

## HISTORICALLY ACCEPTED USE

### Tertiary and Quaternary Committee

#### Executive Summary

**Date:** May 2024

**Medicine (INN):** Azathioprine

**Medicine (ATC):** L04AX01

**Indication/s (ICD10 code/s):** Ulcerative colitis (K51)

**Patient population/s:** Patients diagnosed with Ulcerative Colitis (any severity)

**Level of Care:** Tertiary and Quaternary

**Prescriber Level:** Specialist

**Current standard of Care:** Azathioprine forms part of a standard regimen for management of Ulcerative Colitis in the public sector and has been utilised for a number of decades. The agent was historically included on Adult Hospital Level Standard Treatment Guidelines until 2015 when amendments were made to refer all patients with Inflammatory Bowel Disease to specialist care. Azathioprine has remained on national contract however it was not carried through to the Tertiary and Quaternary EML.

**Rationale:**

Maintenance

- » Timmer 2016<sup>1</sup> explored azathioprine compared to placebo for maintenance of remission for patients with ulcerative colitis.
- » There is low-certainty evidence that azathioprine is superior to placebo (Failure to maintain remission; RR 0.68, 95% CI [0.54 to 0.86], n=232, 4 studies); (Failure to maintain remission in those with successful induction, RR 0.67, 95% CI [0.49 to 0.93], P=0.01, I<sup>2</sup>=29.54%, n=124, 2 studies).
- » Review concluded that “azathioprine may be an effective maintenance treatment for patients who have failed or cannot tolerate mesalazine or sulfasalazine and for patients who require repeated courses of steroids”.
- » There was very low-certainty evidence that there was no difference in adverse events between azathioprine and placebo (RR 2.51 95% CI [0.82 to 7.74], P=0.11, i<sup>2</sup>=0%, n=232, 4 studies).

**Evidence based guideline recommendations:**

Guideline	Recommendations
Ulcerative colitis: management NICE guideline [NG130] Published: 03 May 2019 <sup>2</sup>	<p><b>All extents of disease</b></p> <p>1.4.4 Consider oral azathioprine or oral mercaptopurine to maintain remission:</p> <ul style="list-style-type: none"> <li>• after 2 or more inflammatory exacerbations in 12 months that require treatment with systemic corticosteroids or</li> <li>• if remission is not maintained by aminosalicylates. [2013]</li> </ul> <p>1.4.5 To maintain remission after a single episode of acute severe ulcerative colitis:</p> <ul style="list-style-type: none"> <li>• consider oral azathioprine or oral mercaptopurine</li> <li>• consider oral aminosalicylates if azathioprine and/or mercaptopurine are contraindicated or the person cannot tolerate them. [2013]</li> </ul>

<sup>1</sup> Timmer A, Patton PH, Chande N, McDonald JW, MacDonald JK. Azathioprine and 6-mercaptopurine for maintenance of remission in ulcerative colitis. Cochrane Database Syst Rev. 2016 May 18;2016(5):CD000478. doi: 10.1002/14651858.CD000478.pub4. PMID: 27192092; PMCID: PMC7034525.

<sup>2</sup> Ulcerative colitis: management. NICE guideline [NG130]. Published: 03 May 2019. Available: <https://www.nice.org.uk/guidance/ng130>.

### 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.	<p>YES                  NO</p> <p><input checked="" type="checkbox"/>                  <input type="checkbox"/></p> <p>Disease-modifying anti-rheumatic drugs (29.2)</p>	
2	The medicine is currently registered by SAHPRA for the indication.	<p>YES                  NO</p> <p><input checked="" type="checkbox"/>                  <input type="checkbox"/></p> <p>Registration since 1974, SAHPRA Database</p>	
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.	<p>YES                  NO</p> <p><input checked="" type="checkbox"/>                  <input type="checkbox"/></p> <p>Comment: Registered in 1974, part of standard regimen</p>	
4	There have been no new reported safety or efficacy concerns (Please mark 'yes' if in agreement with statement).	<p>YES                  NO</p> <p><input checked="" type="checkbox"/>                  <input type="checkbox"/></p>	
5	The budget impact is not expected to have an incremental increase, that a de novo review is justified (Please mark 'yes' if in agreement with statement).	<p>YES                  NO</p> <p><input checked="" type="checkbox"/>                  <input type="checkbox"/></p> <p>Comment: Costs - Azamun 50mg TAB 100 tablets = R102.35 (120-150mg daily = R92 per month)<sup>3</sup> Agent already on contract and was previously part of standard of care in Adult Hospital Level STGs</p>	
6	Equitable access across the country is essential, and is limited only by the availability of adequately trained staff and availability of equipment.	<p>YES                  NO</p> <p><input type="checkbox"/>                  <input checked="" type="checkbox"/></p> <p>Comment</p>	

\* 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 that azathioprine, oral be included on the Tertiary Essential Medicines List for use in patients with ulcerative colitis.

<sup>3</sup> Medicines Health Product List (MHPL) – May 2024.