

HISTORICALLY ACCEPTED USE

Tertiary and Quaternary Committee

Executive Summary

Date: May 2024

Medicine (INN): Mesalazine (rectal)

Medicine (ATC): A07EC02

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: Mesalazine (*aminosalicylate*) 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. It was however not carried through to the Tertiary and Quaternary EML, and mesalazine suppositories are currently not on contract. Mesalazine oral was added to the TQ EML in 2015 as an alternative to sulfasalazine for special access for those patients with a Sulphur allergy.

Rationale:

Induction

- » A systematic review by Marshall 2010¹ for induction of response and remission (symptomatic, endoscopic, histological) for patients with distal active ulcerative colitis focussed on rectal mesalazine versus placebo or rectal steroids.
- » Rectal mesalazine was superior to placebo for induction of symptomatic remission (OR 8.30 95% CI [4.28 to 16.12], 8 RCTS, n=756, P<0.0001, i²=55.6%); endoscopic remission (OR 5.31 95% CI [3.15 to 8.92], 7 RCTS, n=729, P<0.0001, i²=30.95%); and histological remission (OR 6.28 95% CI [2.74 to 14.4], 5 RCTS, n=588, P<0.0001, i²=22.11%).
- » Rectal mesalazine was more effective than placebo for symptomatic improvement (OR 8.87, 95% CI [5.30 to 14.83], 8 RCTS, n=811, P<0.0001, i²=41.76%); endoscopic improvement (OR 11.18, 95% CI [5.99 to 20.88], 5 RCTS, n=331, P<0.0001, i²=15.33%); and histological improvement (OR 7.69, 95% CI 3.26 to 18.12], 6 RCTS, n=452, P<0.0001, i²=65.7%).

Maintenance

- » A systematic review by Marshall 2012² for maintenance of remission (symptomatic and endoscopic) for patients with quiescent ulcerative colitis focussed on rectal mesalazine versus placebo or oral mesalazine.
- » Rectal mesalazine was superior to placebo for maintenance of symptomatic remission (RR 2.22 95% CI [1.26 to 3.90], 4 RCTS, n=301, P=0.01, i²=67.1%) – low certainty evidence (GRADE, downgraded for imprecision and inconsistency); and endoscopic remission (RR 4.88 95% CI [1.31 to 18.18], 1 RCT, n=25, P=0.02, i²=NA – GRADE not reported).

¹ Marshall JK, Thabane M, Steinhart AH, Newman JR, Anand A, Irvine EJ. Rectal 5-aminosalicylic acid for induction of remission in ulcerative colitis. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD004115. DOI: 10.1002/14651858.CD004115.pub2.

² Marshall JK, Thabane M, Steinhart AH, Newman JR, Anand A, Irvine EJ. Rectal 5-aminosalicylic acid for maintenance of remission in ulcerative colitis. Cochrane Database of Systematic Reviews 2012, Issue 11. Art. No.: CD004118. DOI: 10.1002/14651858.CD004118.pub2.

- » No difference was found between rectal and oral mesalazine for maintenance of symptomatic remission (RR 1.24, 95% CI [0.92 to 1.66], 2 RCTs, n=69, P=0.15, $i^2=0\%$ - low certainty evidence (GRADE, downgraded for imprecision and serious risk of bias); and endoscopic improvement (RR 1.14, 95% CI [0.90 to 1.45], 2 RCTs, n=91, P=0.31, $i^2=NA$ - low certainty evidence (GRADE, downgraded for Imprecision and serious risk of bias studies).
- » No difference was found between rectal mesalazine and placebo in adverse events (OR 1.35, 95% CI [0.63 to 2.89], 2 RCTs, n=160, P=0.44, $i^2=0\%$) – GRADE not conducted.

Evidence based guideline recommendations:

Guideline	Recommendations
Ulcerative colitis: management NICE guideline [NG130] Published: 03 May 2019 ³	<p><u>Treating mild-to-moderate ulcerative colitis</u></p> <p>Proctitis</p> <p>1.2.1 To induce remission in people with a mild-to-moderate first presentation or inflammatory exacerbation of proctitis, offer a topical aminosaliclylate as first-line treatment. [2019]</p> <p><i>In May 2019, this was an off-label use of some topical aminosaliclylates for children and young people. See NICE's information on prescribing medicines.</i></p> <p>1.2.2 If remission is not achieved within 4 weeks, consider adding an oral aminosaliclylate. [2019]</p> <p>Proctosigmoiditis and left-sided ulcerative colitis</p> <p>1.2.6 To induce remission in people with a mild-to-moderate first presentation or inflammatory exacerbation of proctosigmoiditis or left-sided ulcerative colitis, offer a topical aminosaliclylate as first-line treatment.</p> <p>1.2.7 If remission is not achieved within 4 weeks, consider:</p> <ul style="list-style-type: none"> • adding a high-dose oral aminosaliclylate to the topical aminosaliclylate or • switching to a high-dose oral aminosaliclylate and a time-limited course of a topical corticosteroid. [2019] <p>Extensive disease</p> <p>1.2.11 To induce remission in people with a mild-to-moderate first presentation or inflammatory exacerbation of extensive ulcerative colitis, offer a topical aminosaliclylate and a high-dose oral aminosaliclylate as first-line treatment.</p>

³ Ulcerative colitis: management. NICE guideline [NG130]Published: 03 May 2019. Available: <https://www.nice.org.uk/guidance/ng130/chapter/Recommendations>

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>	Anti-inflammatory medicines (17.3)
2	The medicine is currently registered by SAHPRA for the indication.	<p>YES NO</p> <p><input checked="" type="checkbox"/> <input type="checkbox"/></p>	Registration since 1996, SAHPRA Database
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>	Comment: Registered in 1996, part of standard regimen
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>	Comment: Not currently on contract SEP: Asacol Suppositories, 500mg = R334,40 for 20 suppositories (1g daily = R1 003 per month). Agent was previously part of standard of care in Adult Hospital Level STGs ⁴
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>	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 that mesalazine, rectal be included on the Tertiary Essential Medicines List for use in patients with ulcerative colitis.

⁴ SEP Database December 2023. Available from: <https://www.health.gov.za/nhi-pee/>