It Takes Guts! Induction Therapy for Crohn's Disease

A presentation for HealthTrust Members
January 31, 2024

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Overview

1 Objectives

2 Background

3 Diagnosis

4 Treatment Options

5 Patient Monitoring

1 Objectives

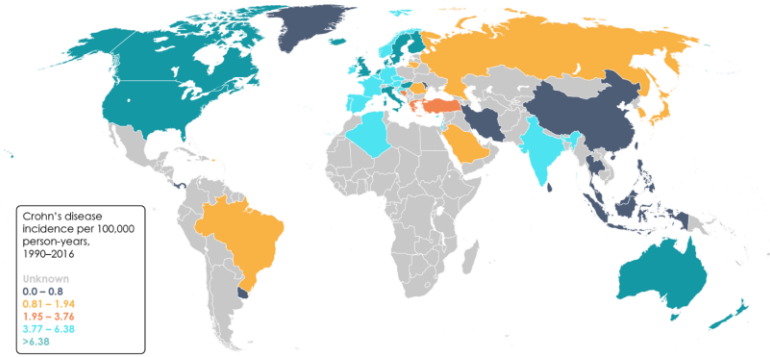
Objectives

1. Identify clinical goals of induction therapy for Crohn's disease
2. Recognize pharmacologic treatment options for induction therapy of Crohn's disease
3. Recall current guideline recommendations to induction therapy

2 Background

Crohn’s Disease

- Crohn’s disease is an idiopathic inflammatory disorder of unknown etiology with genetic, immunologic, and environmental influences.
- In 2015, an estimated 1.3% of US adults (3 million) reported being diagnosed with Inflammatory Bowel Disease (IBD).
- The prevalence of IBD increased from 2001 to 2018 among of all race and ethnicity groups, with the highest increase rate among non-Hispanic Black adults.



Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn’s Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018
Crohn's & Colitis Foundation. What is Crohn’s Disease? Updated 2023. https://www.crohnscolitisfoundation.org/what-is-crohns-disease
Centers for Disease Control. Inflammatory Bowel Disease. Updated 2023. https://www.cdc.gov/ibd/what-is-IBD.htm
Image obtained from https://www.medthority.com/medical-education/inflammatory-bowel-disease-learning-zone/understanding-crohns-disease/

CROHN'S DISEASE

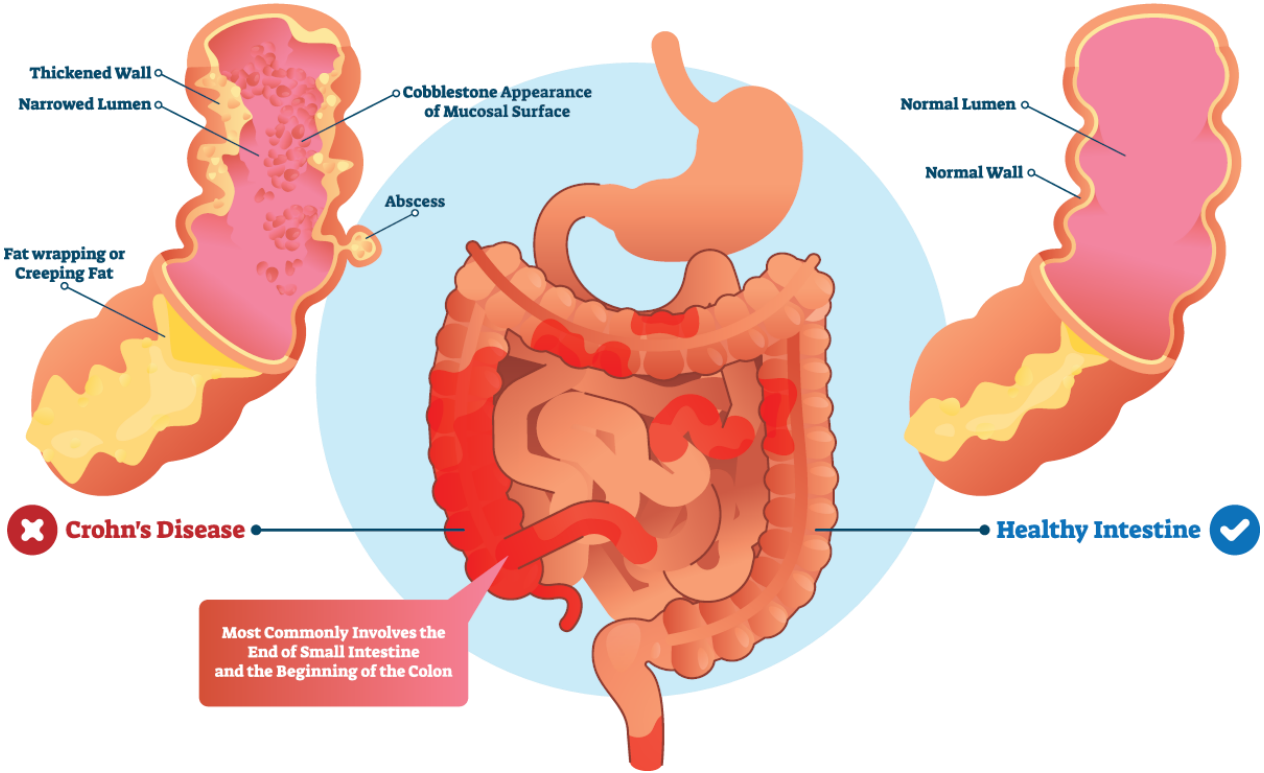


Image obtained from https://wellness-studio.co.uk/crohns-disease/

IBD vs IBS

Inflammatory Bowel Disease (IBD)

- Term for 2 conditions (Crohn's disease and Ulcerative colitis) that are characterized by inflammation of the gastrointestinal (GI) tract
- Can cause destructive inflammation and permanent harm to the intestines
- The disease can be seen during diagnostic imaging
- Increased risk for colon cancer

Irritable Bowel Syndrome (IBS)

- Does not cause inflammation
- Rarely requires hospitalization or surgery
- No sign of disease or abnormality during an exam of the colon
- No increased risk for colon cancer or IBD

Source: Crohn's & Colitis Foundation. What is Crohn's Disease? Updated 2023. https://www.crohnscolitisfoundation.org/what-is-crohns-disease
Centers for Disease Control. Inflammatory Bowel Disease. Updated 2023. https://www.cdc.gov/ibd/what-is-IBD.htm

Differentiating IBD

	Crohn's disease	Ulcerative colitis
Affected location	Can affect any part of the GI tract (from the mouth to the anus) Most often it affects the small intestine near the colon.	Occurs in the large intestine (colon) and the rectum.
Damaged areas	Patches of damaged area that are next to areas of healthy tissue.	Damaged areas are continuous – usually starting at the rectum and spreading further into the colon.
Inflammation	May reach through the multiple layers of the walls of the GI tract.	Present only in the innermost layer of the lining of the colon.

Source: Crohn's & Colitis Foundation. What is Crohn's Disease? Updated 2023. https://www.crohnscolitisfoundation.org/what-is-crohns-disease
Centers for Disease Control. Inflammatory Bowel Disease. Updated 2023. https://www.cdc.gov/ibd/what-is-IBD.htm

Symptoms

- The most common symptom of Crohn's disease is chronic diarrhea.
- Abdominal pain
  - Often localized to the right lower quadrant of the abdomen
  - Worsened postprandially
- Fatigue
  - Thought to arise from a number of factors including inflammation itself, anemia, or various vitamin and mineral deficiencies
- Weight loss
- Anemia
- Growth failure in children

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

Disease Progression and Prognosis

- Crohn's disease, in most cases, is a chronic, progressive, destructive disease.
- The location of Crohn's disease tends to be stable, but can occasionally extend.

- Overall mortality in Crohn's disease is slightly increased, with a standardized mortality ratio of 1.4 times that of the general population.
- The most common causes of excess mortality include GI disease and GI cancer.

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3 Diagnosis

Diagnosis

- Crohn's disease is diagnosed clinically.
- No single laboratory test can make an unequivocal diagnosis.
- Endoscopic, radiographic, and histologic criteria with evidence of chronic intestinal inflammation will be present.

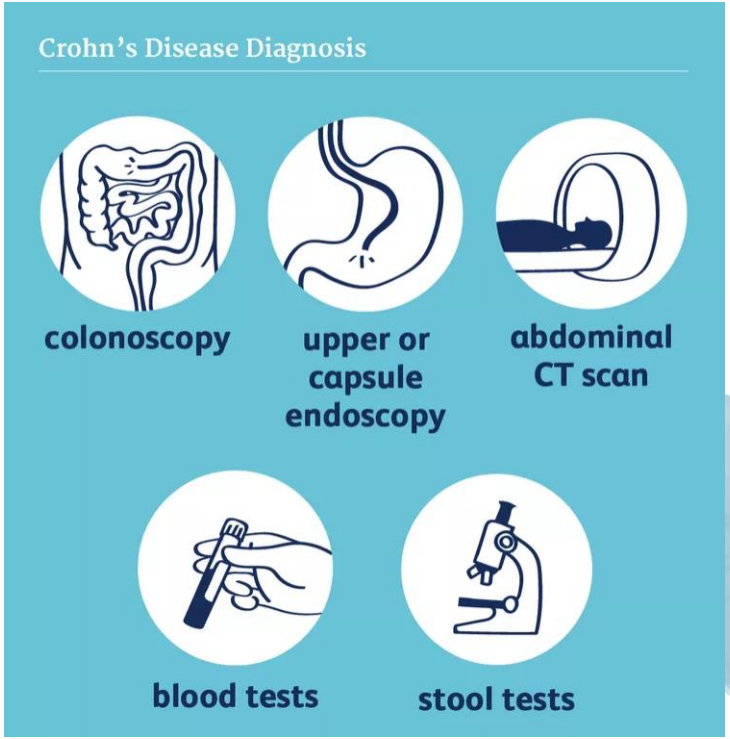

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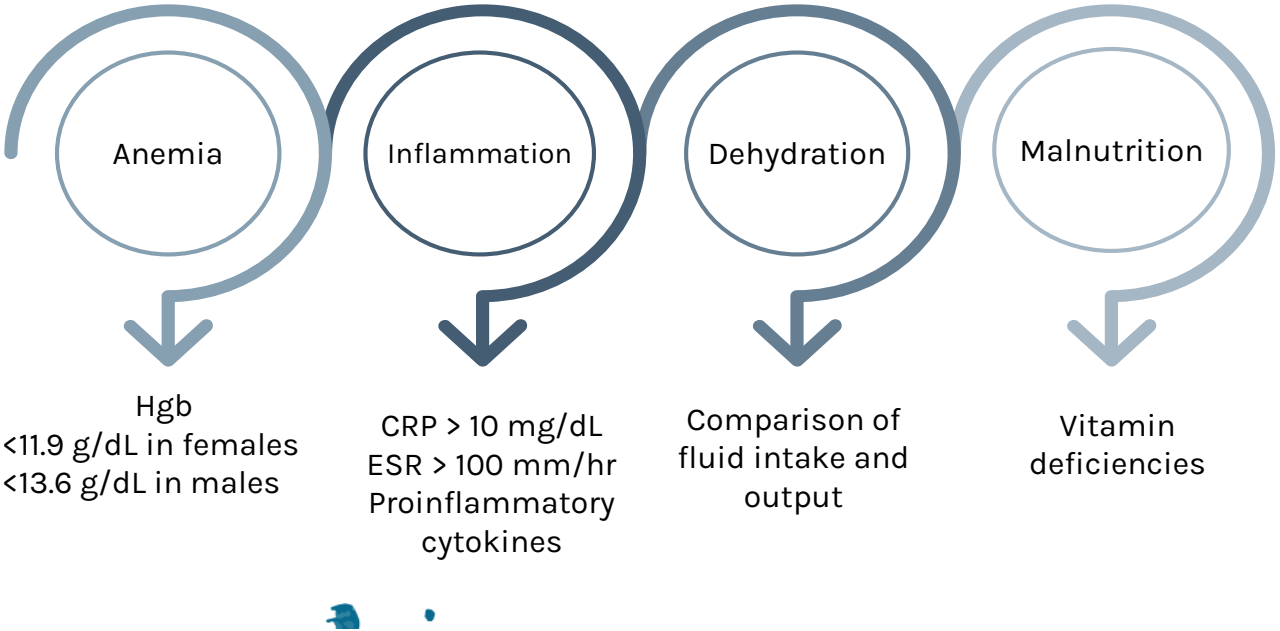
Image obtained from https://www.verywellhealth.com/how-crohns-disease-is-diagnosed-4164398

Clinical Tests

- No single laboratory test can make an unequivocal diagnosis.
- Diagnosis includes evaluation of



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Stool Testing

- In patients who have symptoms of active Crohn's disease, stool testing should be performed including
  - Fecal pathogens
  - *Clostridioides difficile* testing
  - May include studies that identify gut inflammation such as a fecal calprotectin

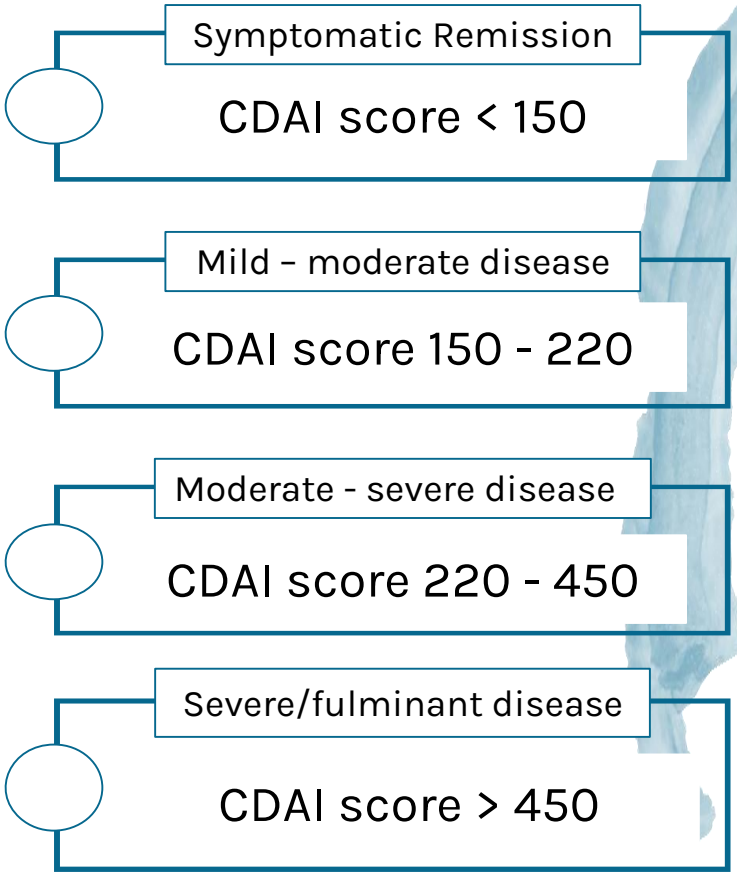
Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

CDAI score

Variable	*Quantity*	*Multiple*	*Total*
Number of liquid or soft stools per day		2	
Abdominal pain (0 = none, 1 = mild, 2 = moderate, 3 = severe)		5	
General well being (0 = well, 1 = slightly under par, 2 = poor, 3 = very poor, 4 = terrible)		7	
Number of complications: arthralgias, iritis, erythema nodosum, pyoderma gangrenosa, aphthous ulcerations, anal fissure, anal fistula, anal abscess, fever > 37° past week, intestinal obstruction		20	
Opiates for diarrhea (no = 0, yes = 1,)		30	
Abdominal mass (no = 0, questionable = 2, yes = 5)		10	
Deviation from normal hematocrit (N = 42 for female, 47 for male)		6	
% deviation from standard weight		1	
Total CDAI			

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

CDAI Classification



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4 Treatment Options

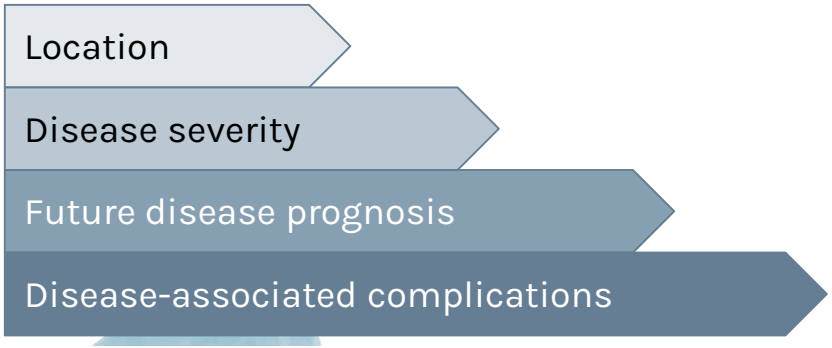
Lifestyle Treatment

- Patients who smoke should be counseled to quit.
- For patients with low risk of progression, it is acceptable to treat active symptoms with
  - Anti-diarrheals
  - Other non-specific medications
  - Dietary manipulation
  - Along with careful observation for inadequate symptom relief, worsening inflammation, or disease progression
- Nonsteroidal anti-inflammatory drugs (NSAIDs) may exacerbate disease activity and should be avoided when possible.
- Assessment and management of stress, depression, and anxiety should be included as part of the comprehensive care.

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

Overall Treatment Recommendations

- Current therapeutic approaches should aim to
  1. “Treat acute disease” or “induce clinical remission”
  2. Then to “maintain response/remission”
- Therefore, treatment is divided into induction and maintenance therapy.



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Classes of Medications

5-aminosalicylates

- Mesalamine
- Sulfasalazine

Antibiotics

- Metronidazole
- Ciprofloxacin

Corticosteroids

- Budesonide
- Prednisone

Immunomodulators

- Azathioprine
- 6-mercaptopurine

Biologics

- Anti-TNF agents
- Agents targeting leukocytes
- Anti-P40 antibody

Investigational Drugs

- JAK inhibitors
- Monoclonal antibodies

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

Abbreviations

- SE = side effects
- BBW = black boxed warning
- IV = intravenous
- IgG = immunoglobulin G, a type of antibody
- IL = interleukin, a type of cytokines, which are proteins that help cells communicate and regulate immune responses.

5-aminosalicylates

- Thought to modulate local chemical mediators of the inflammatory response
- Also thought to be a free radical scavenger or an inhibitor of tumor necrosis factor (TNF)

Sulfasalazine

- Immediate and delayed release: 3 to 6 g/day in divided doses for up to 16 weeks
- SE- blood dyscrasias, nausea, vomiting, diarrhea, and abdominal pain

Mesalamine

- The active component of sulfasalazine
- 1 g 3 to 4 times daily.
- SE - diarrhea, fever, abdominal pain (intolerance syndrome), kidney impairment and nephrotoxicity

Source: Sulfasalazine. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Mesalamine. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com

Corticosteroids

- Depresses the activity of endogenous chemical mediators of inflammation

Budesonide

- Targeted, pH-dependent release in the GI tract
- Capsule: 9 mg once daily in the morning for up to 8 weeks
- SE- hypertension, nausea, headache, respiratory tract infection, muscle spasm, peripheral edema

Prednisone

- 40 to 60 mg once daily for 7 to 14 days, followed by a taper of up to 3 months
- SE- adrenal suppression, CV effects, CNS effects, Cushing syndrome, GI effects, hyperglycemia, infection, and more

Source: Budesonide. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Prednisone. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com

Antibiotics

Metronidazole

- Interacts with DNA to cause loss of helical structure and strand breakage resulting in cell death.
- 20 mg/kg/day (in 3 divided doses) or 1 to 2 g/day in divided doses for 3 months
- SE - CNS effects, disulfiram-like reaction, nausea, vaginitis, headache

Ciprofloxacin

- Promotes breakage of double-stranded DNA.
- Immediate release: 500 mg twice daily, with or without metronidazole, for 4 weeks
- Serious SE- tendinopathy and tendon rupture, peripheral neuropathy, CNS effects, sun sensitivity

Source: Metronidazole. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Ciprofloxacin. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com

Immunomodulators

- Metabolites are incorporated into replicating DNA and halt replication

6-mercaptopurine

- 0.75 to 1.5 mg/kg/day in combination with an TNF agent
- SE- GI effects, bone marrow depression, malaise, skin rash

Azathioprine

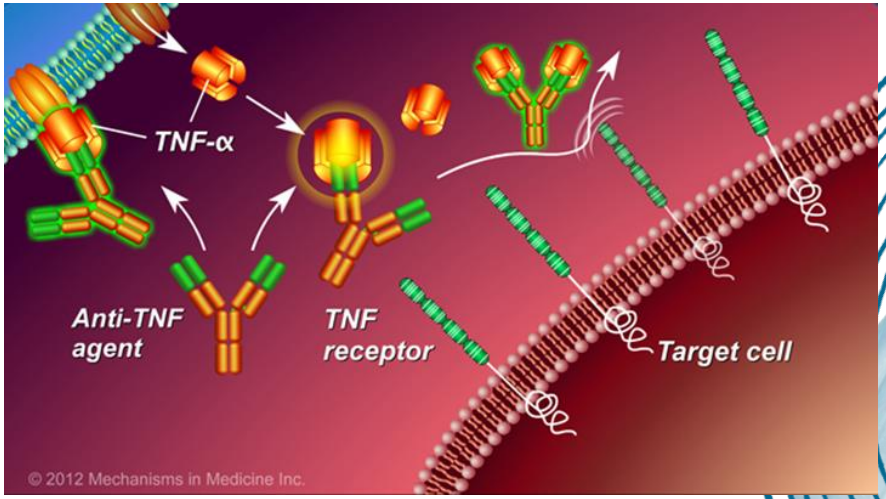
- Derivative of mercaptopurine.
- 50 mg once daily; titrate up to 2.5 mg/kg once daily over ≥12 weeks as indicated and tolerated
- SE- GI effects, hematologic toxicities, infections, hepatotoxicity, malignancy, pancreatitis

Source: Mercaptopurine. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Azathioprine. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com

Biologics

Anti-TNF agents

- Prevents the induction of proinflammatory cytokines, enhancement of leukocyte migration, activation of neutrophils and eosinophils, and the induction of acute phase reactants and tissue degrading enzymes.



Source: Infliximab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Adalimumab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Certolizumab pegol. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Image obtained from https://www.youandibd.com/en-ibd/view/m201-s7-chronic-inflammation-in-ibd-and-how-anti-tnf-therapy-works-slide-show

Biologics

Anti-TNF agents

- BBW for serious infections and malignancy
- SE - dermatologic reactions, tuberculosis, infusion reactions, hepatitis B reactivation, and hepatotoxicity

Infliximab (REMICADE®)

- 5 mg/kg at 0, 2, and 6 weeks, followed by 5 mg/kg every 8 weeks thereafter
- Avsola (infliximab-axxq)
- Inflectra (infliximab-dyyb),
- Renflexis (infliximab-abda)

Adalimumab (HUMIRA®)

- 160 mg (given over 1 or 2 days), then 80 mg 2 weeks later (day 15)
- Hadlima (Citrate-free high-concentration biosimilar)
- Cyltezo (First interchangeable biosimilar)

Certolizumab pegol (CIMZIA®)

- 400 mg, repeat dose 2 and 4 weeks after initial dose
- No available biosimilar agents

Infliximab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Adalimumab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Certolizumab pegol. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com

Biologics

Agents Targeting Leukocyte Trafficking

- Monoclonal antibodies that limit adhesion and transmigration of leukocytes

Vedolizumab (ENTYVIO®)

- IV: 300 mg at 0, 2, and 6 weeks and then every 8 weeks thereafter.
- SE- infusion-related reactions, hepatic injury, serious infection, headache, arthralgia

Natalizumab (TYSABRI®)

- IV: 300 mg infused over 1 hour every 4 weeks.
- BBW- progressive multifocal leukoencephalopathy
- SE - skin rash, abdominal distress, urinary tract infection, influenza, fatigue, headache, infusion-related reaction

Source: Vedolizumab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Natalizumab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com

Biologics

Anti-P40 Antibody

- Human monoclonal antibody that binds to and interferes with the proinflammatory cytokines, interleukin (IL)-12 and IL-23
- Serious SE of hypersensitivity reactions, infection, malignancy, noninfectious pneumonia, and tuberculosis

Ustekinumab (STELARA®)

- Induction of remission:
  - ≤55 kg: IV: 260 mg as single dose.
  - >55 kg to 85 kg: IV: 390 mg as single dose
  - >85 kg: IV: 520 mg as single dose

Source: Ustekinumab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com

Investigational Drugs

Upadacitinib (RINVOQ®)

- Approved for use in rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis
- Inhibits Janus kinase (JAK) enzymes
- BBW for malignancy, infection, mortality, thrombosis, CV events

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- In two phase 3 induction trials (U-EXCEL and U-EXCEED), patients with moderate-to-severe Crohn's disease to receive 45 mg of upadacitinib or placebo.
- A significantly higher percentage of patients who received 45-mg upadacitinib than those who received placebo had
  - Clinical remission (U-EXCEL, 49.5% vs. 29.1%; U-EXCEED, 38.9% vs. 21.1%)
  - Endoscopic response (U-EXCEL, 45.5% vs. 13.1%; U-EXCEED, 34.6% vs. 3.5%)

Source: Upadacitinib. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Loftus E, Panes J, et al. Upadacitinib Induction and Maintenance Therapy for Crohn's Disease. May 25, 2023. N Engl J Med 2023; 388:1966-1980. DOI: 10.1056/NEJMoa2212728
RINVOQ. Abbvie. North Chicago, IL. Updated 2023. https://www.rinvoqhcp.com/rheumatoid-arthritis/dosing-and-moa#mechanism-of-action

Investigational Drugs

Guselkumab (TREMFYA®)

- ➔ Human IgG1 monoclonal antibody selectively binds with IL-23
- ➔ Inhibits the release of proinflammatory cytokines and chemokines
- ➔ Main side effect is infection risk

- ➔ The GALAXI-1 study randomized patients to receive IV guselkumab 200 mg, 600 mg, 1200 mg, or placebo.
- ➔ All 3 dose regimens of guselkumab induced greater clinical and endoscopic improvements vs placebo, with a favorable safety profile.

	Reduction in CDAI from baseline	Clinical remission with CDAI < 150
Placebo	–36.2	16.4%
200 mg	–160.4	57.4%
600 mg	–138.9	55.6%
1200 mg	–144.9	45.9%

Source: Guselkumab. Lexi-Drugs. Lexicomp; 2021. Updated 2023. Accessed November 15, 2023. http://online.lexi.com
Sandborn W, D'Haens G, et al. Guselkumab for the Treatment of Crohn's Disease: Induction Results From the Phase 2 GALAXI-1 Study. Gastroenterology 2022-05-01, Volume 162, Issue 6, Pages 1650-1664.e8.

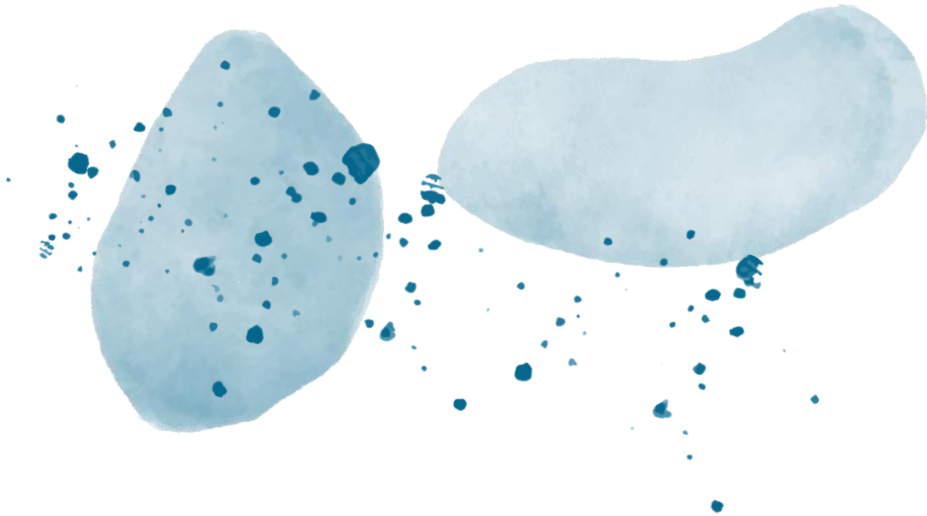
Which medication is available as a capsule that has targeted, pH-dependent release in the GI tract?

A. Prednisone

B. Budesonide

C. Mesalamine

D. Sulfasalazine



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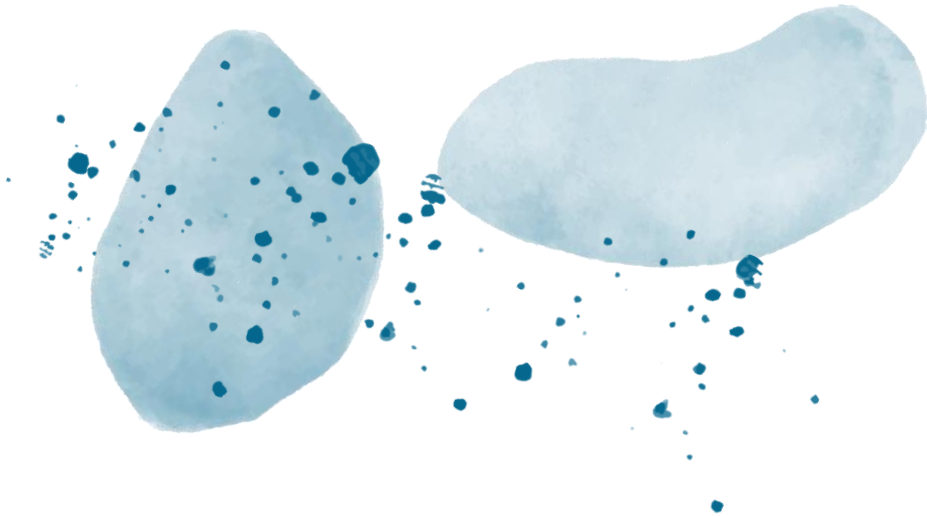

Mild to Moderate Disease

EFFECTIVE

- Sulfasalazine is effective for treating symptoms of Crohn's disease.
- Controlled ileal release budesonide once daily is effective.

INEFFECTIVE

- Oral mesalamine has not consistently been demonstrated to be effective.
- Metronidazole is not more effective than placebo.
- Ciprofloxacin has shown similar efficacy to mesalamine but has not been shown to be more effective than placebo.

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

Moderate to Severe Disease

EFFECTIVE

- ➔ Oral corticosteroids are effective and can be used for short-term use.
- ➔ Ustekinumab in patients who failed previous treatment with corticosteroids, thiopurines, methotrexate, or anti-TNF inhibitors or who have had no prior exposure to anti-TNF inhibitors.
- ➔ Upadacitinib induction treatment was superior to placebo.*
- ➔ Guselkumab induced greater clinical and endoscopic improvements vs placebo.*

*In clinical studies

INEFFECTIVE

- ➔ Azathioprine and 6-mercaptopurine are not more effective than placebo to induce short-term symptomatic remission.
- ➔ Cyclosporine, mycophenolate mofetil, and tacrolimus should not be used for Crohn's disease.

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

Severe and Fulminant Disease

EFFECTIVE

- ➔ IV corticosteroids should be used.
- ➔ Anti-TNF agents (infliximab, adalimumab, certolizumab pegol) can be considered to treat severely active disease.
- ➔ Infliximab may be administered to treat fulminant disease.

INEFFECTIVE

- ➔ Efficacy of adalimumab and certolizumab pegol is less certain.

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

Which of these would be the best first line agent for a patient with mild to moderate Crohn's Disease?

A. Metronidazole

B. Sulfasalazine

C. Adalimumab

D. Ibuprofen

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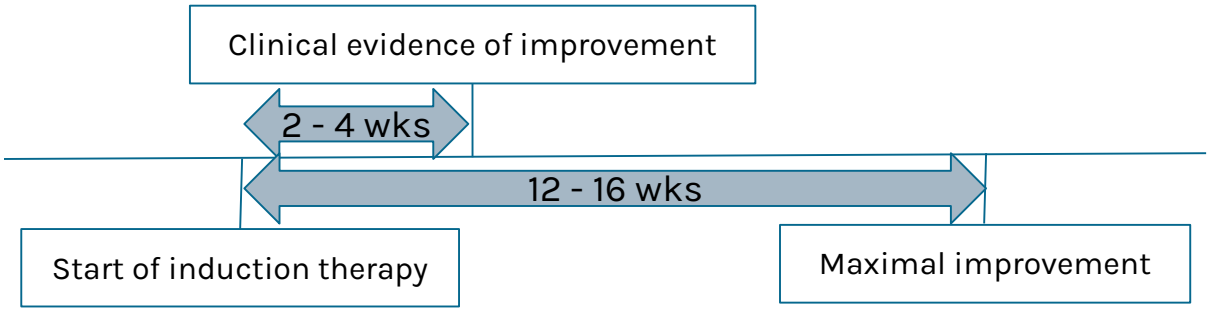
Evaluation of Therapy

- Treatment for active disease should be continued until
  - Symptomatic remission
  - Failure to continue improvement
- In general, clinical evidence of improvement should be evident within 2–4 weeks.
- Maximal improvement should occur with 12–16 weeks.



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5 Patient Monitoring

After starting treatment, when can patients expect to see clinical evidence of improvement?

A. 12 - 16 weeks

B. 8 - 12 weeks

C. 4 - 8 weeks

D. 2 - 4 weeks

After starting treatment, when can patients expect to see clinical evidence of improvement?

A. 12 - 16 weeks

B. 8 - 12 weeks

C. 4 - 8 weeks

D. 2 - 4 weeks

Disease Activity

- Mucosal healing has become an important target in assessing efficacy of treatment for IBD.
- Monitoring of the inflammatory response includes the following

1	2	3	4
Fecal markers	**Serum markers**	**Imaging studies**	**Endoscopic assessment**

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Types of Remission

- An individual may be in
  - Histologic remission
  - Endoscopic remission
  - Clinical remission
  - Surgical remission
- Individuals who require the use of conventional corticosteroids to achieve clinical well-being are said to be “steroid dependent” and are **not** considered to be in remission.

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn’s Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018

Histologic Remission

- Remission is based on appearance of biopsy tissue.
- Histologic changes may include
  - Granulomatous inflammation
  - Focal cryptitis of the duodenum
  - Focally enhanced gastritis
- The landmark feature of histological activity in IBD is defined by the presence of mucosal neutrophilic inflammation.
- Measured through the Geboes Score

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published 27 March 2018
Haley E, Eisner T. 5 Types of Crohn's Disease Remission. January 3, 2023. https://www.mycrohnsandcolitisteam.com/resources/what-does-crohns-disease-remission-look-like

Geboes Score

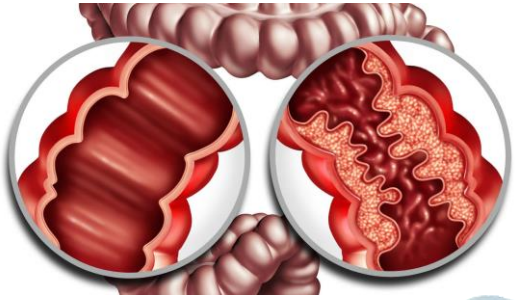
GS	Morphology	RHI
Grade 0: Architectural changes	0.0 No abnormality	0
	0.1 Mild abnormality	0
	0.2 Mild/moderate diffuse or multifocal abnormalities	0
	0.3 Severe diffuse or multifocal abnormalities	0
Grade 1: Chronic inflammatory infiltrate	1.0 No increase	0
	1.1 Mild but unequivocal increase	1
	1.2 Moderate increase	2
	1.3 Marked increase	3
Grade 2A: Eosinophils in lamina propria	2A.0 No increase	0
	2A.1 Mild but unequivocal increase	0
	2A.2 Moderate increase	0
	2A.3 Marked increase	0
Grade 2B: Neutrophils in lamina propria	2B.0 No increase	0
	2B.1 Mild but unequivocal increase	2
	2B.2 Moderate increase	4
	2B.3 Marked increase	6
Grade 3: Neutrophils in epithelium	3.0 None	0
	3.1 <5% crypts involved	3
	3.2 <50% crypts involved	6
	3.3 >50% crypts involved	9
Grade 4: Crypt destruction	4.0 None	0
	4.1 Probable–Local excess of neutrophils in part of the crypts	0
	4.2 Probable–Marked attenuation	0
	4.3 Unequivocal crypt destruction	0
Grade 5: Erosions and ulcerations	5.0 No erosion, ulceration or granulation tissue	0
	5.1 Recovering epithelium + adjacent inflammation	5
	5.2 Probable erosion—focally stripped	5
	5.3 Unequivocal erosion	10
	5.4 Ulcer or granulation tissue	15

GS: histological remission ≤ 2.0, histological response ≤ 3.0. RHI: histological remission ≤ 3, histological response ≤ 9.

Image obtained from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8880199/

Endoscopic Remission

- Endoscopy and colonoscopies reflect amount, location, and severity of inflammation in intestines
- Endoscopic parameters
  - Villous appearance
  - Ulcers
  - Strictures



- Mucosal healing as determined by endoscopy is a goal of therapy.
- Measured through
  - Crohn's Disease Endoscopic Index of Severity (CDEIS)
  - Simple Endoscopic Score for Crohn's disease (SES-CD)

Source: Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018
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Image obtained from https://www.drugwatch.com/health/digestive-health/crohns-disease/

Crohn's Disease Endoscopic Index of Severity (CDEIS)

Table 1
Crohn's disease endoscopic index of severity

	Rectum	Sigmoid and Left Colon	Transverse Colon	Right Colon	Ileum		Total
Deep ulceration (12 if present in the segment, 0 if absent)	0	0	0	0	0	0	1
Superficial ulceration (6 if present in the segment, 0 if absent)	0	0	0	0	0	0	2
Surface involved by the disease (cm)	0	0	0	0	0	0	3
Ulcerated surface measured (cm)	0	0	0	0	0	0	4
	Total 1 + total 2 + total 3 + total 4				=	0	A
	Number (n) of segments totally or partially explored				=	0	n
	Total A divided by n				=	0	B
	3 if ulcerated stenosis anywhere, 0 if not				+	0	C
	3 if non ulcerated stenosis anywhere, 0 if not				+	0	D
	Total score = B + C + D				=	0	CDEIS

Score range: 0–44.
Severe disease: CDEIS $\geq$ 12.
Moderate disease: CDEIS 9–12.
Mild disease: CDEIS = 3–9.
Remission: CDEIS = 0–3.

Image obtained from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8880199/

Simple Endoscopic Score for Crohn's disease (SES-CD)

Table 2
Simple endoscopic severity for Crohn's disease

Variable	0	1	2	3
Size of ulcers (cm)	None	Aphthous ulcers (0.1–0.5)	Large ulcers (0.5–2)	Very large ulcers (>2)
Ulcerated surface	None	<10%	10%–30%	>30%
Affected surface	Unaffected	<50%	50%–75%	>75%
Presence of narrowing	None	Single can be passed	Multiple can be passed	Cannot be passed

Score range: 0–56.
Severe disease: SES-CD ≥16.
Moderate disease: SES-CD = 7–15.
Mild disease: SES-CD = 3–6.
Inactive disease: SES-CD ≤2.
Data from Daperno M, D'Haens G, Van Assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD. Gastrointest Endosc 2004;60(4):505–12; and Peyrin-Biroulet L, et al. Defining disease severity in inflammatory bowel dis-

Image obtained from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8880199/

Clinical Remission

- Indicates resolution of symptoms
  - Abdominal pain, general well being, complications
- Measured through
  - Crohn's Disease Activity Index (CDAI) score

Variable	*Quantity*	*Multiple*	*Total*
Number of liquid or soft stools per day		2	
Abdominal pain (0 = none, 1 = mild, 2 = moderate, 3 = severe)		5	
General well being (0 = well, 1 = slightly under par, 2 = poor, 3 = very poor, 4 = terrible)		7	
Number of complications: arthralgias, iritis, erythema nodosum, pyoderma gangrenosa, aphthous ulcerations, anal fissure, anal fistula, anal abscess, fever > 37° past week, intestinal obstruction		20	
Opiates for diarrhea (no = 0, yes = 1,)		30	
Abdominal mass (no = 0, questionable = 2, yes = 5)		10	
Deviation from normal hematocrit (*N* = 42 for female, 47 for male)		6	
% deviation from standard weight		1	
Total CDAI			

Source: Haley E, Eisner T. 5 Types of Crohn's Disease Remission. January 3, 2023. https://www.mycrohnsandcolitisteam.com/resources/what-does-crohns-disease-remission-look-like

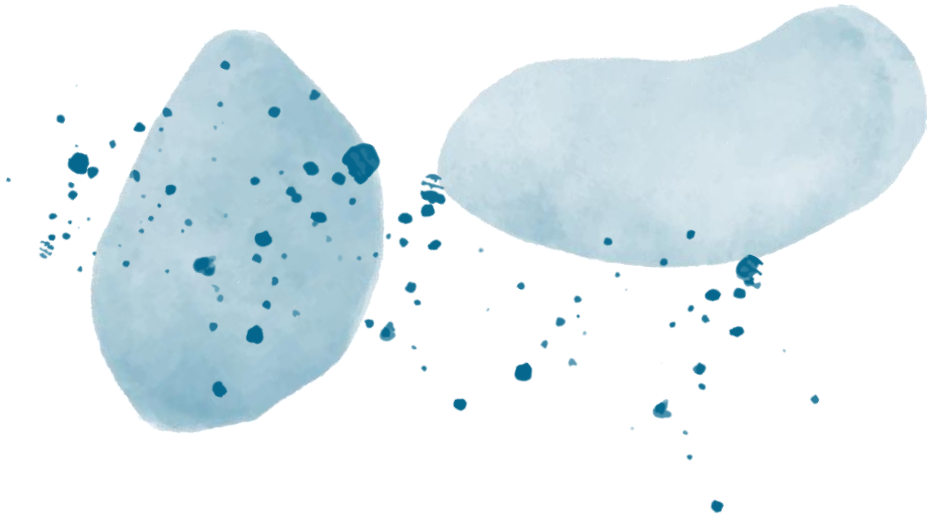
What CDAI score corresponds with symptomatic remission?

A. < 150

B. 150 - 220

C. 220 - 450

D. > 450



What CDAI score corresponds with symptomatic remission?

A. < 150

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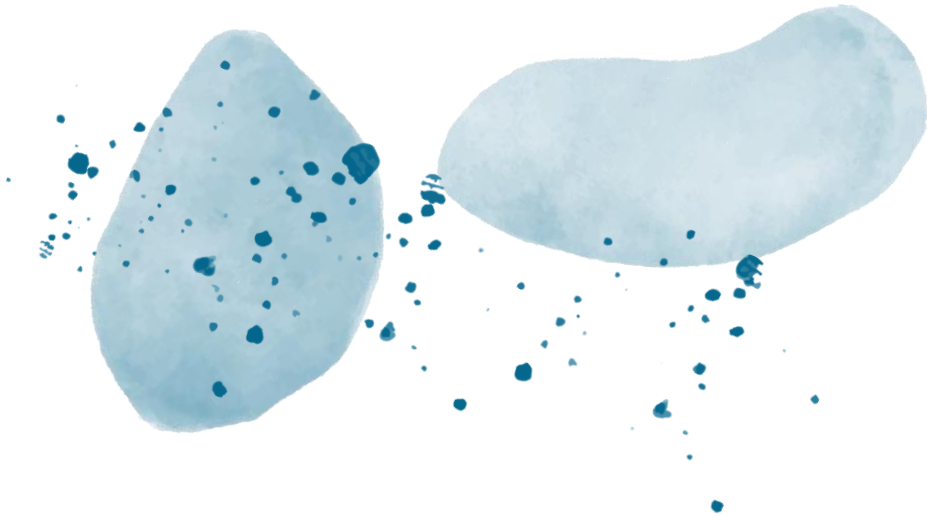
C. 220 - 450

D. > 450



Surgical Remission

- Surgical intervention is often required in the setting of bowel obstruction, abscesses or fistulas, or refractory disease.
- Surgeries for Crohn's disease include
  - Strictureplasty
  - Small bowel resection
  - Colon resection
  - Removal of the rectum
  - Temporary or permanent stoma
- Remission is determined by endoscopic and histologic remission and most importantly, clinical remission.
  - Patients should achieve CDAI < 150
- Detailed follow up and monitoring

Source: Crohn's & Colitis Foundation. What is Crohn's Disease? Updated 2023. https://www.crohnscolitisfoundation.org/what-is-crohns-disease
Centers for Disease Control. Inflammatory Bowel Disease. Updated 2023. https://www.cdc.gov/ibd/what-is-IBD.html
Lichtenstein G, Loftus E, et al.

In Summary

- Crohn's disease has been increasing in incidence and prevalence worldwide.
  - At the same time, the number of therapeutic options is rapidly increasing.
- Mild to moderate disease
  - Sulfasalazine
  - Budesonide
- Moderate to severe disease
  - Corticosteroids
  - Investigational medications such as monoclonal antibodies and biologics
- Severe and fulminant disease
  - IV corticosteroids should be used
  - Anti-TNF agents may be considered

Resources

1. Lichtenstein G, Loftus E, Isaacs K, et al. American College of Gastroenterology Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 2018; 113:481–517; doi: 10.1038/ajg.2018.27; published online 27 March 2018
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Thank you!

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