INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Inflammatory Bowel Disease Guidelines***
-November 2025-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) performed an updated review of guideline-directed pharmacologic treatment of inflammatory bowel disease (IBD), last addressed in 2023. Drugs listed on the IHS National Core Formulary (NCF) relevant to this review include(s) adalimumab-bwwd, azathioprine, mercaptopurine, mesalamine (oral), methotrexate, prednisone, and sulfasalazine. Several updated clinical guidelines have since added recommendations pertaining to biologic and small molecule agents approved by the FDA for these conditions over the past 3 years. Following clinical review and analysis, the NPTC made no modifications to the NCF.

Discussion:

Crohn's disease (CD) and **ulcerative colitis (UC)**, conditions to which the term "inflammatory bowel disease" refers more generally, overlap substantially in their presentation, diagnostic evaluation, and treatment, yet are pathologically and anatomically distinct from each other. UC is characterized by superficial inflammation of colonic mucosa, usually involving the rectum and extending proximally to a variable extent, while CD is associated with transmural inflammation involving the ileum, can include discontinuous lesions in any part of the GI tract, and is associated with complications such as perianal fistula, abscess formation and luminal stricture. Extra-intestinal manifestations of disease, experienced by up to 1/3 of patients and more common in CD, can include arthritis, uveitis, erythema nodosum among others.[1,2]

IBD affects up to 1.3% of the population of the United States. Incidence generally peaks in the 3rd decade of life, though can present in adolescence.[3,4] In the United States, all ethnic groups are affected, though a review of Medicare data suggests that prevalence is lowest among Native American persons (CD: 0.23% vs 0.40% overall; UC: 0.40% vs 0.65% overall).[5] Nonetheless, a 2025 cohort study showed that Native American UC patients had a higher rate of obstructive complications, and those with CD longer average hospital stays than all other ethnic groups.[6]

Conventional agents used to treat IBD include anti-inflammatory agents and immune modulators, including oral and topical amino-salicylates and budesonide, other systemic glucocorticoids, and thiopurines and methotrexate.

Advanced agents target mediators within inflammatory pathways, some gut-specific, including injected biologics classified as tumor necrosis factor (TNF) inhibitors, interleukin (IL) 12/23 inhibitors, and integrin inhibitors; and oral small molecules such as Janus Kinase (JAK) inhibitors, and sphingosine-1-phosphate (S1P) receptor modulators.

Selected medications for Inflammatory Bowel Disease

Classification	Agent	Route	Safety considerations	Notes
Anti-inflammatory	5-aminosalicylates	Oral, rectal		CD: not recommended
	sulfasalazine	Oral		Limited role in IBD
	budesonide	Oral, rectal	HTN, small risk of adrenal suppression	
	prednisone	Oral	Many familiar long-term adverse effects	Used for induction only
Immune modulating	azathioprine	Oral	Lymphoma, myelosuppression, pancreatitis	Pre-treatment thiopurine methyl-transferase testing required
	methotrexate	SC	Bone marrow/ hepatic/ renal/ lung toxicity	CD only, off label
Anti-TNF	infliximab		Opportunistic infection, lymphoma, skin cancer	
	adalimumab			
Anti-interleukin 12/23	ustekinumab	IV->SC	Mild nasaopharyngitis common; risk of serious infection is low	Ustekinumab targets p40 subunit of IL12/23; newer agents target p19 subunit of IL23
	guselkumab	IV/SC->SC		
	mirikizumab	IV->SC		
	rizankizumab	IV->SC		
Anti-integrin	vedolizumab	IV->SC	Risk of serious infection = placebo	High GI specificity
Anti-JAK	upadacitinib	Oral	Thromboembolism, herpes zoster	FDA: use only after biologic failure
S1P receptor mod.	etrasimod	Oral	Cardiac rhythm abnormalities	UC only

Choice of initial therapy is tailored to disease severity, individual risk for complications or relapse, adverse effects of specific therapies, and response to previously used medicines. For both UC and CD, severity is determined by presenting clinical features (e.g., weight loss, rectal bleeding), lab indicators (e.g., CRP, CBC) and endoscopic features, and is summarized with the use of scoring tools such as the Crohn's Disease Activity Index, the Mayo score (UC), or the Montreal classification (CD or UC), among others.[7,8]

Mild to moderate disease:
Oral budesonide in a controlled ileal-release formulation is the preferred initial treatment of CD in most cases, and is tapered off after remission. Guidelines do not support the use of 5-aminosalycilates (5-ASA) for CD, though sulfasalazine can occasionally be used for distal colonic disease. For UC, a rectal 5-ASA agent is initiated for mild disease, where oral mesalamine or an oral colonic-release formulation of budesonide (MMX) can be added depending on proximal extent.[8,9,10]

Moderate to severe disease:
For failure of initial therapy in mild-moderate disease, or for patients who are sicker or at higher risk of disease recurrence or relapse, systemic glucocorticoids are used for induction given the rapid symptom relief they provide. Current guidelines generally support a "top-down" rather than a "step-up" approach, wherein advanced therapies are initiated early, initially using a TNF-inhibitor (often infliximab), paired with azathioprine to reduce the risk of treatment failure due to TNFi anti-drug antibodies.[10,11] This combination confers important risks, including susceptibility to opportunistic infections, increased risk of lymphoma and myelosuppression, and may be a less desirable choice in older patients, and in young men, who carry a greater risk of hepatosplenic T-cell lymphoma associated with thiopurine use.[12]

The anti-IL agent, ustekinumab, and the anti-integrin agent, vedolizumab, in use over the past decade for both CD and UC, have improved safety compared to anti-TNF therapy, and don't require concomitant use of an immune modulator given their comparatively low immunogenicity.

Recently approved agents:
Since the NPTC 2023 review, the anti-interleukins mirikizumab and guselkumab, and the anti-JAK upadacitinib have been FDA approved for both CD and UC; the anti-IL rizankizumab approved for UC (previously approved for CD); and the S1P-rm etrasimod approved for UC alone. For both induction and maintenance of remission, all outperformed placebo: mirikizumab showed a NNT=9 for UC, NNT=4 for CD;[13,14] rizankizumab showed a NNT=7 for UC;[15] guselkumab showed a NNT=7 for UC and NNT=3 for CD;[16,17] oral upadacitinib a NNT=3-5 for UC and NNT=3 for CD;[18,19] and etrasimod a NNT=5-10 for UC.[20] Head to head trials for most advanced therapies are lacking. A 2025 network meta-analysis (NMA) of treatments for CD ranked infliximab + azathioprine, followed by guselkumab as most effective for induction of remission.[21] A similar 2024 NMA of therapies for UC ranked rizankizumab and ozanimod (an older S1P-rm) as most effective for induction, followed by upadacitinib when used after failure of initial treatment, as labeled. When used in treatment-naïve patients (off-label), upadacitinib was ranked most effective.[22]

Findings:
Though the global incidence of IBD appears to be rising, falling surgical intervention rates and increasing prevalence in older patients parallels an increase in the availability of advanced therapies the past 20 years.[23] Monitoring for adverse effects of therapy and colorectal cancer surveillance are lifelong considerations for IBD patients.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

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