, Korelitz BI, Wisch N, Glass JL, Sachar DB, Pasternack BS. Mercaptopurine – A long-term, randomized, double-blind study. *NEJM*. 1980, 302(18):981-987.
- ⁴ Lichtenstein GR, et.al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018; 113: 481-517.
- ⁵ Lamb CA et.al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut*. 2019, 68: s1-s106.
- ⁶ Torres J, et.al. ECCO Guidelines on therapeutics in Crohn's disease: medical treatment. *Journal of Crohn's and Colitis*. 2020, 4-22.
- ⁷ Feuerstein JD, et.al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe luminal and perianal fistulizing crohn's disease. *Gastroenterology*, 2021, 160: 2496-2508.