

Mesalamine: A Comprehensive Overview

Mesalamine, also known as mesalazine or 5-aminosalicylic acid (5-ASA), is an anti-inflammatory medication primarily used to treat inflammatory bowel disease, particularly ulcerative colitis^{[1] [2] [3]}. It represents the active component of sulfasalazine but without the sulfa-related side effects that often limit sulfasalazine use.

Primary Uses and Indications

Mesalamine is primarily indicated for treating mild to moderately active ulcerative colitis in adults and children 5 years or older^{[2] [3] [4]}. The medication serves dual purposes:

- **Active treatment:** Managing symptoms during active disease flares
- **Maintenance therapy:** Preventing symptom recurrence once remission is achieved^{[1] [2] [4]}

The drug is also used for specific forms of inflammatory bowel disease including Crohn's disease (effective only in colonic disease)^[1], proctitis, and proctosigmoiditis^[4]. Recently, Germany introduced guidance to use mesalamine for treating acute uncomplicated diverticulitis^[1].

Mesalamine is available in multiple formulations including oral delayed-release tablets, extended-release capsules, and rectal preparations (suppositories and enemas)^{[2] [4]}. The different formulations allow targeted delivery to specific areas of the intestinal tract.

Mechanism of Action

While the exact mechanism remains incompletely understood, mesalamine exerts its therapeutic effects through several pathways^{[2] [4]}:

- **Anti-inflammatory action:** Blocks cyclooxygenase pathways and inhibits prostaglandin production in the colon
- **Antioxidant properties:** Acts as a potent scavenger of free radicals
- **Immune modulation:** Inhibits Nuclear Factor kappa B (NFkB) activation and reduces pro-inflammatory cytokine production
- **Cellular protection:** Activates peroxisome proliferator-activated receptor gamma (PPAR gamma) receptors in colonic epithelium

The medication works primarily through direct topical contact with intestinal tissues rather than systemic effects^[2].

Common Side Effects

The most frequently reported side effects of mesalamine include^{[5] [6] [7] [8]}:

Gastrointestinal Effects:

- Burping or belching (up to 26% of patients)^[5]
- Abdominal pain (21% of patients)^[5]
- Nausea and vomiting
- Constipation (11% of patients)^[5]
- Diarrhea
- Indigestion (4% of patients)^[5]

General Effects:

- Headache
- Muscle or joint pain
- Back pain
- Fever
- Fatigue

Respiratory/Nasal Effects:

- Nasal congestion
- Runny nose
- Sore throat
- Cold-like symptoms^{[6] [8]}

Most common side effects are mild, temporary, and typically subside within a few weeks of starting treatment^{[5] [6]}. These effects tend to be more pronounced when initiating therapy or increasing doses too rapidly.

Serious Side Effects and Warnings

While generally well-tolerated, mesalamine can cause serious adverse effects requiring immediate medical attention^{[6] [8] [9] [10]}:

Kidney Problems:

- Acute and chronic interstitial nephritis
- Kidney stones (nephrolithiasis)
- Minimal change nephropathy
- Acute renal failure^{[9] [11] [10]}

Chronic interstitial nephritis is particularly concerning as patients often present with asymptomatic reductions in kidney function without typical symptoms like fever or skin

lesions^[11]. If undetected, prolonged exposure can lead to irreversible kidney failure and end-stage kidney disease^[11].

Severe Allergic Reactions:

- Drug reaction with eosinophilia and systemic symptoms (DRESS)
- Stevens-Johnson syndrome (SJS)
- Toxic epidermal necrolysis (TEN)
- Acute generalized exanthematous pustulosis (AGEP)^{[6] [8] [9] [10]}

Cardiac Effects:

- Myocarditis (heart muscle inflammation)
- Pericarditis^{[6] [8] [10]}

Liver Problems:

- Hepatitis
- Liver failure (particularly in patients with pre-existing liver disease)^{[10] [12]}

Mesalamine Intolerance Syndrome:

A paradoxical worsening of ulcerative colitis symptoms including cramping, acute abdominal pain, bloody diarrhea, fever, headache, and rash^{[9] [10] [13]}. This condition can be difficult to distinguish from disease exacerbation and requires immediate drug discontinuation.

Monitoring Requirements

Due to potential serious side effects, regular monitoring is essential^{[9] [11] [10]}:

- **Kidney function:** Regular serum creatinine monitoring, especially during the first years of therapy
- **Liver function:** Particularly important for patients with pre-existing liver disease
- **Complete blood count:** To monitor for blood disorders
- **Urinalysis:** To detect early signs of kidney problems

Association with Vitamin D

Research has revealed a significant beneficial interaction between mesalamine and vitamin D supplementation in treating ulcerative colitis:

Synergistic Benefits:

Multiple studies demonstrate that vitamin D combined with mesalamine is more effective than mesalamine alone for treating ulcerative colitis^{[14] [15] [16] [17]}. Key findings include:

- **Improved clinical efficacy:** The combination shows higher clinical response rates (OR = 4.07, 95% CI 2.64-6.27)^{[14] [16]}
- **Better Mayo scores:** Significant reduction in disease activity scores (MD: -0.41, 95% CI -0.47 to -0.34)^{[14] [16]}

- **Enhanced intestinal barrier function:** Improved markers of mucosal healing^{[14] [16]}
- **Reduced inflammation:** Lower levels of inflammatory markers including IL-6, TNF- α , and CRP^{[14] [16]}

Optimal Patient Population:

The benefits are particularly pronounced in patients with vitamin D deficiency. Studies show that UC patients with baseline vitamin D deficiency (serum 25(OH)D <20 μ g/L) who receive vitamin D supplementation alongside mesalamine demonstrate:

- Greater reduction in Mayo scores (-4 vs -2, P=0.048)^[15]
- Higher clinical remission rates (60.0% vs 22.2%, P=0.019)^[15]

Safety Profile:

The combination therapy shows no significant increase in adverse reactions compared to mesalamine alone (OR = 0.73, 95% CI 0.34-1.32, P = 0.23)^{[14] [16]}.

Mechanism of Vitamin D Enhancement:

Vitamin D enhances mesalamine's effectiveness through several mechanisms^{[16] [17]}:

- **Immune modulation:** Regulates T-cell differentiation and reduces pro-inflammatory cytokine production
- **Intestinal barrier enhancement:** Promotes tight junction protein expression and mucosal integrity
- **Anti-inflammatory effects:** Inhibits NLRP inflammasome activation and reduces oxidative stress
- **Microbiome regulation:** Helps restore healthy gut microbiota balance

Drug Compatibility:

Studies confirm that mesalamine and vitamin D3 have no direct drug interactions and are physically compatible^{[18] [19]}.

Contraindications and Precautions

Mesalamine is contraindicated in patients with^{[10] [20]}:

- Known hypersensitivity to salicylates, aminosalicylates, or mesalamine components
- Severe kidney disease
- History of serious allergic reactions to aspirin or related compounds

Special precautions are needed for patients with:

- Pre-existing kidney or liver disease
- History of kidney stones
- Concurrent use of nephrotoxic medications (including NSAIDs)^[10]

Clinical Significance

Mesalamine remains a cornerstone therapy for ulcerative colitis management, with over 1 million prescriptions dispensed in the United States in 2021^[1]. The medication is included on the World Health Organization's List of Essential Medicines^[1] and is available as a generic medication, making it accessible for long-term management of inflammatory bowel disease.

The emerging evidence supporting vitamin D supplementation as an adjuvant therapy represents an important advancement in optimizing treatment outcomes, particularly for patients with vitamin D deficiency who may experience enhanced therapeutic benefits from this combination approach.

✱

1. <https://en.wikipedia.org/wiki/Mesalazine>
2. <https://go.drugbank.com/drugs/DB00244>
3. <https://medlineplus.gov/druginfo/meds/a688021.html>
4. <https://www.drugs.com/mesalamine.html>
5. <https://www.drugs.com/medical-answers/what-7-mesalamine-side-effects-aware-3576842/>
6. <https://www.webmd.com/drugs/2/drug-3332/pentasa-oral/details>
7. <https://www.crohnscolitisfoundation.org/patientsandcaregivers/ibd-medication/mesalamine-1>
8. <https://www.webmd.com/drugs/2/drug-147055/lialda-oral/details>
9. <https://www.drugs.com/sfx/mesalamine-side-effects.html>
10. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/020049s041lbl.pdf
11. <https://pubmed.ncbi.nlm.nih.gov/32147005/>
12. <https://www.ncbi.nlm.nih.gov/books/NBK547995/>
13. <https://pmc.ncbi.nlm.nih.gov/articles/PMC3088741/>
14. <https://pubmed.ncbi.nlm.nih.gov/35912148/>
15. <https://pubmed.ncbi.nlm.nih.gov/35764562/>
16. <https://pmc.ncbi.nlm.nih.gov/articles/PMC9328974/>
17. <https://www.gavinpublishers.com/article/view/opportunities-and-challenges-of-vitamin-d-as-a-dietary-supplement-in-improving-ulcerative-colitis>
18. <https://www.banglajol.info/index.php/JPharma/article/view/44466/32643>
19. <https://www.drugs.com/drug-interactions/mesalamine-with-vitamin-d3-2336-0-646-5790.html>
20. <https://www.webmd.com/drugs/2/drug-6073-1772/mesalamine-oral/mesalamine-5-aminosalicylic-acid-delayed-release-tabs-in-cap-oral/details>