MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY	Chronic Bowel Disease	**P&T DATE**	2/13/2018
THERAPEUTIC CLASS	Gastrointestinal Disorders	**REVIEW HISTORY** (MONTH/YEAR)	2/17, 2/16, 2/15, 2/13
LOB AFFECTED	Medi-Cal		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

PART 1 INFLAMMATORY BOWEL DISEASE OVERVIEW

Inflammatory bowel disease (IBD) is the chronic inflammation of a part (Ulcerative Colitis) or of an entire (Crohn's Disease) digestive tract. Although the exact etiology of IBD is unknown, effective management of IBD and its symptoms help in improving a patient's quality of life. Health Plan of San Joaquin has adopted the treatment goals and recommendations of the most recent practice guidelines from the American College of Gastroenterology (ACG) and National Institute for Health and Care Excellence (NICE) in the management of Ulcerative Colitis and Crohn's Disease.[1,2] The below criteria, limits, and requirements for certain agents are in place to ensure appropriate use of those agents and to help members towards induction and maintenance of remission of symptoms.

IBD Non-Biologic Agents Formulary Positioning: *(Current as of 1/2018)*

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Average Cost/Rx*	Notes
Oral Amino-salicylates	**Sulfasalazine (Azulfidine)** *Tablets*	IR: 500 mg	--	$21.29	
		DR: 500 mg		$41.93	
	Balsalazide (Colazol) *Capsules*	750 mg	--	$118.34	
	Mesalamine (Pentasa) *Capsules*	CR: 250 mg	**PA**	$1312.60	Reserved for induction of remission in ileal disease.
		CR: 500 mg		$973.26	
	Mesalamine (Lialda) *Tablets*	DR: 1.2 mg	**PA**	$1078.16	Reserved for treatment failure of balsalazide, sulfasalazine, or mesalamine enema for 3 months for induction or maintenance.
	Mesalamine (Apriso) *Capsules*	SR: 0.375 mg	**PA; QL; FL**	$450.50	Reserved for treatment failure of balsalazide, sulfasalazine, or mesalamine enema for 3 months for induction or maintenance. Restricted to 120 capsules per 30 days, 6 fills per 180 days.
	Mesalamine (Asacol HD) *Tablets*	DR: 800 mg	**PA; QL**	$565.65	Reserved for treatment failure of balsalazide, sulfasalazine, or mesalamine enema for 3 months for induction or maintenance. Restricted to 252 tablets per 180 days.
	Mesalamine (Delzicol) *Capsules*	DR: 400 mg	**NF**	$1543.41	Alternatives: sulfasalazine, balsalazide
	Olsalazine (Dipentum) *Capsules*	250 mg	**NF**	--	
Topical Amino-salicylates	**Mesalamine** *Enema Solution*	4 GM/60 ML soln	--	$258.24	
	Mesalamine (Canasa) *Suppository*	1000 mg	**PA**	$1970.36	Reserved for patients unable to administer mesalamine enema.
Cortico-steroids	**Prednisone (Deltasone)** *Tablets, Solution*	1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, 50 mg 5mg/5mL	--	$19.19	
		5mg/mL soln	**NF**		Alternatives: Prednisone 5mg/5mL solution

	Budesonide (Entocort EC) *Capsules*	SR: 3 mg	**PA**	$1105.95	Reserved for induction of remission in those intolerant to conventional glucocorticoids for up to 90 days of therapy.
Immuno-modulators	**6-Mercaptopurine**	50 mg	--	$102.65	
	Azathioprine (Azasan, Imuran)	50 mg	--	$24.20	
		75 mg	NF	$444.10	Alternatives: Azathioprine 50 mg tablet
		100 mg	NF	$395.98	

PA = Prior Authorization; ST = Step Therapy; NF = Non-Formulary; SP = Specialty Pharmacy; IR = Immediate Release; DR = Delayed Release; CR = Controlled Release; SR = Sustained Release * Based on pharmacy claims from 1/2016-12/2016 ^No claims, based on AWP price

Anti-inflammatory Biologic Agents in Crohn's Disease Formulary Positioning: *(Current as of 1/2018)*

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Estimated Cost/Month*	Notes
Tumor Necrosis Factor-α Blockers	**Infliximab-dyyb (Inflectra), Infliximab-abda (Renflexis)**	100 mg	**PA, SP**	--	Reserved for treatment failure to adequate trial or oral immunosuppressive agents. Restricted to specialty pharmacy.
	Adalimumab (Humira) *SQ injection*	40 mg/0.8 ml pen	**PA, SP**	$5,013.85	Reserved for treatment failure to adequate trial or oral immunosuppressive agents. Restricted to specialty pharmacy.
		40 mg/0.8 ml syringe		$4,467.54	
	Certolizumab (Cimzia) *SQ injection*	400 mg	**PA, SP**	$4853.18^	(For Crohn's Disease only) Reserved for treatment failure to Infliximab or Adalimumab. Restricted to specialty pharmacy.
	Golimumab (Simponi) *SQ injection*	100mg	**PA, SP**	$7,652.21	(For Ulcerative Colitis only) Reserved for treatment failure to Infliximab or Adalimumab. Restricted to specialty pharmacy.
	Infliximab (Remicade) *IV infusion*	100 mg	**NF**	$5605.52^	Alternatives: Inflectra and Renflexis
Selective Adhesion Molecule Inhibitor	**Natalizumab (Tysabri)** *IV infusion*	300 mg	**PA**	$7,416^	(For Crohn's Disease only) Reserved for patients with contraindication to TNF biologic. Restricted to specialty pharmacy.
	Vedolizumab (Entyvio) *IV infusion*	300 mg	**NF**	$3,517.83^	Non-Formulary

**Based on pharmacy claims from 1/2017-12/2017 ^No claims, based on AWP price*

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Oral Aminosalicylates

Sulfasalazine (Azulfidine); Balsalazide (Colazol)

- ❒ **Coverage Criteria:** NONE
- ❒ **Limits:** NONE
- ❒ **Required Information for Approval:** NONE

Mesalamine (Pentasa, Delzicol, Apriso, Asacol HD, Lialda), Olsalazine (Dipentum)

- ❒ **Coverage Criteria:**
  - **Pentasa** is reserved for induction of remission and maintenance of ileal disease

- **Apriso, Asacol HD, Lialda** is reserved for treatment failure of balsalazide, sulfasalazine, or mesalamine enema for 3 months for induction or maintenance.

❒ **Limits:**
- **Apriso:**
  - Quantity Limit: 120 capsules per 30 days
  - Fill Limit: 6 fills per 180 days
- **Asacol HD:**
  - Quantity Limit: 252 tablets per 180 days

❒ **Required Information for Approval:**
- **Pentasa**: Documentation of initiating treatment for ulcerative colitis that involves the ileum
- **Apriso, Asacol HD, Lialda**: History of fills for balsalazide, sulfasalazine, or mesalamine enema for 3 months.

❒ **Not on Formulary:** Delzicol, Dipentum (Olsalazine)

Topical Aminosalicylates

Mesalamine Enema

❒ **Coverage Criteria:** NONE
❒ **Limits:** NONE
❒ **Required Information for Approval:** NONE

Mesalamine (Canasa)

❒ **Coverage Criteria:** Canasa is reserved for patients unable to administer mesalamine enema.
❒ **Limits:** NONE
❒ **Required Information for Approval:** Documented inability to administer Mesalamine enema

Corticosteroids

Prednisone (Deltasone)

❒ **Coverage Criteria:** NONE
❒ **Limits:** NONE
❒ **Required Information for Approval:** NONE
❒ **Not on Formulary:** Prednisone 5 mg/mL solution

Budesonide (Entocort EC, Uceris)

❒ **Coverage Criteria:**
- **Entocort EC** is reserved for induction of remission in those intolerant to conventional glucocorticoids for up to 90 days of therapy.

❒ **Limits:** 270 tablets/365 days
❒ **Required Information for Approval:**
- Documented intolerance to conventional glucocorticoids
- History of fills of conventional glucocorticoids for up to 90 days of therapy

❒ **Not on Formulary:** Uceris

Immunomodulators

6-Mercaptopurine, Azathioprine (Azasan, Imuran)

❒ **Coverage Criteria:** NONE
❒ **Limits:** NONE
❒ **Required Information for Approval:** NONE
❒ **Not on Formulary:** Azasan 75mg and 100mg tablets

Tumor Necrosis Factor α Blockers

Infliximab-abda (Renflexis),Infliximab-dyyb (Inflectra), Adalimumab (Humira), Certolizumab Pegol (Cimzia), Golimumab (Simponi)

❒ **Coverage Criteria:**
- **Inflectra/Renflexis/Humira:** Reserved for treatment failure to adequate trial of oral immunosuppressive agents (Azathiopurine, Mercaptopurine, Mesalamine, and Sulfasalazine) OR intolerance to corticosteroids.
  - Must be initiated by a gastroenterologist.

- **Cimzia:** *(for the treatment of Crohn's disease)* Cimzia is reserved for patients who have failed Renflexis/Inflectra OR Humira.
- **Simponi:** *(for the treatment of Ulcerative colitis)* Simponi is reserved for patients who have failed Renflexis/Inflectra OR Humira.

❒ **Limits:** Restrict to Specialty Pharmacy.
❒ **Required Information for Approval:**
- Documented intolerance to conventional glucocorticoids OR treatment failure to IBD non-biologic agents OR have fistulizing disease.
- Therapy initiation by a gastroenterologist.

❒ **Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy. Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.
❒ **Not on Formulary:** Remicade

Selective Adhesion Molecule Inhibitor
Natalizumab (Tysabri)

❒ **Coverage Criteria:** *(for the treatment of Crohn's disease)* Reserved for pts with contraindication to TNF biologic.
❒ **Limits:** NONE
❒ **Required Information for Approval:** Documentation showing contraindication to anti-TNF biologic and a negative anti-JCV antibody detection test result.
❒ **Notes:** Not restricted to Specialty Pharmacy because Natalizumab is a limited distribution drug. Biologics exceeding labeled standard maintenance doses may be approved 1 month at a time. Subsequent fills of the increased maintenance dose will require documentation of symptom improvement.

CLINICAL JUSTIFICATION

Ulcerative Colitis (UC)

The *2010 American College of Gastroenterology Ulcerative Colitis Treatment Guidelines*[1] recommends the following:

Mild-Moderate Distal Colitis

• Oral aminosalicylates (sulfasalazine, olsalazine, mesalamine, or balsalazide), topical mesalamine (enemas or suppositories), or topical corticosteroids (hydrocortisone enemas or foam) as first-line therapies.
  o Topical mesalamine agents are superior to topical steroids or oral aminosalicylates.
  o Combination therapy is more effective than monotherapy.
• Patients who are refractory to the above agents at maximal doses may consider treatment with oral corticosteroids (up to 40-60 mg/day) or infliximab.

Maintaining Remission in Distal Disease
• Topical mesalamine or oral sulfasalazine, mesalamine, and balsalazide are effective in maintaining remission. • Patients who have failed the above agents may consider azathioprine, 6-mercaptopurine, or infliximab. • Topical corticosteroids (prednisone, hydrocortisone, budesonide, etc.) have not yet proven to be effective in maintaining remission in distal colitis.
Mild-Moderate Extensive Colitis

• Oral aminosalicylates (sulfasalazine, olsalazine, mesalamine, or balsalazide) as first-line therapies.
  o Combination therapy with topical therapy is more effective than monotherapy.
• Oral steroids are reserved for patients who are refractory to combination oral aminosalicylates + topical therapy.
• Patients who are refractory to the above agents at maximal doses may consider treatment with azathioprine or 6-mercaptopurine.
• Patients who are steroid refractory or steroid dependent or unable to achieve remission despite being on adequate doses of azathioprine or 6-mercaptopurine should consider infliximab.
  o Incidence of infusion reaction occurs in 10% of patients.
  ▪ The incidence can be decreased by decreasing the interval between infusions to every 8 weeks, use with immunosuppressive agents, and premedication treatment with an oral corticosteroid and antihistamine.

Maintaining Remission in Extensive Disease
• See "Maintaining remission in distal disease."
Severe Colitis

- Patients who are refractory to maximal tolerated doses of oral corticosteroids, oral aminosalicylates, and topical therapies should consider treatment with infliximab.
- Patients who present with toxicity should be admitted to hospital for 3-5 day course of IV steroids.
    - Failure to show significant improvement within 3 – 5 days, treatment with IV cyclosporine should be considered.

Crohn's Disease (CD)

The *2009 American College of Gastroenterology Crohn's Disease Treatment Guidelines*[2] recommends the following:

Mild-Moderate Active Disease

- Sulfasalazine or mesalamine as first-line therapies.
- Short-term oral corticosteroids (prednisone, methylprednisone, dexamethasone)
    - Budesonide may be considered in patients who cannot tolerate conventional corticosteroids. However use is limited to short-term.
    - Budesonide when dosed 6mg/day reduces the time to relapse in ileal and/or right colonic disease, but does not provide significant maintenance benefits beyond 6 months

Moderate-Severe Active Disease

- Prednisone 40–60 mg daily until symptoms resolve (generally 7–28 days).
- Azathioprine and 6-mercaptopurine are effective for maintaining a steroid-induced remission and IM/SQ methotrexate at a dose of 25 mg weekly is effective for steroid-dependent and steroid-refractory CD.
- TNF inhibitors (infliximab, adalimumab, and certolizumab) are considered in patients who have not responded to an adequate trial of corticosteroids or immunosuppressive agents.
    - Natalizumab is an alternative to patients in which TNF inhibitors are inappropriate.

Severe/Fulminant disease

- Patients are managed through hospitalizations (IV fluids, blood transfusions, as appropriate).

Guidelines from both ACG and NICE state aminosalicylates as first line therapy in inducing remission and as effective agents in maintaining remission in UC with no significant differences in efficacy among the different 5-ASA agents. Appropriate agents should be chosen based on anatomic extent of the disease. Contrastingly, efficacy of aminosalicylates is less established in the treatment of CD, showing minimal benefit with sulfasalazine and delayed release mesalamine tablets. Despite this, they are still used as initial treatment due to their favorable side effect profile compared to corticosteroids and immunomodulators. As for the immunomodulators (6-Mercaptopurine and Azathioprine), their use is limited due to the less favorable side effect profile that includes severe bone marrow suppression.

The role of systemic corticosteroids should be limited to achievement in disease remission since chronic use of systemic corticosteroids lead to many side effects (moon face, adrenocortical suppression, edema, etc.). Budesonide (Entocort EC or Uceris) is a systemic corticosteroid that is broken down by the liver. This minimizes some of the corticosteroid-induced side effects. However, the majority of studies have shown budesonide is not effective in maintaining disease remission and use should be limited to 3 months. In several placebo-controlled trials, no difference was found in remission rates between budesonide and placebo when use was beyond 3 months.[3] In one recent European study, 92 patients that previously achieved remission on budesonide 9mg/day were randomized to receive either low-dose budesonide (alternating doses of 3mg and 6mg/day to achieve an average of 4.5mg/day) or placebo over a period of 12 months.[4] 61% of patients on budesonide 4.5mg/day were able to maintain remission as compared to 16% of patients on placebo. More supporting studies are needed to evaluate the efficacy and safety in budesonide when used long-term. When budesonide was compared to conventional corticosteroids (prednisolone), there was no difference in continued remission rates between the two groups. Therefore, budesonide should be an alternative to patients who cannot tolerate conventional corticosteroids.

The use of biologic agents after non-responsiveness to corticosteroids or immunosuppressants is supported, but it is crucial to note the serious safety concerns with these drugs: opportunistic infections, reactivation of latent tuberculosis, and development of hematological malignancies (including hepatosplenic T-cell lymphoma). For CD and UC, infliximab and adalimumab have the highest probability of response and maintain remission followed by certolizumab, then natalizumab, then vedolizumab.[15-16] Natalizumab is associated with a progressive multifocal leukoencephalopathy (PML)—a rare but deadly infection of the brain. A total of 3 cases were reported in patients treated with Tysabri (2 were from MS patients, 1 was from patient with CD).[17] Vedolizumab produced inconsistent results in 2-different placebo-controlled clinical trials.[18-19] In GEMINI-2, vedolizumab was slightly better than placebo. However, in GEMINI-3, where the patient population consisted of more TNF-experienced patients,

vedolizumab was not more effective than placebo. The contradicting evidence in vedolizumab suggest more evidence is needed before its role in treatment of UC and CD can be determined.

PART 2 IBS-C AND IBS-D OVERVIEW

Inflammatory bowel syndrome (IBS) is a common disorder of bowel function that causes change in bowel habits resulting in either constipation (IBS-C) or diarrhea (IBS-D), along with symptoms such as abdominal pain, bloating, and other non-intestinal symptoms. Although the exact etiology of IBS is unknown, effective management of IBS and its symptoms help in improving a patient's quality of life. Health Plan of San Joaquin has adopted the treatment goals and recommendations of the most recent practice guidelines from the American Gastroenterological Association (AGA) and The National Institute for Health Care and Excellence Guidelines (NICE) in the management of IBS-C and IBS-D.[1,2] The below criteria, limits, and requirements for certain agents are in place to ensure appropriate use of those agents and to help members towards induction and maintenance of remission of symptoms.

IBS-C and IBS-D Agents Formulary Positioning: *(Current as of 1/2018)*

Drug	Available Strengths	Fml Limit	Average Cost/Rx*	Notes
Bulk Forming				
Psyllium Husk with Sugar (Metamucil, Natural Fiber, Konsyl)	3.4 gram/7 gram powder	--	$3.50	
	3.4 gram oral powder packet	NF	--	
Psyllium Husk with Aspartame (Metamucil Fiber)	3.4 gram/5.8 gram powder	--	$5.71	
	3.4 gram oral powder packet	NF	--	
Psyllium Seed (Reguloid, Hydrocil Instant)	Reguloid Laxative Powder	--	$6.21	
	Hydrocil Instant Packet	NF-	--	
Psyllium Seed with Dextrose (Natural Fiber Lax, Fiber Smooth, Konsyl-D, Natural Vegetable Laxative Powder)	Fiber oral powder	--	$3.93	
	Metamucil Fiber Wafer 2.5 gram oral Wafer	--	$5.54	
Osmotic				
Polyethylene Glycol 3350 (Miralax, Clearlax, Purelak, Gavilax, Smoothlax)	17gram/dose oral powder jar	QL	$34.85	Limited to 1054 grams per 30 days.
	17g/dose oral powder packet	NF	$62.84	
Peg 3350/Na Sulf/ Bicarb/Cl/KCl (Gavilyte, Golytely, Colyte)	Gavilyte-C 240 gram-22.72 gram-6.72 gram-5.84 gram oral solution	--	$12.14	
	Gavilyte-G 236 gram-22.74 gram-6.74 gram-5.86 gram oral solution	--	$12.78	
	PEG 3350 and ELS	--	$12.76	
	Golytely 236 gram-22.74 gram-6.74 gram-5.86 gram oral solution	NF	--	
	Golytely 227.1 gram-21.5 gram-6.36 gram oral packet	NF	$13.46	
Sodium chloride/ NaHCO3/KCl/Peg (Trilyte, Gavilyte-N, Nulytely)	Trilyte With Flavor Packets 420 gram oral solution	--	$16.04	
	PEG 3350 and ELS	--	$15.76	
	Gavilyte-N 420 gram solution	NF	--	
	Nulytely With Flavor Packets	NF	--	
Chloride Channel Activators				
Lubiprostone (Amitiza)	8 mcg capsule	PA;QL	$297.58	Reserved for patients who have failed treatment with linaclotide (Linzess) or naloxegol (Movantik). Patient must have also failed regularly scheduled, dose optimized polyethylene glycol

	24 mcg capsule	PA; QL	$339.28	(Miralax), AND two of the following: bisacodyl, Senna, lactulose, psyllium, magnesium citrate or hydroxide.
Linaclotide (Linzess)	72 mcg capsule	PA; QL	$360.55	Linzess is reserved for patients with treatment failure of properly titrated and regularly scheduled dosing of polyethylene glycol for 2 months (as evidenced by prescription history fills) AND two of the following: bisacodyl, Senna, psyllium, lactulose, magnesium citrate or hydroxide. Restricted to 30 capsules per 30 days.
	145mcg capsule	PA; QL	$358.19	
	290 mcg capsule	PA;QL	$357.46	
Antimotility				
Loperamide (Imodium)	2 mg capsule	--	$7.56	
	2 mg tablet		$18.17	
	1 mg/5 ml oral solution		$7.90	
	1 mg/7.5 ml oral solution		$24.82	
5-HT3 Antagonist				
Alosetron (Lotronex)	0.5 mg tablet	NF	--	
	1 mg tablet			
Antispasmodics				
Dicyclomine (Bentyl)	10 mg capsule	--	$3.64	
	10 mg /5 mL solution		$30.25	
	20 mg tablet		$2.74	
Hyoscyamine (Anaspaz, Cystospaz, Levsin)	0.125 mg ODT	--	$24.85	
	0.125 mg tablet SL		$11.79	
	0.375 mg ER tablet		$64.35	
	0.125 mg tablet		$19.04	
	125 mcg/5 mL elixir		$0.50	
	0.125 mg/mL drop	AL	$140.33	Restrict use to children and infants < 2 years old only.
Tricyclic Antidepressants				
Amitriptyline (Elavil)	10 mg tablet	--	$5.02	Avoid use in members over 65 years old.
	25 mg tablet	--	$7.97	
	50 mg tablet	--	$18.83	
	75 mg tablet	--	$25.62	
	100 mg tablet	--	$37.92	
	150 mg tablet	--	$49.17	
Clomipramine (Anafranil)	25 mg capsule	NF	$456.90	Avoid use in members over 65 years old.
	50 mg capsule	NF	$593.77	
	75 mg capsule	NF	$242.13	
Desipramine (Norpramin)	10 mg tablet	--	$33.04	Avoid use in members over 65 years old.
	25 mg tablet	--	$3.61	
	50 mg tablet	--	$52.59	
	75 mg tablet	--	$30.91	
	100 mg tablet	--	--	
	150 mg tablet	--	--	
Doxepin (Sinquan)	Silenor 3 mg tablet	NF	--	Avoid use in members over 65 years old.
	Silenor 6 mg tablet	NF	--	
	10 mg/5 ml solution	--	$3.74	Avoid use in members over 65 years old.
	10 mg capsule	--	$17.15	
	25 mg capsule	--	$23.01	
	50 mg capsule	--	$35.20	
	75 mg capsule	--	$52.30	
	100 mg capsule	--	$53.49	
	150 mg capsule	--	$20.89	
Imipramine (Tofranil)	10 mg tablet	--	$6.79	
	25 mg tablet	--	$11.10	
	50 mg tablet	--	$10.06	
Nortriptyline (Pamelor)	10 mg/5 ml oral concentrate	--	$104.31	
	10 mg capsule	--	$7.04	

	25 mg capsule	--	$9.08	
	50 mg capsule	--	$6.55	
	75 mg capsule	--	$10.72	
Trimipramine	25 mg capsule	NF	--	Formulary alternatives = amitriptyline, desipramine, doxepin, imipramine, nortriptyline.
	50 mg capsule	NF	--	
	100 mg capsule	NF	--	
Antibiotics				
Rifaximin (Xifaxan)	550 mg tablet	PA;QL; FL	$1,276.29	For IBS-D: Restricted to 42 tablets per 14 days. Restricted to 3 fills per 365 days. Xifaxan is reserved for patients who have failed treatment with at least one antispasmodic, one TCA, and loperamide; or failed treatment with at least one antispasmodic and one TCA for use in abdominal pain relief. For HE: Xifaxan is reserved for treatment failure of compliant use of lactulose evidenced by consistent lactulose fills.
Mixed Mu-Opioid Receptor				
Eluxadoline (Viberzi)	75 mg tablet	NF	$1033.42	
	100 mg tablet	NF	$1056.03	

**Cost per Rx based on HPSJ utilization historical data from January 2017 through December 2017*

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

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Bulk Forming Laxative

Psyllium Husk with Sugar (powder), Psyllium Husk with Aspartame (powder), Psyllium Seed (powder), Psyllium Seed with Dextrose (powder, wafer)

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A
- ❒ **Other Notes:** None
- ❒ **Non-Formulary:** Psyllium Husk with Aspartame (packet), Psyllium Husk with Sugar (packet), Psyllium Seed (packet)

Osmotic Laxative

Polyethylene Glycol 3350 (powder jar), Peg 3350/Na Sulf/ Bicarb/Cl/KCl (Gavilyte-C, Gavilyte-G, Sodium chloride/ NaHCO3/KCl/Peg (Trilyte), Lactulose, Magnesium oxide (400 mg tablet), Magnesium hydroxide, Magnesium citrate, Glycerin (Adult and Child suppository)

Polyethylene Glycol 3350 (powder jar)

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** 1054g per 30 days
- ❒ **Required Information for Approval:** N/A
- ❒ **Other Notes:** None
- ❒ **Non-Formulary:** Polyethylene Glycol 3350 (powder packet)

Peg 3350/Na Sulf/ Bicarb/Cl/KCl (Gavilyte-C, Gavilyte-G, Sodium chloride/ NaHCO3/KCl/Peg (Trilyte), Lactulose (solution), Magnesium oxide (400 mg tablet), Magnesium hydroxide, Magnesium citrate, Glycerin (Adult and Child suppository)

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A
- ❒ **Other Notes:** None

- ❒ **Non-Formulary:** Polyethylene Glycol 3350 (oral solution), Golytely (solution, powder packet), Gavilyte-N, Nulytely, Suprep Bowel Prep Kit, Prepopik Powder Packet, Moviprep

Chloride Channel Activators

Linaclotide, Lubiprostone

Linaclotide (Linzess)

- ❒ **Coverage Criteria:** Linzess is reserved for patients with treatment failure of properly titrated and regularly scheduled dosing of polyethylene glycol for 2 months (as evidenced by prescription history fills) AND two of the following: bisacodyl, Senna, psyllium, lactulose, magnesium citrate or hydroxide.
- ❒ **Limits:** Limited to 30 capsules per 30 days.
- ❒ **Required Information for Approval:** Proper chart note documentation and pharmacy fill history of at least 2 months of regularly scheduled Miralax, and of two other formulary alternatives.

Lubiprostone (Amitiza)

- ❒ **Coverage Criteria:** Lubiprostone (Amitiza) is reserved for patients who have failed treatment with linaclotide (Linzess) or naloxegol (Movantik). Patient must have also failed regularly scheduled, dose optimized polyethylene glycol (Miralax), AND two of the following: bisacodyl, Senna, lactulose, psyllium, magnesium citrate or hydroxide
- ❒ **Limits:** Limited to 60 capsules per fill
- ❒ **Required Information for Approval:** Proper chart note documentation and pharmacy fill history of at least 2 months of regularly scheduled Miralax AND Linzess or Movantik, in addition to two other formulary alternatives described in the coverage criteria.

Antimotility

Loperamide

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A

Antispasmodics

Dicyclomine, Hyoscyamine

Dicyclomine

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A

Hyoscyamine

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** Hyoscyamine 0.125 mg/mL drop: Restrict use to children and infants < 2 years old only.
- ❒ **Required Information for Approval:** N/A

Tricyclic Antidepressants

Amitriptyline (Elavil); Nortriptyline (Pamelor); Imipramine (Tofranil); Desipramine (Norpramine); Doxepin (Sinquan) capsules, solution

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** N/A
- ❒ **Other Notes:** None
- ❒ **Non-Formulary:** Clomipramine, Doxepin (Silenor) tablets, Trimipramine

Antibiotic

Xifaxan

- **Coverage Criteria:**
  - For use in Hepatic encephalopathy, Xifaxan is reserved for treatment failure of compliant use of lactulose evidenced by consistent lactulose fills.
  - For use in IBS-D, Xifaxan is reserved for patients who have failed treatment with at least one antispasmodic, one TCA, and loperamide; or failed treatment with at least one antispasmodic and one TCA for use in abdominal pain relief.
- **Limits:**
  - Quantity limit: Restricted to 42 tablets per 14 days.
  - Fill limit: Restricted to 3 fills per 365 days.
- **Required Information for Approval:** Proper chart note documentation and pharmacy fill history of at least one antispasmodic and one TCA for use in antispasmodic relief and at least one antispasmodic, one TCA, and loperamide for use in IBS-D.

CLINICAL JUSTIFICATION

The 2014 American Gastroenterological Association (AGA) and 2008 National Institute for Health and Clinical Excellence (NICE) guidelines recommend pharmacological management of irritable bowel syndrome (IBS) based on patient specific symptoms.

- **IBS-C and IBS-D**
  - The use of an antispasmodic is recommended for symptomatic relief by both guidelines.[1,2]
  - The AGA recommends the use of a TCA over no drug treatment for either IBS-C or IBS-D, but recommends against the use of an SSRI.[1]
  - According to the NICE guidelines, TCAs are considered second line treatment if laxatives, loperamide, or antispasmodics have not helped. Low dose TCAs should be used (5–10 mg equivalent of amitriptyline) and titrated as necessary. Patients taking TCAs need to consider possible side effects and need follow up after 4 weeks and then every 6-12 months.[2]
- **IBS-C**
  - The 2014 AGA Management of IBS Guidelines[1] recommends the use of linaclotide, lubiprostone, or PEG laxatives over no drug treatment.
  - The 2008 NICE Guidelines for Irritable Bowel Syndrome in Adults recommends laxatives for IBS-C, and recommends against the use of lactulose.[2]
  - Lubiprostone (Amitiza) in IBS is only approved for women who have severe symptoms that have not responded to other treatments.[1,3]
    - The FDA approved lubiprostone use in IBS-C only in women due to clinical trials consisting of 92% females and only 8% males. Efficacy in males was not proven, but no harm was reported.
  - Linaclotide (Linzess) should only be used if a patient has been experiencing constipation for at least 12 months and optimal doses of previous laxatives have failed. Follow up after 3 months for patients taking linaclotide is also recommended.[2]
- **IBS-D**
  - The 2014 AGA Management of IBS Guidelines[1] recommends the use of rifaximin, alosetron (for global symptoms), or loperamide over no drug treatment.
  - Alosetron is currently non-formulary due to no utilization by HPSJ members and the availability of multiple formulary alternatives.
  - The 2008 NICE Guidelines for Irritable Bowel Syndrome in Adults recommends loperamide as the first line antimotility medication and patients should be educated on dose titration to appropriate stool consistency.[2]
  - A short course of Rifaximin (Xifaxan) can be considered if treatment with antispasmodics, loperamide, and TCAs have failed.
  - Viberzi (Eluxadilone) is non-formulary and has no place in current guidelines.

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REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Biologics Class Review for Crohns 2013-2-19.docx	2/2013	Allen Shek, PharmD
Update to Policy	IBD Class Review 2-17-15.docx	2/2015	Jonathan Szkotak, PharmD
Update to Policy	HPSJ Coverage Policy – Gastrointestinal – Chronic Bowel Disease 2016-02.docx	2/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Gastrointestinal – Chronic Bowel Disease 2017-02.docx	2/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Gastrointestinal – Chronic Bowel Disease 2018-02.docx	2/2018	Johnathan Yeh, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy