Clinical Gastroenterology
*Series Editor:* George Y. Wu

George Y. Wu *Editor*

# Pocket Handbook of GI Pharmaco-therapeutics

*Second Edition*

Humana Press

# Pocket Handbook of GI Pharmacotherapeutics

# CLINICAL GASTROENTEROLOGY

*George Y. Wu, Series Editor*

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# Pocket Handbook of GI Pharmacotherapeutics

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# PREFACE

Since the publication of the first edition of the Pocket Handbook of GI Pharmacotherapeutics, there has been an enormous increase in the number and efficacy of agents to treat gastrointestinal diseases. In some areas, there has been literally a revolution in the development agents that has been little short of miraculous. However, with the expansion of our pharmacological armamentarium has come an increasing complexity in determining and selecting optimal treatment. Now, more than ever, it has become necessary to know how to treat conditions based on the characteristics or stages of the disease. For these reasons, it appeared to be appropriate at this time, to not only update the prescribing information but also include national and international guideline information where available, and provide more treatment algorithms in addition to brand and generic names, indications, contraindications, side effects, drug interactions, doses/routes of administration, durations, and approximate wholesale costs. At the end of the handbook, we again include an index which lists all the drugs in alphabetical order for those interested in specific agents. As in the previous edition, we have sought to present all this information in a format that allows rapid and convenient access.

***George Y. Wu***
***Farmington, CT***

# Relative Cost

Cost codes used are "per month" of maintenance therapy or "per course" of short-term therapy (e.g., antibiotics). Codes are calculated using average wholesale prices for the most common indication and route of each drug at a typical adult dosage. For maintenance therapy, costs are calculated based upon a 30-day supply or the quantity that might typically be used in a given month. When multiple forms are available, these codes reflect the least expensive generally available product. These codes should be used as a rough guideline only. Check with a local pharmacy for exact costs.

| Code | Cost |
|---|---|
| $ | <$25 |
| $$ | $25–$49 |
| $$$ | $50–$99 |
| $$$$ | $100–$199 |
| $$$$$ | ≥$200 |
| $$$$$ $ | ≥$500 |
| $$$$$ $$ | ≥$1000 |
| $$$$$ $$$ | ≥$2000 |
| $$$$$ $$$$ | ≥$4000 |
| $$$$$ $$$$$ | ≥$8000 |

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# I Gastrointestinal Diseases

# 1 Gastroesophageal Disorders

*Houman Rezaizadeh and Erik Olson*

***Contents***



## ABBREVIATIONS

| | |
|---|---|
| BID | Twice daily |
| EGD | Esophagogastroduodenoscopy |
| GERD | Gastroesophageal reflux disease |
| PPI | Proton pump inhibitors |
| QHS | Nightly at bedtime |

## NAUSEA, VOMITING, MOTION SICKNESS

### *Meclizine*

Brand names: Antivert, Less Drowsy (OTC), Medi-Meclizine (OTC), Motion-Time (OTC), Travel Sickness (OTC)
Manufacturer: Pfizer, Generic

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_1,

Mechanism of action: Central anticholinergic action, decreases excitability of middle ear labyrinth and blocks conduction in the middle ear vestibular-cerebellar pathways

Dosage:
- Motion sickness: 25–50 mg 1 h before travel, repeat dose every 24 h as needed
- Vertigo: 25–100 mg po daily in divided doses

Contraindications/cautions:
- Hypersensitivity to meclizine or any component of formulation
- CNS depression
- Caution with asthma, glaucoma, prostatic hyperplasia, pyloric/duodenal obstruction

Adverse effects:
- CNS: Drowsiness, fatigue, headache
- GI: Vomiting, xerostomia
- Ocular: Blurred vision
- Misc: Anaphylactoid reaction

Drug interactions:
- May enhance the CNS depressant effect of other CNS depressant
- May enhance the anticholinergic effect of other anticholinergic drugs

Pregnancy category: B
Lactation: Unknown
Relative cost: $ (Generic available: $–$$)

## *Dimenhydrinate*

Brand names: Dramamine (OTC), Criminate (OTC), Motion Sickness (OTC)
Mechanism of action: Competes with histamine for H-1 receptor sites on effector cells in the GI tract, blood vessels, and respiratory tract. Blocks chemoreceptors, diminishes vestibular stimulation, and depresses labyrinthine function through its central anticholinergic activity
Manufacturer: Generic

Dosage:
Motion sickness, nausea/vomiting or vertigo:
- Oral: 50–100 mg every 4–6 h, not to exceed 400 mg daily
- IM: 50 mg every 4 h, maximum: 100 mg every 4 h
- Rectal: 50–100 mg 3–4× daily

Contraindications/cautions:
- Hypersensitivity to dimenhydrinate or any component of formulation
- CNS depression
- Caution with asthma, glaucoma, prostatic hyperplasia, pyloric/duodenal obstruction
- Caution with antibiotics that have potential to cause ototoxicity
- Caution in the elderly

Adverse effects:
- CVS: Tachycardia
- CNS: Dizziness, drowsiness, excitation, headache, insomnia, lassitude, nervousness, restlessness
- Derm: Rash
- GI: Anorexia, epigastric distress, nausea, xerostomia
- GU: Dysuria
- Ocular: Blurred vision
- Respiratory: Thickened bronchial secretions

Drug interactions:
- May enhance the CNS depressant effect of other CNS depressant
- May enhance the anticholinergic effect of other anticholinergic drugs

Pregnancy category: B
Lactation: Small amounts are excreted in the breast milk. Antihistamines may decrease maternal serum prolactin concentrations when administered prior to the establishment of nursing
Relative cost: $ (Generic available: $)

## *Ondansetron*

Brand names: Zofran, Zofran ODT, Zuplenz
Manufacturer: GlaxoSmithKline
Mechanism of action: Selective 5-HT3-receptor antagonist, blocking serotonin, both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone

Dosage:
Prevention of postoperative nausea and vomiting:
- Oral: 16 mg administered 1 h prior to induction of anesthesia
- IV or IM: 4 mg as a single dose administered ~30 min before the end of anesthesia or as treatment if vomiting after surgery

Treatment of generalized nausea and vomiting: (Off-label use):
- Oral: 4 mg every 6–8 h or 8 mg every 8–12 h as needed

- IV: 4 mg every 6–8 h or 8 mg every 8–12 h as needed. Monitor for QT prolongation with higher doses

Contraindications/cautions:
- Caution in patients allergic to other 5HT-3 receptor antagonists
- QT prolongation (dose dependent)
- Serotonin syndrome in combination with other serotonergic agents
- Dose limitation in patients with hepatic impairment (Child-Pugh Class C)

Adverse effects:
- CNS: Headache, fatigue, malaise, drowsiness, agitation, anxiety, sensation to cold
- Derm: Pruritus
- GI: Diarrhea
- GU: Urinary retention
- Hepatic: AST and ALT increase
- Respiratory: Hypoxia
- Misc: Fever

Drug interactions:
- May enhance the QTc-prolonging effect of QTc-prolonging agents
- May decrease the serum concentrations of CYP3A4 substrates and increase the metabolism of CYP3A4 substrates

Pregnancy: B
Lactation: Unknown
Relative cost: $–$$$ (Generic available: $–$$)

## *Scopolamine Patch*

Brand names: Transderm-Scop
Manufacturer: Sandoz, generic
Mechanism of action: Blocks action of acetylcholine at parasympathetic sites in smooth muscle, secretory glands, and the CNS; increases cardiac output, dries secretions, antagonizes histamine and serotonin; causes blockade of muscarinic receptors at the cardiac SA-node and is parasympatholytic.

Dosage:
- Motion sickness: Apply 1 patch to hairless area behind the ear at least 4 h prior to exposure and every 3 days as needed
- Chemotherapy induced nausea and vomiting: Apply 1 patch every 72 h

Contraindications/cautions:
- Hypersensitivity to scopolamine
- Narrow angle glaucoma

- Caution in patients with hepatic impairment, seizure disorders, hyperthyroidism, GU or GI obstruction, prior psychosis, or ulcerative colitis
- Avoid use in the elderly because of potent anticholinergic adverse effects

Adverse effects:
- CVS: Bradycardia, flushing, orthostatic hypotension, tachycardia
- CNS: Psychosis, agitation, ataxia, confusion, delusions, dizziness, drowsiness, fatigue, hallucinations, headache, irritability, loss of memory, paranoid behavior, restlessness, sedation
- Derm: Dry skin, pruritus, drug eruptions, urticaria
- Endocrine: Thirst
- GI: Constipation, diarrhea, dry throat, dysphagia, nausea, vomiting, xerostomia
- GU: Dysuria, urinary retention
- MSK: Tremor, weakness
- Ocular: Accommodation impaired, blurred vision, conjunctival infection, cycloplegia, dryness, glaucoma, increased intraocular pain, itching, photophobia, pupil dilation, retinal pigmentation
- Respiratory: Dry nose, dyspnea
- Misc: Angioedema, heat intolerance

Drug Interactions:
- May enhance the CNS depressant effect of other CNS depressant
- May enhance the anticholinergic effect of other anticholinergic drugs

Pregnancy category: C
Lactation: Secreted into the breast milk. Should be used with caution if administered to a nursing woman
Relative cost: $$ (generic available: $$)

## GASTROESOPHAGEAL REFLUX DISORDER (GERD) AND PEPTIC ULCER DISEASE (PUD)

### *Proton Pump Inhibitors (PPI)*

PPI class associated effects:
- PPI use and increased risk of *C. diff* infection
- PPI use and increased risk of traveler's diarrhea
- Increase risk of community acquired pneumonia (CAP) with PPI use in patients with following risk factors: (1) Older age; (2) shorter duration of treatment (<30 days); (3) low dose PPI
- Long-term PPI use can cause hypomagnesemia due to decreased intestinal absorption of magnesium, consider monitoring
- Osteoporosis

See algorithms below on gastroesophageal reflux disease, and refractory gastroesophageal reflux disease.

## *Omeprazole*

Brand names: Prilosec, prilosec OTC
Manufacturer: AstraZeneca, Proctor and Gamble, generic

Dosage:
- GERD/erosive esophagitis: 20 mg po qd for 4 weeks
- Gastric ulcer: 40 mg po qd for up to 4–8 weeks
- Duodenal ulcer: 20–40 mg po qd for 4–8 weeks
- *H. pylori* infection: 20 mg po bid in conjunction with triple therapy
- Stress ulcer prophylaxis: 40 mg po qd initially, then 20–40 mg qd
- Gastric hypersecretion: 60 mg po qd initial dose, increase up to 120 mg po tid

Contraindications/cautions:
- Hypersensitivity to omeprazole
- Use with caution in hypocalcemia, hypokalemia, metabolic alkalosis, respiratory alkalosis, Bartter's syndrome (powder for oral suspension contains 1680 mg or 20 meq of sodium bicarbonate)

Adverse effects:
- Gastrointestinal: Abdominal pain, diarrhea, pancreatitis, hepatotoxicity
- Neurologic: Headache
- Renal: Interstitial nephritis
- Musculoskeletal: Hip fracture, rhabdomyolysis

Drug interactions:
- Increases levels of warfarin, cyclosporine, digoxin, phenytoin
- Decreases levels of atazanavir, ketoconazole, itraconazole, cefuroxime
- PPI equivalent dose to omeprazole 20 mg may be administered simultaneously with Harvoni under fasting conditions; higher doses should be avoided as they decrease the efficacy of Harvoni.

Pregnancy category: C
Lactation: Probably safe
Relative cost: $ (generic available: $)

## *Esomeprazole Magnesium (Oral)*
## *Esomeprazole Sodium (IV)*

Brand name: Nexium
Manufacturer: AstraZeneca, generic

Dosage:
- GERD/erosive esophagitis: 20–40 mg daily for treatment
- Maintenance therapy in GERD/erosive esophagitis: 20 mg daily once daily

- Gastric Ulcer: 20–40 mg daily for up to 6 months
- Acute non-variceal upper GI bleed: 80 mg IV bolus followed by continuous infusion at 8 mg/h for 72 h after endoscopic therapy
- *H. pylori* infection: 40 mg po daily in conjunction with triple therapy
- Zollinger–Ellison syndrome: 40 mg twice daily increase up to 240 mg daily based on symptoms

Contraindications/cautions:
- Hypersensitivity to esomeprazole or benzimidazoles
- Use with caution with liver disease

Adverse effects:
- Gastrointestinal: Abdominal pain, constipation, diarrhea, flatulence, nausea, pancreatitis (rare)
- Neurologic: Headache
- Dermatologic: Erythema multiforme, Stevens–Johnson syndrome, toxic epidermal necrolysis
- Musculoskeletal: Hip fracture, rhabdomyolysis

Drug interactions: See omeprazole
Pregnancy category: B
Lactation: Probably safe
Relative cost: Oral–$$, IV–$$$ (Generic available: $–$$)

## *Lansoprazole*

Brand names: Prevacid, generic
Manufacturer: TAP Pharmaceuticals Inc.

Dosage:
- Duodenal ulcer: 15 mg qd or bid for 4–8 weeks
- *H. pylori* treatment: 30 mg bid for 10–14 days in combination with triple therapy
- Erosive esophagitis: 30 mg qd or bid for 4–8 weeks
- Gastric ulcer prophylaxis with NSAID use: 15–30 mg po qd
- Gastric ulcer treatment: 30 mg po qd or bid for 8 weeks
- GERD: 15–30 mg qd for 8 weeks
- Zollinger–Ellison syndrome: 60 mg po qd to 90 mg bid

Contraindications/cautions:
- Hypersensitivity of lansoprazole or any of its components
- Use with caution in phenylketonurics: Oral disintegrating tables contain phenylalanine
- Use with caution in liver disease (dose reduction may be required)

Adverse effects:
- Gastrointestinal: Abdominal pain, diarrhea, nausea
- Neurologic: Headache
- Musculoskeletal: Hip fracture, rhabdomyolysis
- Other: Fatigue

Drug interactions: See omeprazole
Pregnancy category: B
Lactation: Probably safe
Relative cost: $$ (generic available: $–$$)

## *Pantoprazole Sodium Oral and IV*

Brand name: Protonix
Manufacturer: Wyeth-Ayerst, generic

Dosage:
- Erosive esophagitis (short term): 40 mg po qd for 8–16 weeks or 40 mg IV for 7–10 days
- Esophagitis maintenance (GERD): 40 mg po qd
- Duodenal ulcer: 40–80 mg qd for 4–8 weeks
- Acute non-variceal upper GI bleed: 80 mg IV bolus followed by continuous infusion at 8 mg/h for 72 h after endoscopic therapy (Note: Recent data suggests equal efficacy of 40 mg IV BID vs. continuous infusion)
- Gastric hypersecretion (long term): 40 mg po bid, can increase to a maximum of 240 mg qd
- Gastric hypersecretion associated with pathologic conditions: 40 mg po bid or 80 mg IV bid; increase up to 240 mg/day

Contraindications/cautions:
- Hypersensitivity to pantoprazole products
- Use with caution in Bartter's syndrome, hypocalcemia, hypokalemia, metabolic alkalosis (powder for oral suspension contains 1680 mg (20 meq) of sodium bicarbonate)

Adverse effects:
- Gastrointestinal: Diarrhea, pancreatitis, hepatotoxicity
- Renal: Interstitial nephritis
- Endocrine: Hyperglycemia
- Immunologic: Stevens–Johnson syndrome
- Musculoskeletal: Hip fracture, rhabdomyolysis

Drug interactions: See omeprazole
Lactation: Probably safe
Pregnancy category: B
Relative cost: Oral–$, IV–$$$ (generic available: $)

## *Rabeprazole Sodium*

Brand name: Aciphex
Manufacturer: Eisai

Dosage:
- Duodenal ulcer disease: 20 mg po qd after the morning meal for up to 4 weeks
- Gastric hypersecretion: Initial, 60 mg po qd, may increase up to 120 mg; single daily doses up to 100 mg/day may be given; 120 mg dose may require divided doses, 60 mg bid
- Gastroesophageal reflux disease, erosive or ulcerative, maintenance: 20 mg po once daily
- Gastroesophageal reflux disease, erosive or ulcerative, treatment: 20 mg po once daily for 4–8 weeks
- Gastroesophageal reflux disease, symptom control: 20 mg po once daily for 4 weeks
- *H. pylori* treatment with triple therapy: 20 mg po bid for 7 days

Contraindications/cautions:
- Hypersensitivity to rabeprazole/substituted benzimidazoles
- Caution in liver disease

Adverse effects:
- Neurologic: Headache
- Immunologic: Stevens–Johnson syndrome
- Musculoskeletal: Hip fracture, rhabdomyolysis

Drug interactions: See omeprazole
Pregnancy category: B
Lactation: Probably safe
Relative cost: $$

## *Dexlansoprazole*

Brand names: Dexilant, Kapidex [DSC]
Manufacturer: Takeda Pharmaceuticals

Dosage:
- Erosive esophagitis: Short term, 60 mg po qd for up to 8 weeks; maintenance therapy, 30 mg po qd for up to 6 months
- Symptomatic GERD: Short term, 30 mg po qd for up to 4 weeks

Contraindications/cautions:
- Hypersensitivity to dexlansoprazole
- Patients with Child-Pugh class B may require dosage reductions

Adverse effects:
- Gastrointestinal: Diarrhea
- Respiratory: Upper respiratory tract infection
- Musculoskeletal: Increased incidence of osteoporosis related bone fractures

Drug interactions: See omeprazole
Pregnancy category: B
Lactation: Excretion in breast milk unknown
Relative cost: $$$$

## HISTAMINE $H_2$ ANTAGONISTS

See algorithms for gastroesophageal reflux disease and refractory gastroesophageal reflux disease.

### *Famotidine*

Brand names: Pepcid, Pepcid AC
Manufacturer: Merck & Co., Inc.

Dosage:
- Duodenal ulcer disease: 40 mg po qhs or 20 mg po bid or 20 mg IV q12 h
- Duodenal ulcer disease (maintenance): 20 mg po qhs
- Esophagitis/GERD: 20–40 mg po bid for 12 weeks, 20 mg IV q12 h
- Gastric hypersecretion: 20 mg to 160 mg po q 6 h, 20 mg IV q12 h
- Gastric ulcer: 40 mg po qhs, 20 mg IV q 12 h
- GERD short-term system relief: 20 mg po bid for 6 weeks, 20 mg IV q12 h
- Indigestions: 10–20 mg po bid

Contraindications/cautions:
- Hypersensitivity to pepcid or any of its components
- History of hypersensitivity to other H2 receptor antagonists
- Dose adjustment by 50 % or increase interval to 24–36 h for CrCl < 50 mL/min

Adverse effects:
- Gastrointestinal: Constipation, diarrhea, necrotizing enterocolitis in fetus or newborn, increased liver enzymes
- Neurologic: Dizziness

Drug interactions:
- May decrease efficacy of oral iron preparations, antifungals, and atazanavir
- May increase levels of fluvastatin and increase risk of rhabdomyolysis

- H2 blocker equivalent dose to famotidine 40 mg BID may be administered simultaneously with Harvoni under fasting conditions; higher doses should be avoided as they decrease the efficacy of Harvoni. Ideal dosing is 12 h apart.

Pregnancy category: B
Lactation: Probably safe
Relative cost: $$ (generic available: $–$$)

### *Ranitidine Hydrochloride*

Brand name: Zantac
Manufacturer: Boehringer Ingelheim Pharmaceuticals, Inc. (OTC) and GlaxoSmithKline (Rx)

Dosage:
- Duodenal ulcer: 150 mg po bid or 300 mg qhs
- Duodenal ulcer: 50 mg IV q 6–8 h or 6.25 mg/h continuous infusion
- Duodenal ulcer (maintenance): 150 mg po qhs
- Erosive esophagitis: 150 mg po qid initially, then 150 mg po bid
- Gastric ulcer: 150 mg po bid
- Gastric ulcer (maintenance): 150 mg po qhs
- GERD: 150 mg po bid

Contraindications/cautions:
- Hypersensitivity to ranitidine or any of its components

Adverse effects:
- Gastrointestinal: Abdominal pain, constipation, diarrhea, nausea, vomiting, necrotizing enterocolitis in fetus or newborn, pancreatitis
- Neurologic: Dizziness, headache, insomnia, somnolence
- Cardiovascular: Bradyarrhythmia
- Psychiatric: Agitation
- Other: Fatigue

Drug interactions:
- May decrease efficacy or oral iron preparations, antifungals, and atazanavir
- May increase levels of fluvastatin and increase risk of rhabdomyolysis
- Tenofovir may increase ranitidine levels

Pregnancy category: B
Lactation: Probably safe
Relative cost: $ (generic available: $)

## OTHER AGENTS

### *Carafate*

Brand name: Sucralfate
Manufacturer: Axcan Pharma

Dosage:
- Duodenal ulcer disease, active: 1 g po qid or 2 g po bid for 4–8 weeks
- Duodenal ulcer disease, maintenance: 1 g po bid
- Gastric ulcer, maintenance: 1 g po bid
- Stress ulcer, Prophylaxis: 1 g po q 6 h

Contraindications/cautions:
- Hypersensitivity to sucralfate products

Adverse effects:
- Gastrointestinal: Constipation, bezoar
- Other: Aluminum toxicity, renal impaired patients

Drug interactions:
- To reduce the potential of adversely affecting the absorption of other drugs, administer other drugs 2 h prior to sucralfate

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $ (generic available: $)

For algorithms for the treatment of GERD, see Fig. 1.1, and refractory GERD, see Fig. 1.2.

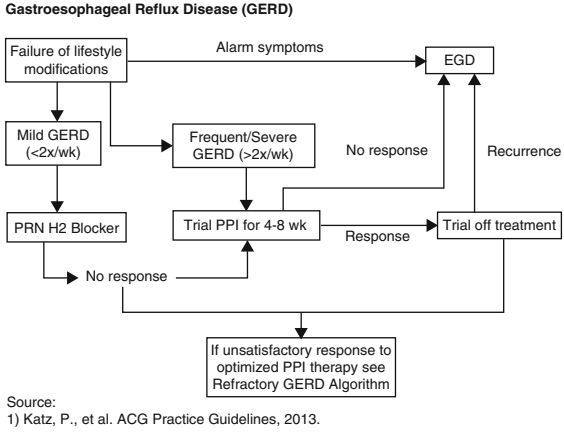


Fig. 1.1 An algorithm for the treatment of GERD. *Source*: (1) Katz P, et al. ACG practice guidelines. 2013

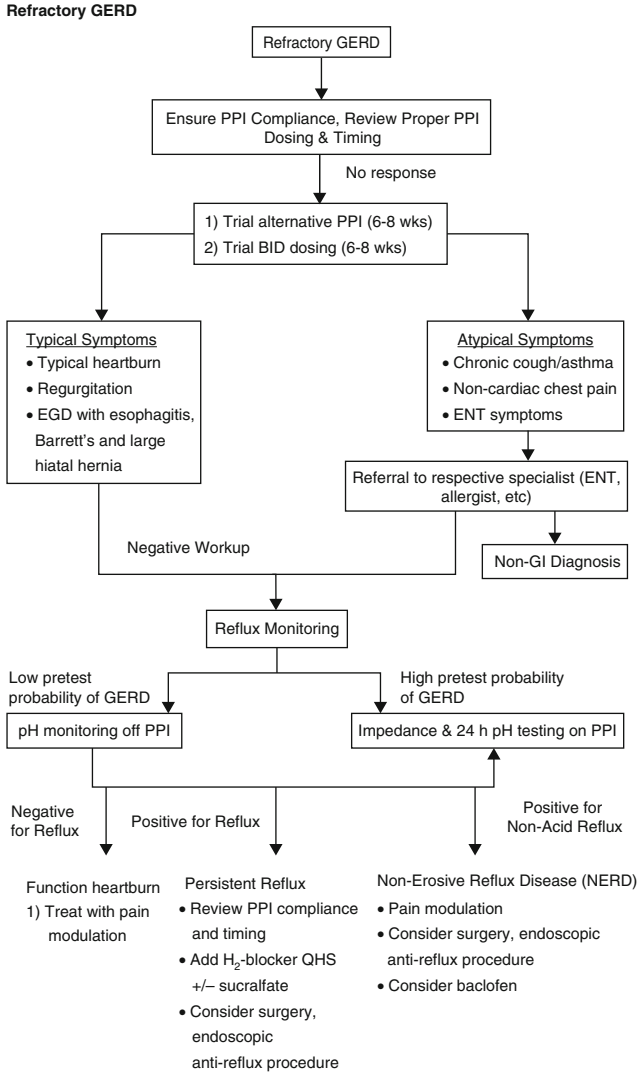


Fig. 1.2 An algorithm for the treatment of refractory GERD. *Source*: (1) Katz P, et al. ACG practice guidelines. 2013; (2) Richter J. Gastroenterol Hepatol. 2014; (3) UpToDate

## REFERENCES

1. UpToDate®2015
2. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol. 2013;108:308–28.
3. Richter JE. Current diagnosis and management of suspected reflux symptoms refractory to proton pump inhibitor therapy. Gastroenterol Hepatol. 2014;10: 547–55.

# 2 Gastrointestinal Bleeding

*Houman Rezaizadeh and Erik Olson*

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## ABBREVIATIONS

TIPS Transjugular intrahepatic portal systemic shunt

## ACUTE NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

- For use of PPIs in non-variceal bleeding, see the algorithm below for upper gastrointestinal bleeding.

### *Pantoprazole Sodium*

Dosage:

- Acute non-variceal upper GI bleed: 80 mg IV bolus followed by continuous infusion at 8 mg/h for 72 h after endoscopic therapy.
- Refer to Chap. 1 for product details
- Esomeprazole

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_2,

- Acute non-variceal upper GI bleed: 80 mg IV bolus followed by continuous infusion at 8 mg/h for 72 h after endoscopic therapy.
- See Chap. 1 for product details.

## ACUTE ESOPHAGEAL VARICEAL HEMORRHAGE

- For use of octreotide in variceal bleeding, see the algorithm below for upper gastrointestinal bleeding.

### *Octreotide Acetate*

Trade name: Sandostatin
Manufacturer: Abraxis, Novartis

Dosage:
- Acute variceal hemorrhage: 50 μg IV bolus followed by 50 μg/h IV infusion
- Small intestinal bacterial overgrowth: 50 μg sc qd for 3 weeks
- VIPoma associated diarrhea: 150–750 μg sc/IV divided in bid-qid dose for 2 weeks, then titrate for response
- Carcinoid tumor symptoms: 50–150 μg sc/IV bid-qid. Maximum 1500 μg/day, titrate based on response for flushing and diarrhea
- Acute carcinoid crisis: 50–500 μg IV prn or 50 μg/h IV infusion for 8–24 h
- Carcinoid crisis prophylaxis: 250–500 μg IV 1×; give 1–2 h preoperatively
- Secretory diarrhea: 50–500 μg sc/IV qd-tid, titrate based on response
- Dumping syndrome: 50–100 μg sc before meals

Contraindications/cautions:
- Sensitivity to octreotide or any of its components

Adverse effects:
- Gastrointestinal: Abdominal discomfort, constipation, diarrhea, flatulence, nausea, pancreatitis, cholelithiasis, ascending cholangitis, cholecystitis, cholestatic hepatitis
- Neurologic: Dizziness, headache
- Cardiovascular: Cardiac dysrhythmia, congestive heart failure (rare), sinus bradycardia
- Endocrine: Hyperglycemia, hypoglycemia, hypothyroidism

Drug interactions:
- Contraindicated with cisapride and pimozide due to risk of QT prolongation
- Use with caution with calcium channel blockers due to risk of bradycardia and cardiac conduction abnormalities.

Pregnancy category: B
Lactation safety: Unknown
Relative cost: $$$$$ (generic available: $)

## *Vasopressin*

Trade name: Pitressin
Manufacturer: Parke-Davis

Dosage:
- Variceal bleed 20 units IV over 20 min followed by 0.2–0.4 units/min; administer with nitroglycerin to control vasoconstrictive complications.
- Prophylaxis for postoperative complications: Initial, 5 units im (0.25 mL) postoperatively; increase to 10 units (0.5 mL) at subsequent injections repeated at 3 or 4 h intervals if necessary

Contraindications/cautions:
- Anaphylaxis or hypersensitivity to the drug or its components
- Chronic nephritis with nitrogen retention contraindicates the use of vasopressin until reasonable nitrogen blood levels have been attained.
- Caution in patients with heart failure, coronary artery disease, epilepsy, and asthma.

Adverse effects:
- Gastrointestinal: Nausea, flatus, abdominal cramps, vomiting
- Neurologic: Throbbing headache, tremor, vertigo
- Cardiovascular: Myocardial infarction, angina, arrhythmias, hypertension
- Respiratory: Bronchospasm
- Endocrine metabolic: Water intoxication syndrome
- Immunologic: Anaphylaxis
- Dermatologic: Gangrenous disorder, sweating, urticaria

Drug interactions:
- Demeclocycline and lithium may decrease antidiuretic effect
- Increased risk of hyponatremia and seizures with polyethylene glycol and sodium phosphate
- Increased antidiuretic effect with carbamazepine and fludrocortisones

Pregnancy category: B
Lactation: Probably safe
Relative cost: $$$$$ (generic available: $)

## *Nitroglycerin*

Trade names:
- Nitroglycerin IV
- Nitrostat
- Tridil

Manufacturers:
- American Regent, Baxter, Bristol-Meyers-Squib, Parke-Davis, Quad, Lymphomed

Dosage:
- 10–20 μg/min continuous IV infusion; titrate in increments of 5–10 mcg/min every 5 min to total dose of 50–180 μg/min until limiting side effects (headache or hypotension); administer along with vasopressin to prevent vasoconstrictive complications of vasopressin

Contraindications/cautions:
- Hypersensitivity to organic nitrates
- Concurrent use of phosphodiesterase inhibitors such as sildenafil or vardenafil (increased hypotensive effect)
- Constrictive pericarditis
- Pericardial tamponade
- Restrictive cardiomyopathy
- Symptomatic hypotension
- Increased intracranial pressure
- Methemoglobinemia

Adverse effects:
- General: Headache, dizziness, flushing
- Cardiac: Hypotension, reflex tachycardia
- Hematological: Methemoglobinemia

Drug interactions:
- Hypotension and cardiovascular collapse with concomitant use of phosphodiesterase inhibitors

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $ (generic available: $)
For prevention of recurrent bleeding due to portal hypertension, see Chap. 9.
For guidance in the treatment of upper gastrointestinal bleeding, see Fig. 2.1. The risk of rebleeding based on endoscopic appearance of a site is shown in Table 2.1.

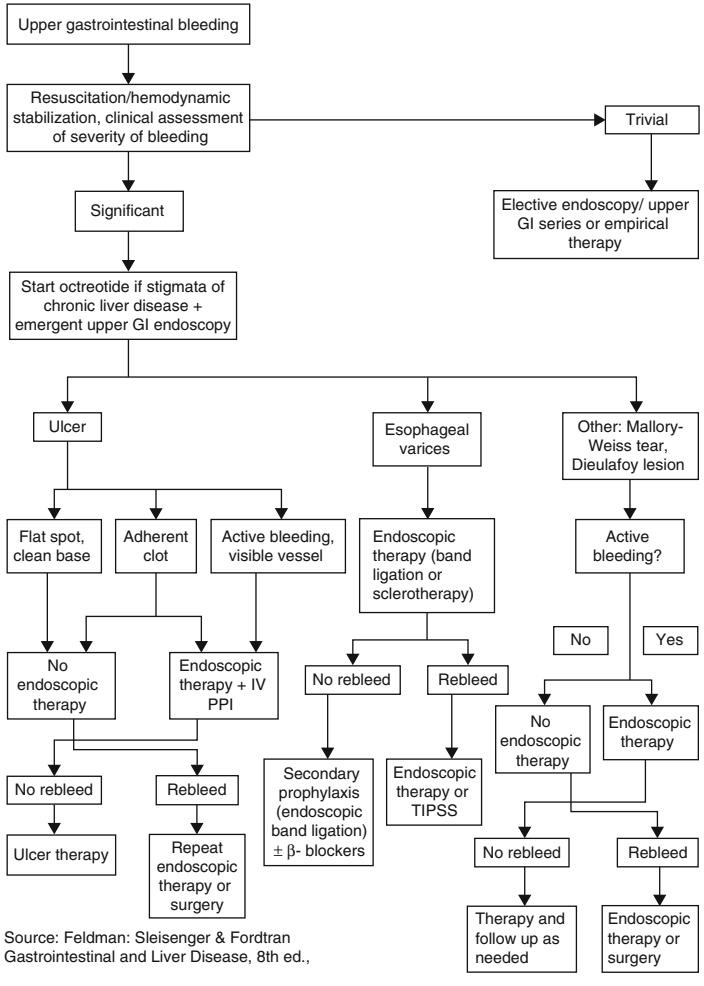


Fig. 2.1 An algorithm for the treatment of upper gastrointestinal bleeding. *Source*: Feldman, Sleisenger & Fordtran gastrointestinal and liver disease. 8th ed. Philadelphia: Saunders; 2006

**Table 2.1 Forrest classification and risk of rebleeding**

| *Forrest classification* | *Endoscopic appearance* | *Rebleeding (%)* |
|---|---|---|
| I | Active bleeding | 55 |
| IIA | Non-bleeding visible vessel | 43 |
| IIB | Adherent clot | 22 |
| IIC | Flat pigment | 10 |
| III | Clean base | 5 |

Adapted from Sleisenger Table 53-3

## REFERENCE

1. Feldman M, Friedman LS, Sleisenger MH, editors. Sleisenger & Fordtran's gastrointestinal and liver disease. 7th ed. Philadelphia: Saunders; 2004.

# 3 Specific GI Motility Disorders

*Houman Rezaizadeh and Erik Olson*

***Contents***



## ACHALASIA, DIFFUSE ESOPHAGEAL SPASM (DES)

### *Medications*

### *Nifedipine*

Brand names: Adalat CC, Procardia, Procardia XL, Afeditab CR, Nifediac CC, Nifedical XL
Manufacturer: Bayer

Dosages:

- Achalasia: Doses ranging from 10 to 30 mg daily may provide minimal benefit
- Diffuse esophageal spasm (DES)/dysphagia predominant symptoms: Doses ranging 10–30 mg daily

Contraindications/cautions:

- Hypersensitivity to nifedipine
- Caution after acute myocardial infarction (within 4 weeks), congestive heart failure, peripheral edema, hypotension, unstable angina pectoris

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_3,

Adverse effects:
- Gastrointestinal: Constipation, heartburn, nausea
- Neurologic: Dizziness, headache
- Cardiovascular: Palpitations, peripheral edema, worsening of angina, myocardial infarction (rare)
- Dermatologic: Flushing

Drug interactions:
- Increased risk of AV block, bradycardia, hypotension with octreotide, beta-blockers, and amiodarone
- Increased risk of hypotension with nitrates

Pregnancy category: C
Lactation: Probably safe
Relative cost: $$ (generic available: $–$$)

## *Botulinum Toxin (Onabotulinum Toxin A)*

Brand names: Botox, Botox Cosmetic
Manufacturer: Allergan, Inc.

Dosage:
- Achalasia: 80–100 units im into lower esophageal sphincter

Contraindications/cautions:
- Anaphylaxis

Adverse effects:
- Gastrointestinal: Dysphagia, indigestion
- Neurologic: Headache, ptosis of eyelid, focal facial paralysis, speech disturbance
- Cardiac: Arrhythmias, hypertension, myocardial infarction, syncope
- Respiratory: Upper respiratory infection, dyspnea
- Musculoskeletal: Muscle weakness, neck pain
- Dermatologic: Injection site pain, erythema multiforme
- Ophthalmic: Dry eyes, acute angle closure glaucoma, punctate keratitis, visual disturbance
- Immunologic: Anaphylaxis

Drug interactions:
- Clindamycin, aminoglycosides, succinylcholine may potentiate neuromuscular effects of botulinum toxin

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$$

### *Isosorbide Dinitrate*

Brand names: Dilatrate-SR, Isordil, Titradose
Manufacturer: Wyeth

Dosage:
- 5–10 mg before meals/chest pain predominant symptoms

Contraindications/cautions:
- Anaphylaxis
- Concurrent use of PDE-5 inhibitors
- Angle closure glaucoma

Adverse effects:
- CNS: Headache
- Gastrointestinal: Nausea, vomiting, bowel incontinence
- Cardiac: Hypotension
- Musculoskeletal: Weakness

Drug interactions:
- PDE-5 inhibitors

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$ (generic available: $$)

## *Gastroparesis*

### *Erythromycin*

Brand names: E-Mycin, E.E.S.-200, E.E.S.-400, Ery-Tab, Eryc, EryPed, erythrocin stearate filmtab, Erythrocot, Ilosone, MY-E, PCE Dispertab, Robimycin

Dosages:
- Gastroparesis: 3 mg/kg iv every 8 h, 40–80 mg po tid before meals
- *Vibrio cholerae* diarrhea: Erythromycin 250 mg qid for 3 days
- Campylobacter gastroenteritis: Erythromycin 500 mg po bid for 5 days

Contraindications:
- Concomitant therapy with astemizole, cisapride, pimozide, or terfenadine
- Hypersensitivity to erythromycin or any component of the product

Adverse effects:
- Gastrointestinal: Diarrhea, loss of appetite, nausea, abdominal cramps, vomiting, elevated liver enzymes, hepatitis, jaundice

- Neurological: Exacerbation of myasthenia gravis, convulsions
- Cardiovascular: Arrhythmias, QT prolongation, torsades de pointes
- Dermatologic: Stevens-Johnson, toxic epidermal necrolysis, erythema multiforme
- Immunologic: Anaphylaxis
- Otic: Reversible hearing loss

Drug interactions:
- phenothiazines, cisapride, dofetilide, pimozide, ranolazine: Increase risk of QT prolongation and cardiac arrhythmias.
- Ergot alkaloids: Increase risk of ergot toxicity, severe vasospasm, and peripheral vascular ischemia

Pregnancy category: B
Lactation: Probably safe
Relative cost: $$–$$$ (generic available: $$–$$$)

## *Metoclopramide*

Brand name: Reglan
Manufacturer: Wyeth, Schwarz Pharma

Dosage:
- Gastroparesis: 5–20 mg po qid

Contraindications:
- Concomitant use of drugs with extrapyramidal adverse effects
- Gastrointestinal hemorrhage, obstruction (mechanical), or perforation
- Hypersensitivity to metoclopramide products
- Pheochromocytoma
- Seizure disorders

Adverse effects:
- Gastrointestinal: Constipation
- Neurologic: Dystonia, sedation, somnolence, tremor, neuroleptic malignant syndrome
- Cardiovascular: Cardiac arrhythmia
- Endocrine metabolic: Body fluid retention
- Psychiatric: Restlessness
- Other: Fatigue

Pregnancy category: B
Lactation: Probably safe
Relative cost: $–$$ (generic available: $–$$)

## *Domperidone*

Brand name: Motilium
Manufacturer: Janssen Pharmaceutica

***Not FDA approved in the USA. Special license and permission required to prescribe. Contact manufacturer for more information.***

Dosage:
- Gastroparesis: 10 mg tid-qid

Contraindications:
- Hypersensitivity to domperidone products
- GI hemorrhage/obstruction
- Concomitant use of ketoconazole

Adverse effects:
- CNS: Headache
- GI: Xerostomia
- Cardiovascular: May prolong QT interval

Pregnancy category: Not classified
Lactation: Probably safe
Relative cost: $$

## *Cisapride*

Brand name: Propulsid
Manufacturer: Janssen Pharmaceutica

***Withdrawn from US market March 2000. Available for compassionate use only. For more information contact manufacturer.***

Dosage:
- Gastroparesis: 5–10 mg po qid (limited availability)

Contraindications:
- Hypersensitivity to cisapride products
- GI hemorrhage/obstruction
- Serious cardiac arrhythmias

Adverse effects:
- CNS: Headache, extrapyramidal effects
- GI: Cramping, constipation, nausea
- Respiratory: Increased incidence of viral infection

Pregnancy category: C
Lactation: Compatible
Relative cost: $$$$

## DUMPING SYNDROME AND ACCELERATED GASTRIC EMPTYING

### *Octreotide*

See Chap. 2

### *Dexlansoprazole*

See Chap. 1

## RAPID TRANSIT DYSMOTILITY OF THE SMALL BOWEL

### *Loperamide*

Brand names: Diamode, Imodium, Imodium A-D, Imogen, Imotil, Imperim, Kao-Paverin Caps, Kaodene A-D
Manufacturer: Multiple

Dosage:
- Rapid transit: Loperamide 4 mg before meals and before dinner

Adverse Effects:
- Gastrointestinal: Abdominal pain, nausea, vomiting, xerostomia, necrotizing enterocolitis in fetus or newborn (rare)
- Neurologic: Dizziness, somnolence
- Endocrine metabolic: Hyperglycemia
- Other: Fatigue

Drug interactions:

- Potassium salts: Anticholinergic drugs decrease GI transit, increase local exposure to potassium, thereby causing ulcerative lesions

Pregnancy Category: B
Lactation: Probably safe
Relative cost: $ (generic available: $)

# 4 General GI Motility Disorders

*Houman Rezaizadeh and Erik Olson*

***Contents***



## DIARRHEA

### *Dicyclomine Hydrochloride*

Brand name: Bentyl
Class: Anticholinergics
Manufacturer: Axcan Scandipharm
Dosage: Irritable bowel syndrome: 10–40 mg po qid

Contraindications/cautions:

- Age <6 months
- Hypersensitivity
- Active infection
- Breastfeeding
- Gastrointestinal obstruction
- Glaucoma
- Myasthenia gravis
- Obstructive uropathy
- Reflux esophagitis
- Severe ulcerative colitis or toxic megacolon
- Unstable cardiovascular status in acute hemorrhage

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_4,

Adverse effects:
- Gastrointestinal: Constipation, nausea, xerostomia
- Neurologic: Dizziness, somnolence
- Cardiovascular: Tachyarrhythmia
- Renal: Urinary retention
- Dermatologic: Diminished sweating
- Ophthalmic: Blurred vision

Drug interactions:
- Potassium salts: Anticholinergic drugs decrease GI transit and increase local exposure to potassium, thereby causing ulcerative lesions

Pregnancy category: B
Lactation: Possibly unsafe
Relative cost: $ (generic available: $)

## *Hyoscyamine Sulfate*

Brand name: Levsin
Class: Anticholinergics/Antispasmodic
Manufacturer: Schwarz Pharma
Dosage:
Irritable bowel syndrome: 0.125–0.25 mg sl/po q4 h as needed

Contraindications/cautions:
- Glaucoma
- Hypersensitivity to hyoscyamine products or other anticholinergic drugs
- Intestinal obstruction, intestinal atony (in elderly, debilitated), severe ulcerative colitis, paralytic ileus, toxic megacolon
- Myasthenia gravis
- Obstructive uropathy
- Unstable cardiovascular states in acute hemorrhage

Adverse effects:
- Gastrointestinal: Xerostomia
- Neurologic: Dizziness, somnolence
- Cardiovascular: Tachyarrhythmia
- Renal: Urinary retention
- Dermatologic: Diminished sweating
- Ophthalmic: Blurred vision, elevated intraocular pressure

Drug interactions:
- Potassium salts: Anticholinergic drugs decrease GI transit and increase local exposure to potassium, thereby causing ulcerative lesions

Pregnancy category: C
Lactation: Possibly safe
Relative cost: $ (generic available: $)

### *Diphenoxylate Hydrochloride/Atropine Sulfate*

Brand name: Lomotil
Class: Antidiarrheals
Manufacturer: Pfizer U.S. Pharmaceuticals

Dosage:
- Diarrhea; Adjunct: 2 tab or 10 mL solution po qid (maximum dose 20 mg/day (diphenoxylate))

Contraindications/cautions:
- Diarrhea associated with enterotoxin producing bacteria or pseudomembranous enterocolitis; may prolong and/or worsen diarrhea
- Hypersensitivity to diphenoxylate or atropine products
- Obstructive jaundice, may precipitate hepatic coma

Adverse effects:
- Gastrointestinal: Abdominal discomfort, nausea and vomiting, pancreatitis, toxic megacolon
- Neurologic: Dizziness, sedation, somnolence
- Psychiatric: Euphoria

Drug interactions:
- Potassium salts: Anticholinergic drugs decrease GI transit and increase local exposure to potassium, thereby causing ulcerative lesions.

Pregnancy category: C
Lactation: Probably safe
Relative cost: $$ (generic available: $-$$)

### *Loperamide*

Brand name: Imodium
Class: Antidiarrheals
Manufacturer: Janssen, L.P.

Dosage:
- Diarrhea; 4 mg po after first loose stool initially; then 2 mg after each subsequent stool; not to exceed 16 mg/day

Contraindications/cautions:
- Abdominal pain in the absence of diarrhea
- Bacterial enterocolitis, caused by invasive organisms including Salmonella, Shigella, and Campylobacter; do not use as primary therapy
- Dysentery, acute; do not use as primary therapy
- Hypersensitivity to loperamide or to any of the excipients
- Infants below 24 months of age
- Pseudomembranous colitis, associated with the use of broad spectrum antibiotics.

Adverse effects:
- Gastrointestinal: Abdominal pain, nausea, vomiting, xerostomia, necrotizing enterocolitis in fetus or newborn (rare)
- Neurologic: Dizziness, somnolence, fatigue
- Endocrine: Hyperglycemia

Drug interactions:
- Potassium salts: Anticholinergic drugs decrease GI transit and increase local exposure to potassium, thereby causing ulcerative lesions

Pregnancy category: C
Lactation: Probably safe
Relative cost: $ (generic available: $)

## *Imipramine*

Brand name: Tofranil
Class: Tricyclic antidepressants
Manufacturer: Generic

Dosage:
- Irritable bowel syndrome: 10–100 mg/day po; start low and titrate as necessary

Contraindications/cautions:
- Hypersensitivity to imipramine
- Concomitant use of monoamine oxidase (MAO) inhibitors
- Use in patients during acute recovery after a myocardial infarction

Adverse effects:
- Gastrointestinal: Bloating, constipation, xerostomia
- Neurologic: Asthenia, dizziness, headache, somnolence
- Cardiovascular: Cardiac dysrhythmia, heart block, hypertension, myocardial infarction (rare), orthostatic hypotension, palpitations, syncope
- Renal: Urinary retention

- Endocrine: Weight gain
- Ophthalmic: Blurred vision

Drug interactions:
- Antiarrhythmics, class Ia: Increased risk of QT prolongation and cardiac arrhythmias
- MAO inhibitors: Combination may result in CNS overstimulation, hyperpyrexia, seizures, and death
- Potassium salts: Anticholinergic drugs decrease GI transit and increase local exposure to potassium, thereby causing ulcerative lesions.
- Pimozide: Increased risk of CNS depression, psychomotor impairment, QT prolongation

Pregnancy category: D
Lactation: Probably safe
Relative cost: $ (generic available: $)

## *Amitriptyline*

Brand name: Elavil
Class: Tricyclic antidepressants
Manufacturer: Generic

Dosage:
- Chronic pain: Start: 0.1 mg/kg po qhs, titrate slowly over 2–3 weeks; maximum of 150 mg/day

Contraindications/cautions:
- Hypersensitivity
- Concomitant use of monoamine oxidase (MAO) inhibitors
- Use in patients during acute recovery after a myocardial infarction
- Concomitant cisapride use

Adverse effects:
- Gastrointestinal: Bloating, constipation, xerostomia
- Neurologic: Asthenia, dizziness, headache, somnolence
- Cardiovascular: Cardiac dysrhythmia, heart block, hypertension, myocardial infarction (rare), orthostatic hypotension, palpitations, syncope
- Endocrine metabolic: Weight gain
- Ophthalmic: Blurred vision

Drug interactions:
- Antiarrhythmics, class Ia: Increase risk of QT prolongation and cardiac arrhythmias
- MAO inhibitors: Combination may result in CNS overstimulation, hyperpyrexia, seizures, and death

- Potassium salts: Anticholinergic drugs decrease GI transit and increase local exposure to potassium, thereby causing ulcerative lesions
- Pimozide: Increase risk of CNS depression, psychomotor impairment, QT prolongation

Pregnancy category: D
Lactation: Probably unsafe
Relative cost: $ (generic available: $)

## *Alosetron*

Brand name: Lotronex
Class: Serotonin (5-HT3) receptor antagonists
Manufacturer: GlaxoSmithKline

Dosage:
- Restricted access in USA: Irritable bowel syndrome, 0.5 mg po bid (in women only) for 4 weeks; after 4 weeks of 0.5 mg twice per day, may increase to 1 mg bid

Contraindications/cautions:
- Hypersensitivity
- Preexisting constipation; do not initiate therapy
- Concurrent use of fluvoxamine; increases alosetron plasma concentrations and half-life
- History of Crohn's disease, diverticulitis, gastrointestinal perforation and/or adhesions, impaired intestinal circulation or ischemic colitis, intestinal obstruction, intestinal stricture, or toxic megacolon
- Severe hepatic impairment; alosetron is extensively metabolized in the liver
- History of hypercoagulable state, thrombophlebitis
- Patients unable to understand or comply with Patient–Physician Agreement
- Side effects:
- Gastrointestinal: Abdominal pain, constipation, nausea, ischemic colitis
- Neurologic: Headache (rare)

Drug interactions:
- Fluvoxamine: Increases alosetron levels and increases risk of adverse effects

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$$$$

## CONSTIPATION

### *Psyllium*

Brand name: Metamucil, Fiberall
Class: Laxative
Manufacturer: Psyllium—Generic, Metamucil—Procter and Gamble Pharmaceuticals
Dosage: Constipation: 15–60 g/day po with at least 8 glasses of water

Contraindications:
- Hypersensitivity to psyllium
- Intestinal obstruction
- Fecal impaction
- Adverse effects:
- Gastrointestinal: Abdominal distention and flatulence
- Immunologic: Potentially severe (but rare) allergic reactions, anaphylaxis, and asthma

Drug interactions: No major drug interactions known

Pregnancy category: Likely safe
Lactation: Safety unknown, probably safe
Relative cost: $ (generic available: $)

### *Methylcellulose*

Brand name: Citrucel
Class: Laxative
Manufacturer: GlaxoSmithKline
Dosage: Constipation: 15–60 g/day po with at least 8 glasses of water

Contraindications:
- Hypersensitivity to psyllium
- Intestinal obstruction
- Fecal impaction

Adverse effects:
Gastrointestinal: Abdominal distention and flatulence, nausea

Drug interactions: No major drug interactions

Pregnancy category: B
Lactation: Probably safe
Relative cost: $ (generic available: $)

## *Docusate*

Brand name: Docusate sodium (Colace)/Docusate calcium (Surfak)
Class: Emollient stool softeners
Manufacturer: Colace—Roberts Pharmaceutical Corp, Docusate—generic
Dosage: Constipation: 100 mg po qd/bid (50–200 mg) or 50–100 mg pr as an enema

Contraindications:
- Hypersensitivity to psyllium
- Intestinal obstruction
- Concomitant use of mineral oil
- Acute abdominal pain, nausea, vomiting

Adverse effects:
- Gastrointestinal: Abnormal taste in mouth, diarrhea, nausea
- Musculoskeletal: Cramps

Drug interactions:
- Mineral oil: Increase mineral oil absorption and adverse effects

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $ (generic available: $)

## *Magnesium Citrate*

Brand name: Evac-Q-Mag
Class: Saline laxatives
Manufacturer: Generic

Dosage:
- Constipation: 150–300 mL/day or 11–18 g po divided qd-bid (1 mL Mg citrate contains 9.4 mg elemental Mg)
- Preparation of bowel for procedure: 150–300 mL PO once, may repeat as needed

Contraindications/cautions:
- Abdominal pain, nausea/vomiting, rectal bleeding
- Heart block
- Low-salt diet
- Severe renal disease

Adverse effects:
- Gastrointestinal: Diarrhea
- Neurologic: Asthenia, dizziness
- Respiratory: Hypoventilation

Drug interactions:
- Doxercalciferol: Increase risk of hypermagnesemia

Pregnancy category: B
Lactation: Probably safe
Relative cost: $ (generic available: $)

## *Mineral Oil*

Brand name: Fleet, Zymenol
Class: Lubricant laxative
Manufacturer: Generic

Dosage: Constipation: 15–45 mL po once daily at bedtime, maximum 45 mL or Enema—1 bottle (133 mL) into rectum once.

Contraindications/cautions:
- Hypersensitivity to psyllium
- Children less than 2 years of age (rectal administration)
- Children less than 6 years of age (oral administration)
- Colostomy/ileostomy
- Diverticulitis, appendicitis
- Ulcerative colitis, rectal bleeding
- Adverse effects:
- Gastrointestinal: Incontinence of feces, intestinal malabsorption, fat-soluble vitamins, rectal discharge, rectal bleeding
- Dermatologic: Anal irritation, pruritus ani
- Other: Chronic abuse of laxatives is accompanied by concerns of lipid pneumonia, lymphoid hyperplasia, and foreign body reactions

Drug interactions:
- Docusate: Increase mineral oil absorption and adverse effects

Pregnancy category: C
Lactation: Possibly unsafe
Relative cost: $ (generic available: $)

## *Polyethylene Glycol*

Brand name: Glycolax, Miralax
Class: Osmotic laxatives
Manufacturer: Miralax: Schering-Plough; Glycol ax: Kremers Urban, LLC; Polyethylene glycol: Generic

Dosage:
- Constipation: 17 g (about 1 heaping tablespoon) per day dissolved in 4-ounces of water, juice, soda, coffee, or tea
- Preparation of bowel for procedure: Polyethylene glycol/electrolytes (Golytely)—4 L po once

Contraindications/cautions:
- Hypersensitivity to any component, such as polyethylene glycol
- Bowel obstruction, known or suspected

Adverse effects:
- Gastrointestinal: Diarrhea, flatulence, nausea, abdominal cramps, bloating

Drug interactions: No major interactions
Pregnancy category: C
Lactation: Probably unsafe
Relative cost: $ (generic available: $)

## *Lactulose*

See Chap. 10

## *Senna*

Brand name: Senokot, Ex-Lax, Senexon, Senna-Gen
Class: Stimulant laxatives
Manufacturer: Senokot—Purdue Pharma; Ex-lax—Novartis Consumer Health; Senna—generic

Dosage: Constipation: 0.12–0.25 g/day po (2–4 tabs po qd-bid)

Contraindications/cautions:
- Acute surgical abdomen
- Bowel obstruction
- Fecal impaction
- Hypersensitivity to anthraquinone laxatives or to any of the ingredients
- Patients with nausea, vomiting, or other symptoms of appendicitis
- Undiagnosed abdominal pain

Adverse effects:
- Gastrointestinal: Abdominal pain, nausea, abdominal bloating, abdominal cramps, flatulence, diarrhea, pseudomelanosis coli, cathartic colon
- Renal: Urine discoloration, nephritis
- Other: Laxative abuse

Pregnancy category: C
Lactation: Probably safe
Relative cost: $ (generic available: $)

## *Bisacodyl*

Brand name: Bisac-Evac, Bisco-Lax, Dulcolax, Dacodyl
Class: Stimulant laxatives
Manufacturer: Dulcolax—Boehringer-Ingelheim Consumer Healthcare, Bisacodyl—generic

Dosage: Constipation: 5–15 mg po once daily up to 30 mg/day or 10 mg suppository pr once daily

Contraindications/cautions:
- Hypersensitivity to drug
- Nausea, vomiting
- Intestinal obstruction

Adverse effects:
- Gastrointestinal: Abdominal colic, abdominal discomfort, diarrhea, Proctitis (with suppository use), atony of colon

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $ (Generic available: $)

## *Castor Oil*

Brand name: Alphamul, Emulsoil, Neoloid, Purge
Class: Stimulant laxatives
Manufacturer: Generic

Dosage: Constipation: 15–60 mL po once daily

Contraindications/cautions:
- Hypersensitivity to drug
- Intestinal obstruction
- Acute abdominal pain, nausea, vomiting
- Symptoms of appendicitis
- Pregnancy

Adverse effects:
- Gastrointestinal: Abdominal pain, nausea, vomiting
- Musculoskeletal: Cramps

Pregnancy category: X
Lactation: Possibly unsafe
Relative cost: $ (generic available: $)

## *Lubiprostone*

Brand name: Amitiza
Class: Chloride-channel activator, laxative
Manufacturer: Sucampo Pharmaceuticals, Inc. and Takeda Pharmaceuticals America, Inc.

Dosage: Idiopathic constipation, chronic: 24 mg po twice daily with food

Contraindications/cautions:
- Hypersensitivity
- History of mechanical gastrointestinal obstruction

Adverse effects:
- Gastrointestinal: Abdominal distension, abdominal pain, diarrhea, flatulence, nausea
- Neurologic: Headache

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$$$$

## *Linaclotide*

Brand Name: Linzess
Class: Agonize guanylate cyclase-C, c-GMP concentrations are increased resulting in Cl- and $HCO_3$ secretion into intestinal lumen
Manufacturer: Actavis, Ironwood

Dosage: Idiopathic Constipation: 145 mcg po qd, IBS-C: 240 mcg po qd.
- Children <6 years of age

Adverse Effects:
- GI: Diarrhea, abdominal pain, flatulence, dyspepsia, GERD, vomiting, dehydration
- CNS: Headache
- Respiratory: URI, sinusitis

Pregnancy: Category C
Lactation: Unknown safety
Relative Cost: $$$

## *Irritable Bowel Syndrome*

Diarrhea predominant (IBS-D):

## *Rifaximin*

Dosing: 550 mg tid × 14 days
See Chap. 9

## *Alosteron*

See Chap. 4

## *Eluxadoline*

Brand Name: Viberzi (Forest Pharmaceuticals)
Mechanism of Action: Mixed mu opioid receptor agonist, delta opioid receptor antagonist, and kappa opioid receptor agonist which act locally to reduce abdominal pain and diarrhea without constipating side effects

Dosage:
- Patients with gallbladder: 100 mg po bid, decrease to 75 mg po bid if intolerant or drug/drug interactions
- Patients without a gallbladder: 75 mg po bid

Contraindications/Cautions:
- Biliary obstruction, sphincter of Oddi disease or dysfunction, pancreatic duct obstruction, alcohol abuse, severe hepatic impairment, mechanical GI obstruction, abuse potential

Adverse Effects:
- CNS: Dizziness, fatigue, drowsiness
- Dermatologic; skin rash
- GI: Constipation, nausea, abdominal pain, sphincter of ODDI spasm, abdominal distention, flatulence, gastric reflux
- Hepatic: Increased ALT and AST
- Respiratory: Upper respiratory infection, bronchitis, asthma, wheezing

Drug Interactions:
- Alcohol: Toxic effects of eluxadoline
- Alosteron, Analgesics, anticholinergics: Increased constipation
- Antihepacivirals, atazanavir, cyclosporine, eltrombopag, gemfibrozil, lopinavir, rifampin, ritonavir, rosuvastatin, saquinavir, tipranavir: Increase serum concentrations of Eluxadoline

Pregnancy: Adverse events not observed in animal reproduction studies
Lactation: Unknown
Relative Cost: $$$
Irritable Bowel Syndrome (Constipation predominant, IBS-C)

### *Amitiza*

See this chapter

### *Linzess*

See this chapter

# 5 Inflammatory Bowel Disease

*Houman Rezaizadeh and Erik Olson*

***Contents***



## 5-AMINOSALICYLATES (5-ASA)

For suggested use, see algorithms at end of chapter.

### *Sulfasalazine*

Brand names: Azulfidine, Azulfidine Entabs, Sulfazine, Sulfazine EC
Manufacturer: Sulfasalazine—generic, Azulfidine—Pfizer U.S. Pharmaceuticals

Dosages:
- Ulcerative colitis—initially, 3–4 g po qd in evenly divided doses not exceeding 8 h intervals; maintenance, 2 g po qd in divided doses not exceeding 8 h intervals. Supplement with folic acid 1 g/day.

Contraindications/cautions:
- Hypersensitivity to sulfasalazine, sulfa drugs, salicylates
- Intestinal or urinary obstruction
- Porphyria

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_5,

Adverse effects:
- Gastrointestinal: Dyspepsia, nausea, vomiting
- Neurologic: Headache
- Reproductive: Reversible oligozoospermia
- Hematologic: Hemolysis, neutropenia, agranulocytosis, folate deficiency
- Dermatologic: Rash
- Others (rare): Pulmonary infiltrate, nephritis, hepatitis

Drug interactions:
- Methenamine—may produce insoluble precipitate in urine

Pregnancy category: B—consider additional supplementation with folic acid
Lactation: Safety unknown
Relative cost: $$ (generic available: $$)

## *Mesalamine*

Brand names: Asacol, Canasa, Pentasa, Rowasa, Lialda, Apriso

Manufacturer:
- Asacol—Procter and Gamble Pharmaceuticals
- Pentasa—Shire Pharmaceuticals
- Rowasa—Solvay Pharmaceuticals Inc.
- Canasa—Axcan Pharma
- Lialda—Shire Pharmaceuticals
- Apriso—Salix Pharmaceuticals

Dosage:
- Crohn's disease: 1000 mg po qid
- Ulcerative colitis: Chronic, active and maintenance of remission, 800 mg tablet po tid (Asacol), 1000 mg po qid (Pentasa), 4 g rectally as a retention enema administered nightly and retained for 8 h for 3–6 weeks (Rowasa), 2.4–4.8 g po qd (Lialda), 1.5 g po qd (Apriso)

Contraindications/cautions:
- Hypersensitivity to mesalamine or salicylates
- Active peptic ulcer disease

Adverse effects:
- Gastrointestinal: Abdominal pain, constipation, diarrhea, nausea, vomiting, hepatitis
- Neurologic: Asthenia, dizziness, headache
- Musculoskeletal: Arthralgia
- Dermatologic: Pruritus, urticaria
- Others (rare): Paradoxical exacerbation of inflammatory bowel disease, pancreatitis, pericarditis, pneumonitis, nephritis

Drug interactions:
- Azathioprine or 6-MP: May increase risk of myelosuppression

Pregnancy category: B
Lactation: Possibly unsafe
Relative cost: $$$$

## *Olsalazine*

Brand name: Dipentum
Manufacturer: Pharmacia Corp.

Dosage:
- Ulcerative colitis: Maintenance of remission, 500 mg po bid

Contraindications/cautions:
- Hypersensitivity to olsalazine or salicylates

Adverse effects:
- Gastrointestinal: Abdominal pain, secretory diarrhea, dyspepsia, nausea
- Neurologic: Headache, blurred vision
- Others (rare): Hypertension, hypotension, pericarditis, hepatitis

Drug interactions:
- Azathioprine or 6-MP: May increase risk of myelosuppression

Pregnancy category: C
Lactation: Possibly unsafe
Relative cost: $$$$

## *Balsalazide*

Brand name: Colazal
Manufacturer: Salix Pharmaceuticals

Dosage: Active ulcerative colitis: 2.25 g po tid

Contraindications/cautions:
- Hypersensitivity to balsalazide, mesalamine, or salicylates

Adverse effects:
- Gastrointestinal: Abdominal pain, diarrhea, nausea, vomiting
- Neurologic: Headache
- Respiratory: Respiratory tract infection
- Musculoskeletal: Arthralgia

Drug interactions:
- Increased myelosuppression with mercaptopurine and azathioprine

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$$$$

## STEROID THERAPIES

For suggested use, see algorithms at end of the chapter.

### *Glucocorticoids (Prednisone, Methylprednisolone)*

Brand name: Generic
Manufacturer: Generic

Dosage:
- Crohn's disease: 40–60 mg po qd only for acute flare for a duration of 6–12 weeks
- Ulcerative colitis: 40–60 mg po qd during acute flares
- Autoimmune hepatitis: If single drug therapy then start with 60 mg po qd and taper over 4 weeks to 20 mg po qd maintenance dose until end point. If combination therapy with azathioprine then start with 30 mg po qd and taper over 4 weeks to 10 mg po qd maintenance dose until endpoint.

Contraindications/cautions:
- Hypersensitivity to prednisone
- Systemic fungal infections
  - Caution in congestive heart failure, seizure disorder, diabetes, hypertension, TB infection, osteoporosis

Adverse effects:
- Gastrointestinal: Nausea, vomiting, dyspepsia, appetite change
- Cardiovascular: Hypertension
- Endocrine metabolic: Body fluid retention, decreased body growth, hypernatremia, osteoporosis, hypercortisolism, hyperglycemia, primary adrenocortical insufficiency
- Immunologic: Immunosuppression
- Dermatologic: Atrophic condition of skin, impaired wound healing
- Psychiatric: Depression, euphoria, mood swings, anxiety
- Ophthalmic: Cataract, glaucoma

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection

Pregnancy category: C
Lactation: Probably safe
Relative cost: $$ (generic available: $-$$)

### *Budesonide*

Brand name: Enterocort EC
Manufacturer: Prometheus Therapeutics and Diagnostics

Dosage: Crohn's disease: For induction of remission for mild—moderate Crohn's disease affecting ileum and/or ascending colon, 9 mg po qd for up to 8 weeks. Tapered dose to 6 mg po qd used to maintain remission for up to 3 months, then taper to complete cessation is recommended.

Contraindications/cautions:
- Hypersensitivity to budesonide
- Caution in patients with TB, HTN, DM, osteoporosis, peptic ulcer disease, glaucoma, cataracts

Adverse effects (generally well-tolerated with fewer side effects than corticosteroids):
- Gastrointestinal: Nausea, abdominal pain, vomiting, dyspepsia
- Dermatologic: Easy bruising, acne
- Respiratory infection
- Neurological: Dizziness, headache

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection

Pregnancy category: C
Lactation: No data from controlled trials
Relative cost: $$$$

### *Hydrocortisone Retention Enema*

Brand name: Cortenema
Manufacturer: ANI Pharmaceuticals, Inc

Dosage: Ulcerative colitis, especially distal forms: 1 enema pr nightly for up to 21 day or until patient goes into remission

Contraindications/cautions:
- Hypersensitivity to hydrocortisone
- Systemic fungal infections
- Immediate or early post-op period after ileocolostomy

Adverse effects:
- Local pain or burning
- Rectal bleeding
- Other possible systemic effects of glucocorticoids including:
  - Gastrointestinal: Nausea, vomiting, dyspepsia, appetite change
  - Cardiovascular: Hypertension
  - Endocrine metabolic: Body fluid retention, decreased body growth, hypernatremia, osteoporosis, hypercortisolism, hyperglycemia, primary adrenocortical insufficiency
  - Immunologic: Immunosuppression
  - Dermatologic: Atrophic condition of skin, impaired wound healing
  - Psychiatric: Depression, euphoria, mood swings, anxiety
  - Ophthalmic: Cataract, glaucoma

Drug interactions:
- May have increased risk of infection if used in conjunction with other immunosuppressants

Pregnancy category: C
Lactation: No data from controlled trials
Relative cost: $$$$

## IMMUNOMODULATORY THERAPIES

For suggested use, see algorithms at end of the chapter.

### *6-Mercaptopurine*

Brand name: Purinethol (6-Mercaptopurine)
Manufacturer: Gate Pharmaceuticals

Dosages:
- Crohn's disease: For induction or maintenance of remission. 75–125 mg po qd. Start 50 mg po qd, maximum dose of 1.5 mg/kg po qd.
- Ulcerative colitis (UC):6-Mercaptopurine: For induction or maintenance of remission. 75–125 mg po qd. Start 50 mg po qd, maximum dose of 1.5 mg/kg po qd.

Contraindications/cautions:
- Hypersensitivity to azathioprine
- Caution with impaired renal function
- Pregnancy

Adverse effects:
- Gastrointestinal: Nausea, vomiting, GI ulceration, pancreatitis, hepatotoxicity
- Renal: Nephrolithiasis, urate nephropathy

- Hematologic: Myelosuppression, anemia
- Immune: Immunosuppression

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection

Pregnancy category: D
Lactation: Safety unknown
Relative cost: $$$ (generic available: $$)

## *Azathioprine*

Brand names: Azasan, Imuran (Azathioprine)
Manufacturer: Generic

Dosage:
- Ulcerative colitis: 100–250 mg daily, start with 50 mg daily, maximum dose of 2.5 mg/kg po qd.
- Crohn's disease: 100–250 mg daily, start with 50 mg daily, maximum dose of 2.5 mg/kg po qd.

Contraindications/cautions:
- Hypersensitivity to drug/class/component
- Pregnancy
- Caution if impaired renal function

Adverse effects:
- Gastrointestinal: GI hypersensitivity reaction, nausea, vomiting, pancreatitis, hepatotoxicity, hepatic veno-occlusive disease
- Hematologic: Leukopenia, megaloblastic anemia, thrombocytopenia, bone marrow suppression
- Immune: Chronic immunosuppression
- Other: Lymphoma, malignancy, infection

Drug interactions:
- Increased risk of serious infection with leflunomide and TNF blockers
- Increased risk of myelosuppression with ACE inhibitors, clozapine, sulfasalazine, interferon alfa, balsalazide, mycophenolate mofetil, and a number of anticancer drugs

Pregnancy category: D
Lactation: Possibly unsafe
Relative cost: $$$ (generic available: $$)

## *Methotrexate*

Brand name: Rheumatrex, Trexall
Manufacturer: Dava pharmaceuticals, Teva pharmaceuticals, generic

Dosage:
- Crohn's disease (moderate to severe): 25 mg/week injected IM for induction and maintenance of remission in refractory Crohn's disease

Contraindications/cautions:
- Hypersensitivity to methotrexate
- Contraindicated in pregnancy
- Chronic liver disease
- Active infection

Adverse effects:
- Gastrointestinal: Gingivitis, stomatitis, pharyngitis, nausea, abdominal pain, vomiting, enteritis, pancreatitis, diarrhea
- Hepatobiliary: Hepatotoxicity, acute hepatitis, hepatic failure, chronic fibrosis, and cirrhosis
- Neurologic: Headache, drowsiness, blurred vision, malaise, dizziness
- Cardiovascular: Pericarditis, pericardial effusion, thromboembolic events
- Pulmonary: Pulmonary fibrosis, alveolitis, interstitial pneumonitis,
- Hematologic: Pancytopenia, leucopenia, anemia, thrombocytopenia, lymphoproliferative disorders
- Dermatologic: Rash, pruritus, urticaria
- Renal: Nephropathy, renal failure, azotemia, hematuria, proteinuria
- Infectious: Opportunistic infections
- Other: Lymphoma, malignancy, hypersensitivity reactions

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection.

Pregnancy category: X
Lactation: Not recommended
Relative cost: $$$$ (generic available: $$$)

## *Cyclosporine*

Brand name: Cyclosporine, Sandimmune
Manufacturer: Novartis Pharmaceuticals

Dosages:
- Ulcerative colitis (severe): 2–4 mg/kg IV qd, 5–10 mg/kg po qd.

Contraindications/cautions:
- Hypersensitivity to cyclosporine
- Caution with impaired liver or renal function

Adverse effects:
- Gastrointestinal: Gingival hyperplasia, diarrhea, nausea and vomiting, hepatotoxicity, pancreatitis, GI bleed
- Neurologic: Neurotoxicity, intracranial hypertension, headache, tremor, encephalopathy, seizure
- Cardiovascular: Hypertension, myocardial infarction
- Renal: Reversible or irreversible renal insufficiency, hyperkalemia
- Hematological: Leukopenia, thrombocytopenia, hemolytic anemia
- Endocrine: Diabetes mellitus, hirsutism, dyslipidemia, hyperuricemia
- Immune: Allergic reactions, anaphylaxis
- Other: Infections, malignancy, optic disc edema, pruritus

Drug interactions:
- Bosentan: Increased bosentan levels and risk of toxicity and also decreased cyclosporine levels and efficacy

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$$ (Generic available: $-$$$)
For algorithms for the treatment of mild to moderate ulcerative colitis, see Fig. 5.1, and severe ulcerative colitis, see Fig. 5.2.

## BIOLOGICAL THERAPIES

For suggested use, see algorithms at end of the chapter.

### *Infliximab*

Brand name: Remicade
Manufacturer: Centocor, Inc

Dosage:
- Crohn's disease, fistulizing and moderate to severe: 5 mg/kg IV over 2 h at week 0, 2, and 6 and then q8 weeks.
- Ulcerative colitis, treatment-refractory: 5 mg/kg IV over 2 h at week 0, 2, and 6 and then q8 weeks.

Contraindications/cautions:
- Hypersensitivity to infliximab
- Active infection

- Congestive heart failure; NYHA Class III, IV
- Caution if latent tuberculosis, hepatitis B carrier, chronic infection
- Caution if CNS demyelinating disorder, seizure disorder, vasculitis, or immunosuppression

Adverse effects:
- Gastrointestinal: Abdominal pain, nausea, vomiting, hepatotoxicity (rare)
- Cardiovascular: Worsening of congestive heart failure, acute coronary syndrome
- Hematologic: Leukopenia, neutropenia, pancytopenia, thrombocytopenia, hepatosplenic T cell lymphoma
- Immunologic: Complication of infusion, drug induced lupus erythematosus, delayed hypersensitivity reaction
- Infectious: Opportunistic infection, upper respiratory tract and other infections, disseminated tuberculosis, hepatitis B reactivation

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection.
- Abatacept, anakinra: May increase risk of serious infection

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$$$$

## *Adalimumab*

Brand name: Humira
Manufacturer: Abbott Laboratories

Dosage:
- Crohn's disease (moderate to severe): 160 mg sc at week 0 (may administer as 4 injections in 1 day or 2 injections daily for 2 consecutive days), 80 mg sc at week 2, then 40 mg sc every other week starting at week 4.

Contraindications/cautions:
- Hypersensitivity to adalimumab
- Active infection

Adverse effects:
- Gastrointestinal: Nausea, abdominal pain, elevated liver enzymes
- Neurologic: Headache, demyelinating disease exacerbation
- Cardiovascular: Hypertension, congestive heart failure exacerbation
- Hematologic: Pancytopenia, aplastic anemia
- Immunologic: Anaphylaxis, angioneurotic edema, lupus-like syndrome, flare of rheumatoid arthritis

- Dermatologic: Injection site reaction, erythema multiforme, rash
- Infectious: Tuberculosis reactivation, sepsis, opportunistic infections
- Other: Lymphoma, malignancy

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection.
- Abatacept, anakinra: May increase risk of serious infection.

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$$$$

## *Certolizumab Pegol*

Brand name: Cimzia
Manufacturer: UCB, Inc.

Dosage:
- Crohn's disease (moderate to severe): 400 mg sc at week 0, week 2, and week 4 to induce remission. Maintenance dose is 400 mg sc every 4 weeks.

Contraindications/cautions:
- Hypersensitivity to certolizumab
- Active infection

Adverse effects:
- Gastrointestinal: Nausea, abdominal pain, elevated liver enzymes, diarrhea
- Neurologic: Headache, demyelinating disease exacerbation
- Cardiovascular: Hypertension, congestive heart failure exacerbation
- Hematologic: Pancytopenia, aplastic anemia
- Immunologic: Hepatitis B reactivation, anaphylaxis, lupus-like syndrome
- Dermatologic: Injection site reaction, erythema multiforme, rash
- Infectious: Tuberculosis reactivation, sepsis, opportunistic infections (invasive fungal infections)
- Other: Lymphoma, malignancy, hypersensitivity reactions

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection.
- Abatacept, anakinra: May increase risk of serious infection.

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$$$$

## *Natalizumab*

Brand name: Tysabri
Manufacturer: Biogen Idec, Elan Pharmaceuticals, Inc.
Mechanism of action: Alpha-4 integrin inhibitor

Dosage:
- Crohn's disease (moderate to severe): Available only through a restricted prescribing program for inducing and maintaining clinical response in remission in adults with moderate to severe Crohn's disease who have had inadequate response to other therapies. 300 mg infused over 1 h q4 weeks.

Contraindications/cautions:
- Hypersensitivity to natalizumab
- Contraindicated in patients taking other immunosuppressants or TNF inhibitors
- Current or history of PML
- Active infection

Adverse effects:
- CNS: Headache, fatigue, depression
- Dermatologic: Rash
- Gastrointestinal: Nausea, gastroenteritis, abdominal discomfort, hepatotoxicity
- Genitourinary: UTIs
- Neuromuscular: Arthralgias, extremity pain, back pain
- Respiratory: URIs, LRIs
- Hypersensitivity/infusion-related reactions
- Infections: Use may be associated with increased risk of infections, opportunistic infections, and serious herpes infections
- Progressive multifocal leukoencephalopathy (PML)

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection.
- Echinacea may diminish the therapeutic effect of immunosuppressants
- Immunosuppressants may enhance toxicity and risk of concurrent infection

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$$$$

## *Vedolizumab*

Brand name: Entyvio
Manufacturer: Takeda Pharmaceuticals USA, Inc.

Mechanism of Action: Alpha-4 integrin inhibitor (unlike natalizumab, however, vedolizumab it does not cross blood brain barrier)

Dosage:
- Crohn's or ulcerative colitis (moderate to severe): IV: 300 mg at 0, 2, and 6 weeks and then every 8 weeks thereafter. Discontinue therapy in patients who show no evidence of therapeutic benefit by week 14.

Contraindications/cautions:
- Hypersensitivity to vedolizumab
- Contraindicated in patients taking other immunosuppressants or TNF inhibitors
- Current or history of PML
- Active infection
- Liver injury

Adverse effects:
- CNS: Headache
- Immunologic: Antibody development
- Neuromuscular: Arthralgia
- Respiratory: Nasopharyngitis
- Hypersensitivity/infusion-related reactions
- Infections: Use may be associated with increased risk of infections, opportunistic infections, and serious herpes infections

Drug interactions:
- Live vaccines: Inadequate immunological vaccine response and increased risk of disseminated infection.
- Echinacea may diminish the therapeutic effect of immunosuppressants
- Immunosuppressants may enhance toxicity and risk of concurrent infection

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$$$$
For an algorithm for the treatment of mild to moderate Crohn's Disease, see Fig. 5.3. A diagram of 6-MP metabolism is shown in Fig. 5.4.

## *Suggested Monitoring for IBD drugs*

- 5-ASA agents: BUN/Cr (for sulfasalazine supplement with folic acid 1 g/day).
- AZA, 6-MP: Liver enzymes, CBC
- Anti-TNFα
  - Initial: PPD/quantiferon, hepatitis B serologies, +/− chest X-ray
  - Annual PPD/quantiferon in high-risk populations

- Alpha-4 integrin inhibitors:
  - Initial: Anti-JC virus antibodies
  - Every 6–12 months, repeat anti-JC virus antibodies (consider with vedolizumab)
  - Monitor for signs of PML (new onset or worsening of neurological signs and symptoms—progressive weakness or clumsiness, disturbance of vision, confusion or changes in personality)

An algorithm for determining anti-TNFα resistance and therapeutic drug monitoring is shown in Fig. 5.5.

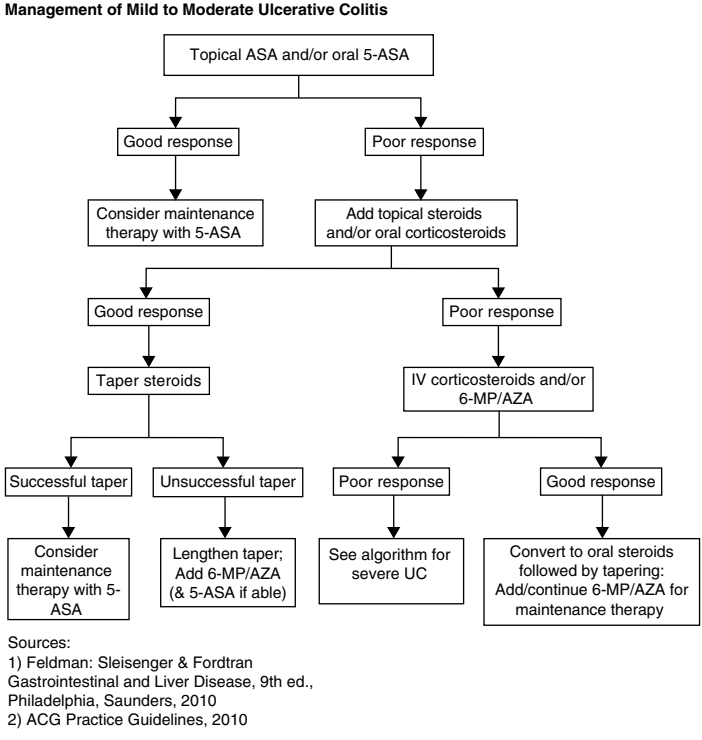


Fig. 5.1 An algorithm for the treatment of mild to moderate ulcerative colitis

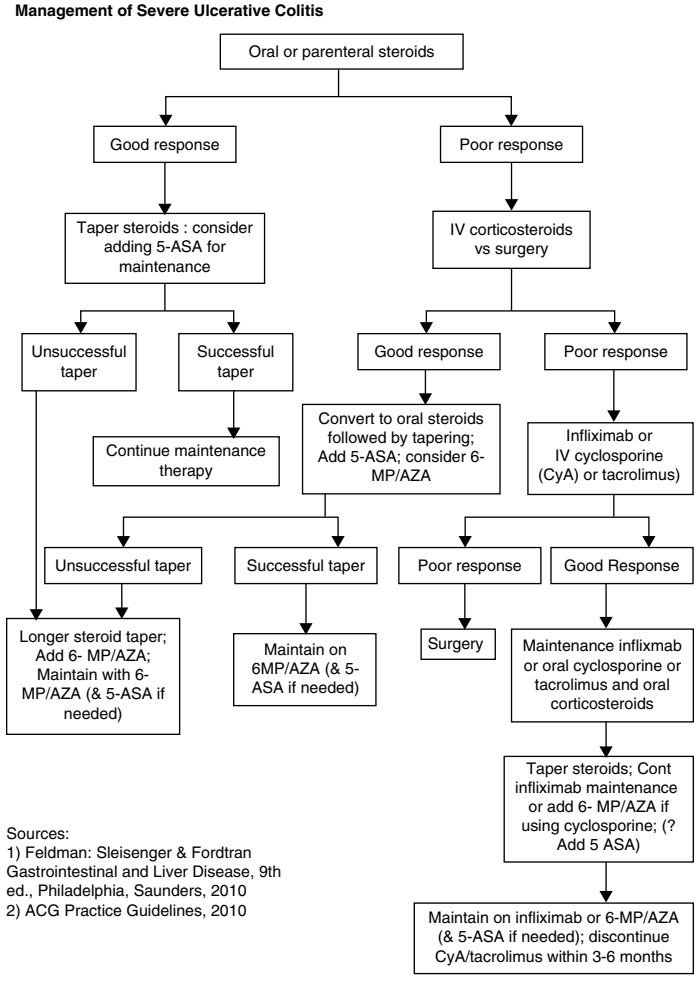


Fig. 5.2 An algorithm for the treatment of severe ulcerative colitis

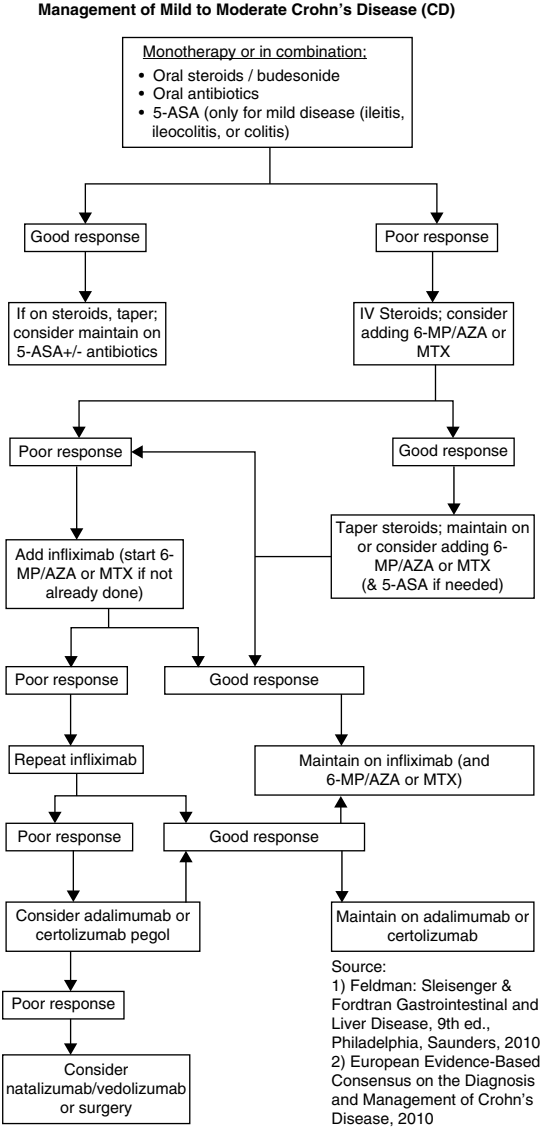


Fig. 5.3 An algorithm for the treatment of mild to moderate Crohn's disease

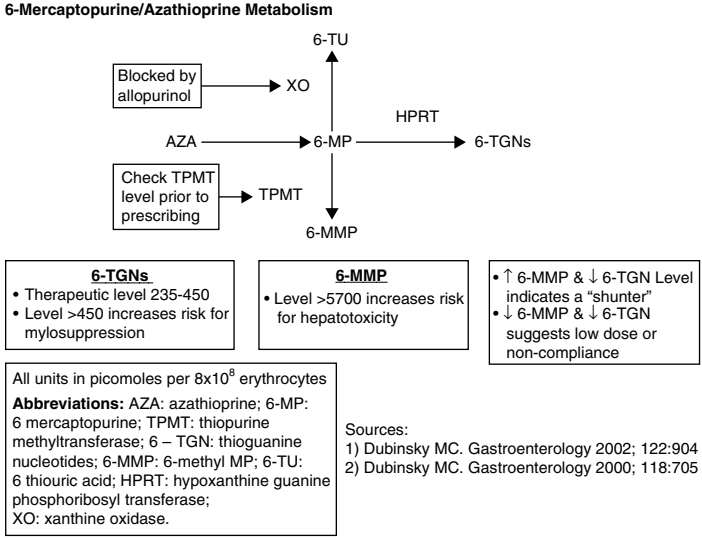


Fig. 5.4 A diagram of 6-MP metabolism

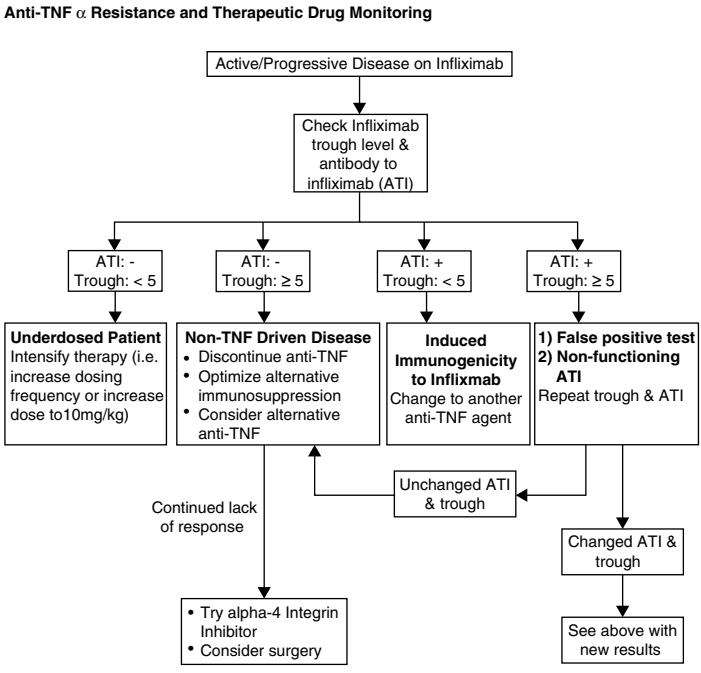


Fig. 5.5 An algorithm for determining anti-TNFα resistance and therapeutic drug monitoring

## REFERENCES

1. Van Assche G, Dignass A, Panes J, Beaugerie L, Karagiannis J, Allez M, Ochsenkühn T, Orchard T, Rogler G, Louis E, Kupcinskas L, Mantzaris G, Travis S, Stange E. The second European evidence-based consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. J Crohn's Colitis. 2010;4(1):7–27.
2. Dubinsky MC, Lamothe S, Yang HY, et al. Pharmacogenomics and metabolite measurement for 6-mercaptopurine therapy in inflammatory bowel disease. Gastroenterology. 2000;118:705–13.
3. Dubinsky MC, Yang H, Hassard PV, Seidman EG, Kam LY, Abreu MT, et al. 6-MP metabolite profiles provide a biochemical explanation for 6-MP resistance in patients with IBD. Gastroenterology. 2002;122:904–15.

4. Feldman ML, Sleisenger MH, Fordtran JS, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease: pathophysiology, diagnosis, management. Philadelphia: Saunders/Elsevier; 2010.
5. Hendy P, Hart A, Irving P. Anti-TNFdrug and antidrug antibody level monitoring in IBD: a practical guide. Frontline Gastroenterol. 2014. doi:10.1136/flgastro-2014-100527.
6. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol. 2010;105:501–23.
7. Steenholdt C, Brynskov J, Thomsen OO, Munck LK, et al. Individualised therapy is more cost-effective than dose intensification in patients with Crohn's disease who lose response to anti-TNF treatment: a randomised, controlled trial. Gut. 2014;63:919–27.
8. UpToDate® 2015
9. Vaughn BP, Martinez-Vazquez M, Patwardhan VR, et al. Proactive therapeutic concentration monitoring of infliximab may improve outcomes for patients with inflammatory bowel disease: results from a pilot observational study. Inflamm Bowel Dis. 2014;20:1996–2003.

# 6 General GI Infections

*Houman Rezaizadeh and Erik Olson*

***Contents***



For suggested use of antibiotics below, see specific tables and algorithms at the end of this chapter on uncomplicated diverticulitis, *Clostridium difficile*, and spontaneous bacterial peritonitis.

## CEFOTAXIME

Brand name: Claforan
Manufacturer: Sanofi-Aventis

Dosages:
- Diverticulitis: 1–2 g IV q 6 h, maximum 12 g/day, duration varies

Contraindications/cautions:
- Hypersensitivity to drug/class or component of drug
- Caution if impaired renal function or with nephrotoxic agent use
- Caution if seizure disorder
- Caution if hypersensitivity to penicillin

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_6,

Adverse effects:
- Gastrointestinal: Nausea, diarrhea, elevated LFTs.
- Neurological: Seizures, headache
- Renal: Interstitial nephritis, elevated BUN/creatinine
- Hematological: Neutropenia, hemolytic anemia, thrombocytopenia, agranulocytosis, eosinophilia
- Dermatological: Stevens–Johnson syndrome, erythema multiforme, toxic epidermal necrolysis
- General: Fever, pruritus, headache

Drug interactions:
- Inadequate typhoid vaccine (live oral) response if given within 3 days before or after antibiotic course
- May decrease efficacy of oral contraceptives
- Increased nephrotoxicity with aminoglycosides

Pregnancy category: B
Lactation: Probably safe
Relative cost: $$ (generic available: $–$$)

## CEFTRIAXONE

Brand name: Rocephin
Manufacturer: Roche Laboratories

Dosages:
- Diverticulitis: 1–2 g IV q24 h, max 4 g q24 h, duration varies

Contraindications/cautions:
- Hypersensitivity to drug/class or component of drug
- Parenteral calcium containing product use, concurrent or <48 h after last dose
- Caution if hypersensitivity to penicillin
- Caution if impaired liver and renal function or vitamin K deficiency

Adverse effects:
- Gastrointestinal: Pseudomembranous colitis, biliary sludge, jaundice
- Respiratory: Bronchospasm, allergic pneumonitis
- Hematological: Neutropenia, leucopenia, hemolytic anemia, thrombocytopenia, hypoprothrombinemia, agranulocytosis
- Immunological: Serum sickness, anaphylaxis

Drug interactions:
- IV calcium chloride/calcium gluconate may cause calcium ceftriaxone precipitates in lungs, gallbladder

- Inadequate typhoid vaccine (live oral) response if given within 3 days before or after antibiotic course
- May decrease efficacy of oral contraceptives
- Increased nephrotoxicity with aminoglycosides

Pregnancy category: B
Lactation: Probably safe
Relative cost: $$$ (generic available: $–$$)

## LEVOFLOXACIN

Brand name: Levaquin
Manufacturer: Ortho-McNeil Pharmaceutical
Dosages: 500 mg IV qd

Contraindications/cautions:
- Hypersensitivity to drug/class or component of drug
- Prolonged QT interval/hypokalemia
- Caution if proarrhythmic condition
- Caution if seizure or CNS disorder
- Caution if dehydration
- Caution if renal function impaired

Adverse effects:
- Gastrointestinal: Pseudomembranous colitis, hepatotoxicity
- Neuropsychiatric: Toxic psychosis, depression, suicidal ideation
- Cardiovascular: Prolonged QT, torsades de pointes
- Renal: Nephrotoxicity
- Immunological: Anaphylaxis, hypersensitivity
- Musculoskeletal: Tendon rupture

Drug interactions:
- Increased risk of QT prolongation with anti-arrhythmics, class Ia and class III, cisapride, phenothiazines, ziprasidone, fluconazole, haloperidol, erythromycin, tacrolimus, tricyclic antidepressants

Pregnancy category: C
Lactation: Probably safe
Relative cost: $$$ (generic available: $–$$)

## NORFLOXACIN

Brand name: Noroxin
Manufacturer: Merck & Co. Inc.

Dosage:
- SBP prophylaxis: 400 mg qd or bid

Contraindications/cautions:
- Hypersensitivity to drug/class or component of drug
- Pregnancy
- Breastfeeding
- Safety not established for patients <18-year-old
- Prolonged QT interval

Adverse reactions:
- Gastrointestinal: Pseudomembranous colitis, nausea, vomiting, abdominal pain, elevated LFTs
- Neurological: Seizures
- Cardiac: QT prolongation (rare), torsades de pointes (rare)
- Musculoskeletal: Tendon rupture (rare), arthropathy (animal studies)
- Immunological: Hypersensitivity reaction, anaphylaxis
- Dermatological: Phototoxicity, skin reactions

Drug interactions:
- Increased risk of QT prolongation with anti-arrhythmics, class Ia and class III, cisapride, phenothiazines, ziprasidone, fluconazole, haloperidol, erythromycin, tacrolimus, tricyclic antidepressants

Pregnancy: C
Lactation: Probably safe
Relative cost: $$$

## CIPROFLOXACIN

Manufacturer: Generic
Brand Names: Cipro, Cipro XR

Dosages:
- Infections: 250–500 mg po bid or 200–400 mg IV q12 h
- SBP prophylaxis: 250–500 mg po q12 h or 200–400 mg IV q12 h

Contraindications/cautions:
- Hypersensitivity to drug/class or component of drug
- Use with caution if QT prolongation
- Use with caution if seizure disorder is present

Adverse reactions:
- Gastrointestinal: Nausea, vomiting, diarrhea, abdominal pain, pseudomembranous colitis, hepatotoxicity

- Neurological: Seizures, increased intracranial pressure
- Cardiac: QT prolongation
- Renal: Nephrotoxicity (rare), crystalluria (rare)
- Hematological: Myelosuppression (rare), blood dyscrasias (rare)
- Musculoskeletal: Tendon rupture (rare), arthropathy (animal studies)
- Immunological: Anaphylaxis, anaphylactic shock, vasculitis, serum sickness
- Dermatological: Photosensitivity, skin reactions, phototoxicity, psychosis, peripheral neuropathy

Drug interactions:
- Increased risk of QT prolongation with anti-arrhythmics, class Ia and class III, cisapride, phenothiazines, ziprasidone, fluconazole, haloperidol, erythromycin, tacrolimus, tricyclic antidepressants

Pregnancy: C
Lactation: Probably safe
Relative cost: $$$ (generic available: $–$$)

## SULFAMETHOXAZOLE AND TRIMETHOPRIM

Brand name: Bactrim
Manufacturer: AR Scientific, Inc.
Other brand names: Bethaprim, Cotrim, Cotrim DS, Septra, Septra DS, Sulfatrim, Uroplus, Uroplus DS

Dosage:
- SBP prophylaxis: 160/800 (DS tab*) po qd.

Contraindications/cautions:
- Hypersensitivity to drug/class or component of drug
- Megaloblastic anemia
- Folate deficiency
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Near-term pregnancy
- Breastfeeding

Adverse reactions:
- Gastrointestinal: Nausea, vomiting, hepatic necrosis, pseudomembranous colitis
- Pulmonary: Pulmonary infiltrates
- Renal: Interstitial nephritis, nephrotoxicity, hyperkalemia
- Hematologic: Agranulocytosis, aplastic anemia, blood dyscrasias, methemoglobinemia, myelosuppression

- Immunological: Hypersensitivity reaction
- Dermatologic: Rash, urticaria, photosensitivity, Stevens–Johnson syndrome, toxic epidermal necrolysis

Drug interactions:
- Methenamine: May produce insoluble precipitate in urine
- Topical benzocaine, butamben, tetracaine, lidocaine, prilocaine: Increases risk of methemoglobinemia

Pregnancy: C
Lactation: Safety conditional
Relative cost: $ (generic available: $–$$)
For an algorithm for the treatment of diverticulitis and cholangitis, see Figs. 6.1 and 6.2, respectively

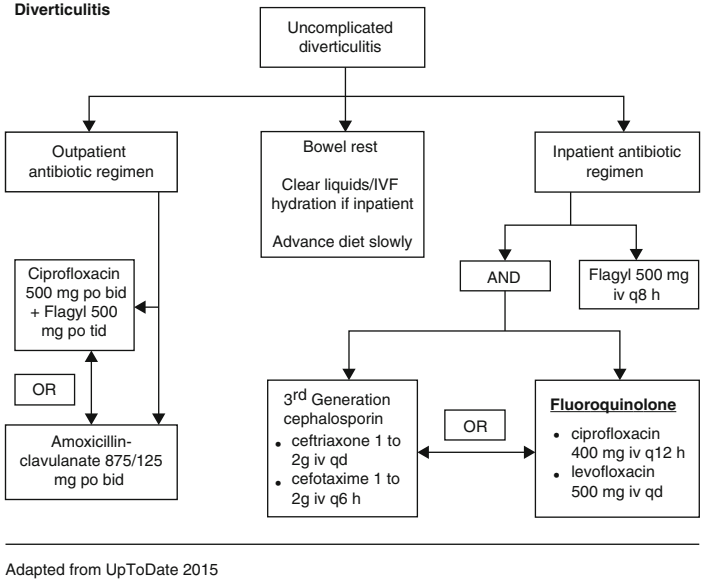


Fig. 6.1 An algorithm for the treatment of diverticulitis. Adapted from UpToDate 2015

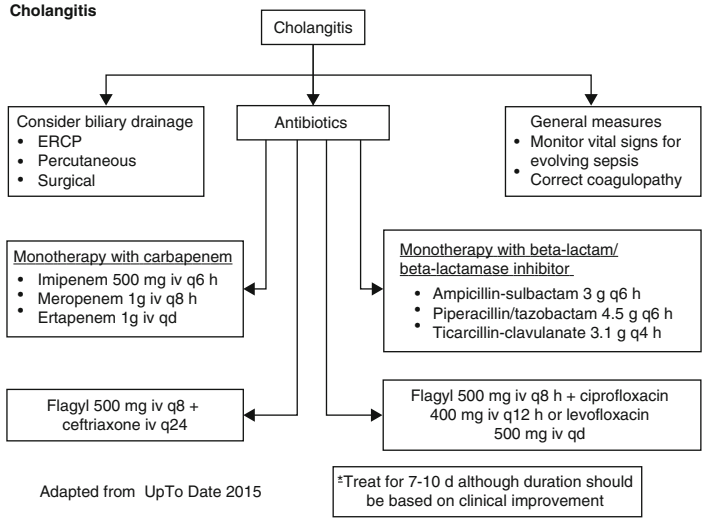


Fig. 6.2 An algorithm for the treatment of cholangitis. Adapted from UpToDate 2015

## SPONTANEOUS BACTERIAL PERITONITIS (SBP)

Indications of prophylactic antibiotics for prevention of SBP in cirrhosis with ascites:

– Patients with low protein ascites (<1 g/dl) during hospitalization (po or IV)
– Previous spontaneous bacterial peritonitis
– Active variceal hemorrhage (po or IV)

For the treatment of spontaneous bacterial peritonitis (SBP), see an algorithm, Fig. 6.3, and laboratory criteria for making a diagnosis of SBP in Table 6.1.

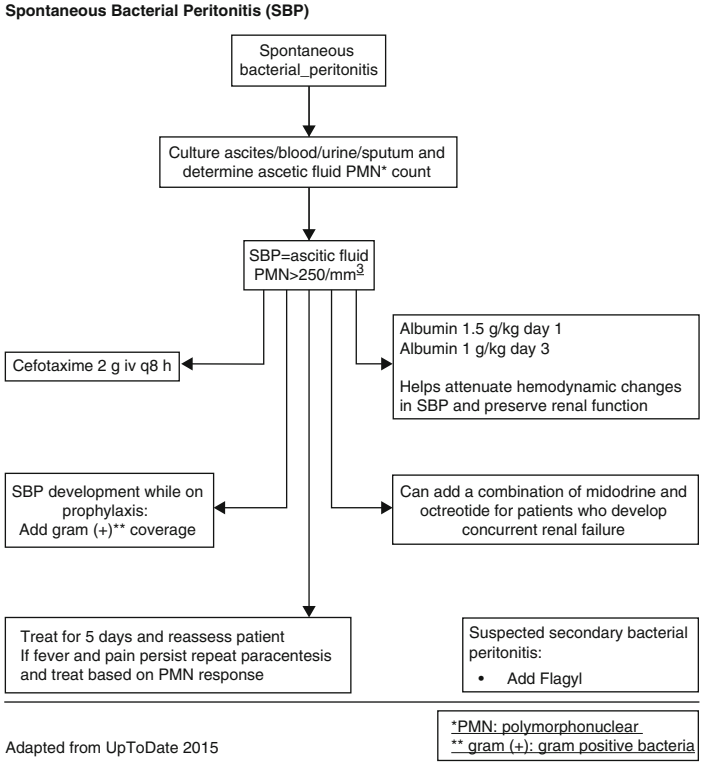


Fig. 6.3 An algorithm for the treatment of spontaneous bacterial peritonitis. Adapted from UpToDate 2015

**Table 6.1 Spontaneous bacterial peritonitis (SBP). Adapted from AASLD guidelines 2012**

| *Ascitic fluid* | *Prior B-lactam Exposure or nosocomial setting* | *Prior FQ exposure, vomiting, shock, Grade 2 HE, Creatinine >3* | *High suspicion of infection/No ascitic fluid Cx result* | *Antibiotic choice(s)* |
|---|---|---|---|---|
| >250 PMN's | No | No | N/A | IV 3rd Generation Cephalosporin Cefotaxamine 2G Q8 h |
| >250 PMN's | Yes | No | N/A | Anbx Therapy Base on Local bacterial susceptibility in patients with cirrhosis (i.e. Zoysn, Cefepime) |
| >250 PMN's | No | Yes | N/A | Oral Ofloxacin 400 mg BID |
| <250 PMN's | No | No | Yes | Empiric IV Cefotaxamine 2G Q8 h |

## REFERENCES

1. Runyon B, Management of adult patients with ascites due to cirrhosis: Update 2012. AASLD. 2012. http://www.aasld.org/sites/default/files/guideline_documents/adultascitesenhanced.pdf. Accessed 30 Dec 2015.
2. Neil S, Smalley W, Hirano I. American gastroenterological association institute guideline on the management of acute diverticulitis. Gastroenterology. 2015; 149(7):1944–949.
3. UptoDate 2015

# 7 Specific GI Microbial Infections

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***Contents***



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## BACTERIAL INFECTIONS

### *Clostridium difficile*

For suggested use of antibiotics in the treatment of *Clostridium difficile*, see the treatment algorithm at the end of this chapter.

## METRONIDAZOLE

Brand name: Flagyl
Manufacturer: Searle

Dosages:
- First line in pseudomembranous enterocolitis: 500–750 mg po tid or 250–500 mg po qid for 7–14 days. Intravenous metronidazole has been used to treat patients with pseudomembranous colitis who are unable to take the medication orally
- General infections: 500–750 g po q6–8 h for 7–14 days
- Amebic liver abscess: 500–750 mg tid for 5–10 days
- Intestinal amebiasis: 750 mg tid for 5–10 days
- Giardiasis: 250 mg tid for 5–7 days or 2 g po qd for 3 days

Contraindications/cautions:
- Hypersensitivity to metronidazole, nitroimidazole derivatives, or any component of the formulation
- Pregnancy (1st trimester—found to be carcinogenic in rats)
- Caution if blood dyscrasia, liver dysfunction, CNS disorder

Adverse Effects:
- Gastrointestinal: Abdominal discomfort, loss of appetite, metallic taste, nausea and vomiting
- Neurologic: Ataxia, dizziness, headache, peripheral neuropathy, seizure
- Reproductive: Candida infection of genital region, symptomatic cervicitis/vaginitis, vaginal discharge
- Hematologic: Leukopenia, thrombocytopenia
- Immunologic: Jarisch–Herxheimer reaction
- Other: Disulfiram-like reaction with alcohol, ototoxicity

Drug Interactions:
- Disulfiram-like reaction with ritonavir, tipranavir, diazoxide
- Increases levels and toxicity of tacrolimus, cyclosporine, lithium, and phenytoin

Pregnancy category: B
Lactation: Not recommended
Relative cost: $ (generic available: $)

## VANCOMYCIN

Brand name: Vancocin
Manufacturer: ViroPharma

Dosage:
- Pseudomembranous enterocolitis: 500 mg to 2 g po qd divided every 6–8 h for 7–10 days. IV form is ineffective.

Contraindications/cautions:
- Hypersensitivity to vancomycin products.
- Caution if impaired renal function.
- Use with caution if hearing loss occurs.

Adverse Effects:
- Gastrointestinal: Nausea and vomiting
- Cardiovascular: Hypotension accompanied by flushing
- Renal: Nephrotoxicity (rare)
- Hematologic: Neutropenia (rare)
- Immunologic: Anaphylaxis (rare)
- Dermatologic: Erythematous rash on face and upper body (red neck or red man syndrome—infusion rate related)
- Otic: Ototoxicity (rare)

Drug Interactions:
- Increased nephrotoxicity with tenofovir, cidofovir, acyclovir, cyclosporine, ganciclovir

Pregnancy category: B
Lactation: Probably safe
Relative cost: $$$$ (generic available: $-$$$)

## CHOLESTYRAMINE

Brand name: Prevalite, Questran, Questran Light
Manufacturer: Generic

Dosage:
- Bile acid sequestrant. May be used to bind the *C. difficile t*oxins for excretion into the feces. 2–4 g po bid-qid to maximum of 16 g/day

Contraindications/cautions:
- Complete biliary obstruction
- Hypersensitivity to bile-sequestering resins

Adverse Effects:
- Gastrointestinal: Abdominal discomfort, constipation, flatulence, nausea and vomiting, fecal impaction
- Hematologic: Clotting and bleeding disorders due to hypoprothrombinemia

Drug Interactions:
- May decrease efficacy of amiodarone, thyroid hormones, leflunomide, and raloxifene

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $ (generic available: $)

## COLESTIPOL

Brand name: Colestid
Manufacturer: Pharmacia Corp.

Dosage:
- Bile acid sequestrant. May be used to bind the *C. difficile* toxins for excretion into the feces. 2–16 g/day given once or in divided doses orally.

Contraindications/cautions:
- Hypersensitivity to colestipol or any other component.
- Use with caution if constipation occurs.

Adverse Effects:
- Gastrointestinal: Constipation, abdominal discomfort, flatulence, indigestion, diarrhea, nausea, vomiting, bleeding hemorrhoids, difficulty swallowing, abnormal liver enzymes

Drug Interactions:
- May decrease efficacy of amiodarone, thyroid hormones, leflunomide, and raloxifene

Pregnancy category: N/A
Lactation: Safety unknown
Relative cost: $$$ (generic available: $$-$$$)

## FIDAXOMICIN

Brand name: Dificid
Manufacturer: Optimer Pharmaceuticals/Biocon

Dosages:
- 200 mg bid for 10 days

Contraindications/cautions:
- Hypersensitivity to fidaxomicin or any component of the formulation

Adverse Effects:
- Gastrointestinal: Nausea, GI hemorrhage, abdominal pain, vomiting

Drug Interactions:
- No known drug interactions

Pregnancy category: B
Lactation: Excretion in breast milk unknown
Relative cost: $$$$$
For recommendations on the antibiotic treatment of *C. difficile* colitis based on severity, see Table 7.1.

## *Helicobacter pylori*

For suggested use of the antibiotics in the treatment of *H. pylori*, see the algorithm on *H. pylori* treatment regimens at the end of this chapter.

**Table 7.1 *Clostridium difficile* treatment**

| *Clinical definition* | *Supportive data* | *Treatment* |
|---|---|---|
| Initial episode, mild or moderate | WBC > 15,000 cell/ul or lower creatinine < 11.5× | Metronidazole 500 mg TID po duration: 10–14 days |
| Initial episode, severe | WBC > 15,000 cell/ul or higher creatinine > 11.5× premorbid level | Vancomycin 125 mg QID po duration: 10–14 days |
| Initial episode, severe, complicated | Shock, ileus, or megacolon | Vancomycin 500 mg QID po or NG + metronidazole 500 mg Q8 h IV +/− rectal instillation vancomycin |
| First recurrence | ***** | Same as for initial episode |
| Second recurrence | ***** | Vancomycin tapered and/or pulsed regimen<br>Alt: Fidaxomicin 200 mg po BID × 10 days or fecal transplant |
| Subsequent relapse | ***** | Fidaxomicin 200 mg po BID × 10 days (if not used in prior regimens)<br>Fecal microbiota transplant |

Adapted from: http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/cdiff2010a.pdf
UptoDate 2015

## AMOXICILLIN

Brand names: Amoxicot, Amoxil, Amoxil Pediatric Drops, Biomox, Dispermox, Trimox, Wymox
Manufacturer: Generic; Amoxil—GlaxoSmithKline; Dispermox—Ranbaxy; Trimox—Apothecon Inc.

Dosage: For *H. pylori* eradication—1 g po bid in combination with PPI and other antibiotics.

Contraindications/cautions
- Hypersensitivity to amoxicillin
- Infectious mononucleosis: Risk of developing skin rash
- Caution in phenylketourics
- Hypersensitivity to cephalosporins: Risk of cross-reactivity

Adverse Effects:
- Gastrointestinal: Diarrhea, nausea, vomiting
- Immunologic: Immune hypersensitivity reaction
- Dermatologic: Rash

Drug Interactions:
- Typhoid vaccine, live oral: Antibiotic may inactivate vaccine.

Pregnancy category: B
Lactation: Safe
Relative cost: $ (generic available: $)

## CLARITHROMYCIN

Brand names: Biaxin, Biaxin Filmtab, Biazin XL
Manufacturer: Generic; Biaxin-Abbott Laboratories

Dosage:
- *H. pylori* eradication—500 mg po bid in combination with PPI and other antibiotics

Contraindications/cautions
- Concomitant cisapride, pimozide, astemizole, terfenadine, ergotamine, or dihydroergotamine
- Hypersensitivity to clarithromycin, erythromycin, or any macrolide antibiotics
- Dose adjustment required in renal failure patients

Adverse Effects:
- Gastrointestinal: Abdominal discomfort, abdominal pain, diarrhea, disorder of taste, indigestion, nausea, liver failure

- Neurologic: Headache
- Immunologic: Immune hypersensitivity reaction (severe), anaphylaxis, Stevens–Johnson syndrome, toxic epidermal necrolysis

Drug Interactions:
- Phenothiazines, cisapride, dofetilide, pimozide, ranolazine: Increased risk of QT prolongation and cardiac arrhythmias.
- Ergot alkaloids: Increased risk of ergot toxicity, severe vasospasm, and ischemia.
- Eplerenone: Risk of hyperkalemia.

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$ (generic available: $)

## METRONIDAZOLE

Refer to Sect. 7 under Bacterial Infections.

## LEVOFLOXACIN

Brand name: Levaquin
Manufacturer: Ortho-McNeil-Janssen Pharmaceuticals
Pharmacology: Inhibits DNA gyrase promoting breakage of DNA strands

Dosage: *H. pylori* eradication: See table 7.2

Contraindications/Cautions:
- Hypersensitivity to FQs
- Prior cardiac history or underlying QTc prolongation
- In the elderly concern for toxic psychosis and tendon rupture
- Caution in people with G6PD deficiency and risk of hemolytic reactions
- In patients with myasthenia gravis may increase muscle weakness

Adverse Effects:
- GI: Nausea, diarrhea, constipation, abdominal pain, dyspepsia, vomiting
- GU: Vaginitis
- CV: Chest pain, edema
- CNS: Headache, insomnia, dizziness
- Derm: Skin rash, pruritus

Drug Interactions:
- Concomitant administration with other QTc prolonging agents
- Antacids may decrease absorption

Pregnancy Category: C
Lactation: Small amounts excreted in breast milk, consider cessation of drug or breast feeding during administration
Relative cost: $$$ (generic available: $-$$)

## TINIDAZOLE

Brand name: Tindamax
Manufacturer: Mission Pharmacal Company
Pharmacology: Causes cytotoxicity by damaging DNA and preventing further synthesis

Dosage: See table

Contraindications/Cautions:
- Hypersensitivity to nitroimidazole derivatives (including metronidazole)

Adverse Effects:
- CNS: Fatigue, malaise, dizziness
- GI: Metallic taste, nausea, anorexia, flatulence, dyspepsia, vomiting, constipation
- GU: Pelvic pain, urine abnormality
- MS: Weakness
- Respiratory: URI

Drug Interactions:
- Alcohol and disulfiram: Result in toxic effects of disulfiram

Pregnancy Category: C
Lactation: Contraindicated in nursing mothers and 3 days after cessation of treatment
Relative cost: $$$ (generic available: $$-$$$)
For recommendations on the antibiotic treatment of *H. pylori*, see Table 7.2.

## *E. COLI* (EP AND EI) GASTROENTERITIS

- Ciprofloxacin 500 mg po bid for 3–5 days.
- Bactrim 1 double strength tab po bid for 3–5 days.

**Table 7.2 *H. pylori* treatment regimens**

| *H. pylori* | *Drug* | *Duration* | *Eradication rates* | *Comments* |
|---|---|---|---|---|
| Standard | PPI BID, Clarithromycin 500 mg BID, Amoxicillin 1000 mg BID | 10–14 days | 70–85 % | Non-PCN allergy patients |
| PCN allergy | PPI BID, Clarithromycin 500 mg BID, Metronidazole 500 mg BID | 10–14 days | 70–85 % | PCN allergy |
| Quadruple therapy/ salvage therapy | Bismuth 525 mg QID, Metronidazole 250 mg QID, Tetracycline 500 mg QID, Ranitidine, or PPI SD | 10–14 days (Note:7 days for Salvage Therapy) | 75–90 % | PCN allergy, salvage therapy if failed response to Macrolide-based therapy initially |
| Sequential | PPI + Amoxicillin 1G BID × 5 days followed by PPI + Clarithromycin 500 mg BID + Tinidazole 500 mg BID × 5 days | 5 + 5 Days | >90 % | Not validated in the USA |
| FQ-based therapy | PPI SD, amoxicillin 1G BID, levofloxacin 500 mg day | 10 Days | 87 % | Not validated in the USA |

Chey, William D., and Benjamin C.Y. Wong. "American College of Gastroenterology Guideline on the Management of Helicobacter Pylori Infection." *The American Journal of Gastroenterology Am J Gastroenterology*: 1808–825. Print

## SHIGELLA COLITIS

- Ciprofloxacin: Drug of choice—500 mg po bid for 5 days
  - 1 g po once for mild disease due to Shigella species other than *S. dysenteria*e 1

- Bactrim: 1 double strength tab (160 mg trimethoprim (TMP)/800 mg sulfamethoxazole (SMX)) po bid for 5 days
- Azithromycin: 500 mg po qd for 1 day, then 250 mg po qd for 4 days

## SALMONELLA GASTROENTERITIS

1. Usually symptomatic management with fluids and electrolyte replacement
2. In severely ill immunocompromised adults and children or elderly patients:

   - Ciprofloxacin 500 mg po bid for 3–7 days,
   - Levofloxacin 500 mg po qd,
   - Trimethoprim-sulfamethoxazole 160 mg/800 mg po bid,
   - Amoxicillin 500 mg po tid, or
   - If intravenous therapy were required: A third-generation cephalosporin (ceftriaxone 1–2 g IV qd or cefotaxime 2 g IV q8 h)

## CAMPYLOBACTER GASTROENTERITIS

1. Usually symptomatic management with fluids and electrolyte replacement
2. In severely ill, elderly, pregnant, or immunocompromised patients, and those with bloody stools, high fever, extraintestinal infection, worsening or relapsing symptoms, or symptoms lasting longer than 1 week

   - Erythromycin 500 mg po bid for 5 days or
   - Ciprofloxacin 500 mg po bid

## *Vibrio cholerae*

1. Usually management with fluids and electrolyte replacement either orally or intravenously
2. As adjunct to appropriate rehydration

   - Tetracycline 500 mg po qid for 3 days,
   - Doxycycline 300 mg once,
   - Erythromycin 250 mg po qid for 3 days,
   - Azithromycin 1000 mg po once, or
   - Ciprofloxacin 1000 mg po once

## YERSINIA GASTROENTERITIS

1. Usually symptomatic management with fluids and electrolyte replacement
2. In severely ill, elderly, pregnant, or immunocompromised patients, or those having an underlying comorbid illness

- Ciprofloxacin 500 mg bid for 5 days or
- Trimethoprim-sulfamethoxazole in children (TMP 8 mg/kg/day and SMX 40 mg/kg/day in two divided doses
- If septicemia: Ceftriaxone 2 g/day combined with gentamicin 5 mg/kg/day in one to three divided doses for 3 weeks

### *Listeria monocytogenes*

Isolated gastrointestinal illness does not require antibiotic treatment.

## TRIMETHOPRIM-SULFAMETHOXAZOLE

Brand name: Bactrim
Manufacturer: Roche

Dosage:
- See above

Contraindications/cautions:
- Hypersensitivity to drug or components
- Megaloblastic anemia due to folate deficiency
- Marked hepatic damage or renal disease

Adverse Effects:
- Gastrointestinal: Nausea, vomiting, anorexia
- Dermatologic: Urticaria

Drug Interactions:
- Inhibits CYP2C8 and CYP2C9. Avoid concomitant use with BCG, dofetilide, methenamine, procaine

Pregnancy: C
Lactation: Contraindicated
Relative cost: $ (generic available: $)

## CIPROFLOXACIN

Brand name: Cipro
Manufacturer: Bayer Pharmaceuticals

Dosage:
- See above

Contraindications/cautions:
- Hypersensitivity to drug or components
- Associated with tendonitis and tendon rupture
- May exacerbate muscle weakness in patient with myasthenia gravis

Adverse Effects:
- Gastrointestinal: Nausea, diarrhea, vomiting, aminotransferase elevations
- Dermatologic: Rash
- Renal: May increase creatinine

Drug Interactions:
- Inhibits CYP1A2. Avoid use with warfarin, imipramine, ondansetron, cisapride.

Pregnancy: C
Lactation: Contraindicated
Relative cost: $$ (generic available: $)
For recommendations on the antibiotic treatment of Whipple's Disease, see Table 7.3.

**Table 7.3 Overview of antibiotics used to treat Whipple's disease**

| *Drug* | *Dosage* | *Comments* |
|---|---|---|
| Penicillin G + Streptomycin | 6–24 million units IV daily (in divided doses) + 1 g im qd | Induction therapy (first 10–14 days) |
| Ceftriaxone | 2 g IV once daily | Induction therapy (first 10–14 days) or salvage therapy; less widely used than penicillin G + Streptomycin |
| Trimethoprim-Sulfamethoxazole | 160 mg/800 mg po bid | Long-term therapy; first-line drug; good CNS penetration but CNS relapses may occur |
| Penicillin VK | 500 mg po qid | Alternative for long-term therapy; limited experience |
| Doxycycline (or tetracycline) | 100 mg po bid (500 mg po qid) | Clinical relapses including CNS are well described |
| Cefixime | 400 mg po bid | Alternative for long-term therapy; limited experience |
| Rifampin | 600 mg po qd | Second-line drug; good CNS penetration |
| Chloramphenicol | 500 mg po qid | Second-line drug; worrisome side effects |
| Erythromycin | 500 mg po qid | Second-line drug; limited experience |
| Pefloxacin | 400 mg po bid | Second-line drug; limited experience |

*Source*: Feldman: Sleisenger & Fordtran Gastrointestinal and Liver Disease, 8th ed., Philadelphia, Saunders, 2006

## AZITHROMYCIN

Brand name: Zithromax
Manufacturer: Pfizer, Inc.

Dosage:
- Shigella and Enterohemorrhagic *E. coli*—500 mg po qd for 1 day, then 250 mg po qd for 4 days

Contraindications/cautions:
- Hypersensitivity to drug or components
- Use with caution in impaired renal function, impaired hepatic function.
- Use with caution in QT prolongation.

Adverse Effects:
- Gastrointestinal: Cholestatic jaundice, pseudomembranous colitis, diarrhea, nausea, abdominal pain, dyspepsia
- Cardiovascular: QT prolongation
- Dermatologic: Angioedema, Stevens–Johnson syndrome, pruritus

Drug Interactions:
- Increased risk of QT prolongation with cisapride, phenothiazines, pimozide, ranolazine, antiarrhythmics class IA and class III, chloroquine, droperidol, haloperidol, erythromycin, flecainide, methadone, pentamidine, ziprasidone

Pregnancy: B
Lactation: Enters breast milk/use caution
Relative cost: $$$ (generic available: $-$$)

## ERYTHROMYCIN

Brand name: E-mycin
Manufacturer: Abbott

Dosage:
- See above

Contraindications/cautions:
- Hypersensitivity to drug or components

Adverse Effects:
- Gastrointestinal: Abdominal pain, anorexia, pancreatitis, pseudomembranous colitis, diarrhea
- Cardiovascular: QT prolongation, torsade de pointes, ventricular arrhythmia
- Otic: Hearing loss

Drug Interactions:
- Substrate of CYP2B6 and CYP3A4, P-glycoprotein, Inhibits CYP1A2, CYP3A4, P-glycoprotein

Pregnancy: B
Lactation: Enters breast milk/use caution
Relative cost: $ (generic available: $)

## DOXYCYCLINE

Brand names: Adoxa, Doryx, Doxy Lemmon, Doxy-Caps, Doxy-D, Monodox, Oracea, Periostat, Vibra-Tabs, Vibramycin, Vibramycin Calcium, Vibramycin Hyclate, Vibramycin Monohydrate
Manufacturer: generic

Dosage:
- *Vibrio cholerae*—300 mg po × 1

Contraindications/cautions:
- Hypersensitivity to drug or components
- Children less than 8 years old
- Caution in impaired liver function, impaired renal function
- Avoid sun/UV light exposure
- Caution if history of, or predisposition to, candidiasis.
- Pregnancy

Adverse Effects:
- Dermatologic: Photosensitivity, skin discoloration, rash, erythema multiforme, Stevens–Johnson syndrome
- Gastrointestinal: Hepatotoxicity, esophagititis, pseudomembranous colitis, pancreatitis, diarrhea, nausea, dyspepsia
- Hematologic: Neutropenia, thrombocytopenia, hemolytic anemia
- Other: Tooth discoloration in children less than 8 years old, headache, joint pain, pericarditis

Drug Interactions:
- Contraindicated with acitretin due to increased risk of pseudotumor cerebri and papilledema
- Increased levels and risk of digoxin, lithium toxicity if given together.
- Increased phototoxicity with hydroquinone/retinoic acid combinations

Pregnancy: D
Lactation: Unsafe
Relative cost: $ (generic available: $)

## TETRACYCLINE

Brand name: Sumycin
Manufacturer: Generic

Dosage: 1–2 g/day po divided bid-qid. Give at least 1 h before or 2 h after meals.

Contraindications/cautions:
- Hypersensitivity to drug or components
- Use with caution in impaired renal function, impaired hepatic function.
- Use with caution in systemic lupus erythematosus.
- Pregnancy

Adverse Effects:
- Gastrointestinal: Hepatotoxicity, pseudomembranous colitis, pancreatitis, diarrhea, nausea, dyspepsia, abdominal discomfort
- Hematologic: Neutropenia, thrombocytopenia, hemolytic anemia
- Dermatologic: Photosensitivity, skin discoloration, rash, erythema multiforme, Stevens–Johnson syndrome
- Other: Tooth discoloration in less than 8 years old, headache, dizziness

Drug Interactions:
- Contraindicated with acitretin due to increased risk of pseudotumor cerebri and papilledema
- Increased levels and risk of digoxin, lithium toxicity if given together.
- Increased phototoxicity with hydroquinone/retinoic acid combinations

Pregnancy: D
Lactation: Possibly unsafe
Relative cost: $ (generic available: $)

## FUNGAL INFECTIONS

### *Oropharyngeal Candidiasis*

1. HIV-negative patients:
   Topical therapy, with either clotrimazole troches (10 mg troche five times daily) or nystatin suspension (200,000–400,000 units five times daily)
2. HIV-positive patients:
   For initial episode of oropharyngeal candidiasis in HIV-infected patients with mild disease—topical therapy

   For patients with recurrent infection, moderate to severe disease, or in those with advanced immunosuppression (CD4 < 100)—fluconazole 200 mg loading dose, followed by 100 mg qd for 7–14 days after clinical improvement

### *Esophageal Candidiasis*

- Fluconazole 200 mg loading dose followed by 100 mg po qd for 14–21 days
- Voriconazole 200 mg po bid
- If IV therapy needed—caspofungin 50 mg intravenously for 7–21 days
- Clotrimazole 10 mg troche five times daily for 14 days

## FLUCONAZOLE

Brand name: Diflucan
Manufacturer: Pfizer, Inc.

Dosage:
- Esophageal candidiasis: 100 mg po/IV qd. Start 200 mg po/IV × 1. Continue for more than 3 weeks total and for more than 2 weeks after symptom resolution.

Contraindications/cautions:
- Hypersensitivity to drug or components
- Caution in impaired liver function, renal function
- Caution in QT prolongation, pro-arrhythmic conditions, electrolyte abnormalities, heart disease, elderly

Adverse Effects:
- Gastrointestinal: Hepatotoxicity, nausea, vomiting, abdominal pain, diarrhea, dyspepsia, taste changes
- Neurologic: Seizures, headache, dizziness
- Cardiac: QT prolongation, torsades de pointes
- Hematologic: Leucopenia, agranulocytosis, thrombocytopenia
- Dermatologic: Stevens–Johnson syndrome, angioedema, rash

Drug Interactions:
- Decreased levels of antifungal drug with concomitant use of barbiturates, carbamazepine, rifampin, rifabutin
- Increased risk of QT prolongation with cisapride, droperidol, phenothiazines, pimozide, quinidine, ranolazine, amiodarone

Pregnancy: C
Lactation: Probably safe
Relative cost: $$$ (generic available: $-$$$)

## VORICONAZOLE

Brand name: Vfend
Manufacturer: Pfizer, Inc.

Dosage:
- Esophageal candidiasis: 200 mg po q12 h. Treat for 14 days minimum and for 7 days after symptom resolution. Give 1 h before or after meal.

Contraindications/cautions:
- Hypersensitivity to drug or components
- Caution in impaired liver function, renal function
- Caution in proarrhythmic conditions, electrolyte abnormalities, galactose intolerance, lactase deficiency, hematologic malignancy

Adverse Effects:
- Gastrointestinal: Hepatitis, fulminant hepatic failure, nausea, vomiting, diarrhea, abdominal pain, increase in liver transaminases, increase in alkaline phosphatase
- Cardiac: QT prolongation, torsades de pointes, tachycardia
- Dermatologic: Stevens–Johnson syndrome, angioedema, rash
- Other: Color vision changes, photophobia, hallucinations, renal failure, peripheral edema.

Drug interactions:
- Decreased levels of antifungal drug with concomitant use of barbiturates, carbamazepine, rifampin, rifabutin
- Increased risk of QT prolongation with cisapride, droperidol, phenothiazines, pimozide, quinidine, ranolazine, amiodarone

Pregnancy: D
Lactation: Safety unknown
Relative cost: $$$$ (generic available: $$-$$$)

## CASPOFUNGIN

Brand name: Cancidas
Manufacturer: Merck & Co., Inc.

Dosage:
- Esophageal candidiasis: 50 mg IV q24 h for 7–21 days

Contraindications/cautions:
- Hypersensitivity to drug or components
- Caution in impaired liver function

Adverse Effects:
- Gastrointestinal: Hepatotoxicity, nausea, vomiting, diarrhea, abdominal pain, increase in liver enzymes, increase in alkaline phosphatase

- Pulmonary: Adult respiratory distress syndrome, pulmonary edema
- Other: Fever, chills, hypercalcemia, hypokalemia, flushing, eosinophilia

Drug Interactions:
- Cyclosporine may increase caspofungin levels and risk of hepatotoxicity
- Carbamazepine, dexamethasone, efavirenz, nevirapine, phenytoin, rifabutin, rifampin may decrease caspofungin levels
- Caspofungin may decrease sirolimus, tacrolimus levels

Pregnancy: C
Lactation: Safety unknown
Relative cost: $$$$$

## CLOTRIMAZOLE

Brand name: Mycelex Troche
Manufacturer: Janssen Pharmaceuticals

Dosage:
- Esophageal candidiasis: 10 mg troche five times daily for 14 days

Contraindications/cautions:
- Hypersensitivity to drug or components

Adverse Effects:
- Gastrointestinal: Abnormal liver function

Drug Interactions:
- Avoid concomitant use with tolvaptan

Pregnancy: C
Lactation:
Relative cost: $$$ (generic available: $-$$)

### *Cryptosporidium hominis*

- Nitzoxanide 500 mg po bid for 7 days

See below for product details

### *Cyclospora cayetanensis*

- Bactrim 160/800 mg po bid for 7 days

See this chapter.

## NITAZOXANIDE

Brand name: Alinia
Manufacturer: Romark Laboratories, LC

Dosage:
- Infectious diarrhea: 500 mg po q12 h for 3 days. Give with food.
- *Cryptosporidium hominis*: 500 mg po bid for 7 days

Contraindications/cautions:
- Hypersensitivity to drug or components
- Caution in impaired liver function, renal function
- Caution in biliary disease, diabetes, HIV, immunodeficiency

Adverse Effects:
- Gastrointestinal: Abdominal pain, diarrhea, nausea
- Other: Headache

Drug Interactions:
- May increase levels of warfarin and phenytoin

Pregnancy: B
Lactation: Safety unknown
Relative cost: $$$

## VIRAL INFECTIONS

### *Cytomegalovirus (CMV) Gastrointestinal Disease*

- Ganciclovir (5 mg/kg po bid) or foscarnet (90 mg/kg po bid) for induction therapy for 3–6 week.
- Switch to oral valganciclovir (900 mg bid) to complete induction therapy when presenting clinical manifestations have resolved.

### *Herpes Simplex Esophagitis*

- Acyclovir 400 mg po five times a day for 14–21 days. If unable to swallow—acyclovir 5 mg/kg IV q8 h for 7–14 days or IV foscarnet 40 mg/kg/dose every 8–12 h for 14–21 days.

## GANCICLOVIR

Brand name: Cytovene
Manufacturer: Roche Laboratories

Dosage:
- CMV prophylaxis in solid organ transplant: 5 mg/kg IV q12 h for 7–14 days, then 5 mg/kg IV q24 h 7 times a week or 6 mg/kg q24 h 5 times a week. Alternative: 1000 mg po tid. Give with food.
- CMV gastrointestinal disease: 5 mg/kg IV bid×3–6 weeks for induction therapy

Contraindications/cautions:
- Hypersensitivity to drug or components
- Hypersensitivity to acyclovir
- Absolute neutrophil count less than 500
- Platelets less than 25,000
- Caution in impaired renal function
- Caution in myelosuppression, elderly

Adverse Effects:
- Gastrointestinal: Pancreatitis, perforation, diarrhea, vomiting, increased liver transaminases
- Neurologic: Seizures, neuropathy
- Hematologic: Pancytopenia, anemia
- Other: Depression, retinal detachment, hypertension, nephrotoxicity, impaired fertility, fever

Drug interactions:
- Increased risk of nephrotoxicity with cidofovir, aminoglycosides, carboplatin, cisplatin, clofarabine, efavirenz/emtricitabine/tenofovir, tacrolimus
- Increased risk of myelosuppression with clozapine, azathioprine, cisplatin, methotrexate
- Increased risk of seizures with imipenem

Pregnancy: C
Lactation: Unsafe
Relative cost: $$$

## VALGANCICLOVIR

Brand name: Valcyte
Manufacturer: Roche Laboratories

Dosage:
- CMV colitis: 900 mg po qd for 14–21 days

Contraindications/cautions:

Hypersensitivity to drug or components
- Hypersensitivity to ganciclovir
- Absolute neutrophil count less than 500

- Hemoglobin less than 8 mg/dL
- Platelets less than 25,000
- Caution in impaired renal function
- Caution in myelosuppression, elderly, chemotherapy, pregnancy

Adverse Effects:
- Gastrointestinal: Diarrhea, vomiting, abdominal pain
- Neurologic: Seizures, neuropathy, agitation, psychosis
- Hematologic: Aplastic anemia, leucopenia, thrombocytopenia, neutropenia, myelosuppression
- Other: Infertility, nephrotoxicity

Drug Interactions:
- Increased risk of nephrotoxicity with cidofovir, aminoglycosides, carboplatin, cisplatin, clofarabine, efavirenz/emtricitabine/tenofovir, tacrolimus
- Increased risk of myelosuppression with clozapine, azathioprine, cisplatin, methotrexate
- Increased risk of seizures with imipenem

Pregnancy: C
Lactation: Unsafe
Relative cost: $$$$$

## FOSCARNET

Brand name: Foscavir
Manufacturer: AstraZeneca Pharmaceuticals, LP

Dosage:
- CMV colitis—60 mg/kg q8 h or 90 mg/kg q12 h for 2 weeks as infusion, followed by maintenance regimens of 90–120 mg/kg qd

Contraindications/cautions:
- Hypersensitivity to drug or components
- Caution in impaired renal function
- Caution in myelosuppression, seizure, cardiac disease, electrolyte abnormalities, combination with nephrotoxic agents

Adverse Effects:
- Gastrointestinal: Pancreatitis, nausea, vomiting, diarrhea
- Neurologic: Paresthesias
- Hematologic: Anemia, granulocytopenia, leukopenia, thrombocytopenia
- Other: Hypomagnesemia, hypokalemia, hypocalcemia, nephrotoxicity, fever

Drug Interactions:
- Increased nephrotoxicity with cidofovir, aminoglycosides, carboplatin, cisplatin, clofarabine, efavirenz/emtricitabine/tenofovir, gallium, tenofovir
- May cause QT prolongation with droperidol, erythromycin, amiodarone

Pregnancy: C
Lactation: Safety unknown
Relative cost: $$$$$

## ANTIHELMINTHIC THERAPIES

### *Amebiasis*

1. To eliminate intraluminal infection
   - Metronidazole 500–750 mg po tid for 7–10 days
   - Tinidazole 2 g po qd for 3 days
2. To eliminate intraluminal encysted organisms
   - Paromomycin—25–30 mg/kg/day po in three divided doses for 7 days
   - Iodoquinol—650 mg po tid for 20 days

### *Giardiasis*

- Metronidazole 250 mg po tid for 5 days
- Tinidazole po 2 g single dose

## PARASITIC INFESTATIONS

### *Angiostrongyliasis*

- Supportive and corticosteroids

### *Ascariasis (A. lumbricoides)*

- Treatment of choice: Mebendazole 100 mg po bid for 3 days
- Alternative treatments: Pyrantel pamoate 11 mg/kg or albendazole 400 mg once

### *Cutaneous Larva Migrans*

- Treatment of choice: Ivermectin 200 ug/kg po qd for 1–2 days
- Alternative treatments: Albendazole 400 mg po qd for 3 days

### *Cysticercosis (Taenia Solium)*

- Treatment of choice: Albendazole 400 mg po bid for 8–30 days. Concurrent steroids for CNS disease
- Alternative treatments: Praziquantel 50–100 mg/kg/day po in 3 doses for 30 days

### *Dracunculiasis (Guinea worm disease)*

- Metronidazole 250 mg po tid for 10 days plus worm removal

### *Echinococcosis (Hydatid cyst)*

- Treatment of choice: Perioperative albendazole followed by surgery
- Alternative treatments: Albendazole 400 mg po bid for 1–6 months

### *Enterobiasis (Pinworm)*

- Pyrantel pamoate 11 mg/kg po once
- Albendazole 400 mg po once
- Mebendazole 100 mg po once
- Repeat after 2 weeks

### *Hook Worm (Ancylostomiasis)*

- Albendazole 400 mg po once,
- Mebendazole 100 mg po bid for 3 days, or
- Pyrantel pamoate 11 mg/kg po for 3 days

### *Lymphatic Filariasis (W. bancrofti, B. malayi, B. timori)*

- Diethylcarbamazine 6 mg/kg po once

### *Loaisis (M. streptocerca, O. volvulus, D. medinensis)*

- Diethylcarbamazine 6 mg/kg po once

### *Tropical Pulmonary Eosinophilia*

- Diethylcarbamazine 6 mg/kg/day po in 3 doses for 12–21 days

### *Trypanosoma Cruzi (Chagas Disease)*

- Benznidazole for acute infection only

### *Onchocerciasis (River blindness)*

- Ivermectin 150 μg/kg po once; repeat every 6–12 months

### *Fluke Infections*

- Liver flukes (*Clonorchis sinensis*), intestinal flukes (*Fasciolopsis buski*): Praziquantel 75 mg/kg/day po in 3 doses for 1 day
- Lung fluke (*Paragonimus westermani*): Praziquantel 75 mg/kg/day po in 3 doses for 2 days
- Sheep liver fluke: Triclabendazole 10 mg/kg po once

### *Schistosomiasis*

- *S. mansoni, S. haematobium*: Praziquantel 40 mg/kg/day po in 2 doses × 1 day
- *S. japonicum, S. mekongi*: Praziquantel 60 mg/kg/day po in 3 doses × 1 day

### *Strongyloidiasis*

- Treatment of choice: Ivermectin 200 μg/kg/day po for 2 days. For 7 days if immunocompromised
- Alternative treatments: Albendazole 400 mg daily po for 3 days

### *Tapeworm Intestinal Infections (Taenia saginata)*

- Praziquantel 5–10 mg/kg po for 1 day

### *Trichinellosis (Roundworm)*

- Treatment of choice: Steroids for severe symptoms plus mebendazole 200–400 mg po tid for 3 days, then 400–500 mg po tid for 10 days
- Alternative treatments: Albendazole 400 mg po bid for 8–14 days

### *Trichuriasis (Whipworm)*

- Treatment of choice: Mebendazole 100 mg po bid for 3 days or albendazole 400 mg po qd for 3 days.
- Alternative treatments: Ivermectin 200 μg/kg/day po for 3 days

For suggested use of the medications below in helminth infection, see Table 7.4.

**Table 7.4 Protozoan infections**
**Antihelminthic therapies**

| *Infection* | *Treatment of choice* | *Alternative treatments* |
|---|---|---|
| Angiostrongyliasis | Supportive and corticosteroids | |
| Ascariasis | Mebendazole 100 mg bid for 3 days | Pyrantel pamoate 11 mg/kg or Albendazole 400 mg po once |
| Cutaneous larva migrans | Ivermectin 200 ug/kg po qd for 1–2 days | Albendazole 400 mg po once daily for 3 days |
| Cysticercosis | Albendazole 400 mg po bid for 8–30 days. Concurrent steroids for CNS disease | Praziquantel 50–100 mg/kg/day po in 3 doses × 30 days |
| Dracunculiasis | Metronidazole 250 mg po tid for 10 days plus worm removal | |
| Echinococcosis/ Hydatid cyst | Perioperative albendazole | Albendazole 400 mg po bid for 1–6 months |
| Enterobiasis/ Pinworm | Pyrantel pamoate 11 mg/kg po once or albendazole 400 mg po once or mebendazole 100 mg po once. Repeat after 2 weeks | |
| Hookworm/ Ancylostomiasis | Albendazole 400 mg po once or mebendazole 100 mg po bid for 3 days or pyrantel pamoate 11 mg/kg po for 3 days | |

(continued)

**Table 7.4 (continued)**

| *Infection* | *Treatment of choice* | *Alternative treatments* |
|---|---|---|
| Onchocerciasis | Ivermectin 150 μg/kg po once, repeat every 6–12 months | |
| *Fluke infections* | | |
| Liver flukes<br>Intestinal flukes | Praziquantel 75 mg/kg/day po in 3 doses for 1 day | |
| Lung fluke | Praziquantel 75 mg/kg/day po in 3 doses for 2 days | |
| Sheep liver fluke | Triclabendazole 10 mg/kg po once | |
| *Schistosomiasis* | | |
| S. mansoni, S. haematobium | Praziquantel 40 mg/kg/day po in 2 doses for 1 day | |
| S. japonicum, S. mekongi | Praziquantel 60 mg/kg/day po in 3 doses for 1 day | |
| Strongyloidiasis | Ivermectin 200 μg/kg/day po for 2 days for 7 days if immunocompromised | Albendazole 400 mg po qd for 3 days |
| Tapeworm intestinal infections | Praziquantel 5–10 mg/kg po once | |
| Trichinellosis | Steroids for severe symptoms plus mebendazole 200–400 mg po tid for 3 days, then 400–500 mg po tid for 10 days | Albendazole 400 mg po bid for 8–14 days |
| Trichuriasis (whipworm) | Mebendazole 100 mg po bid for or albendazole 400 mg po once daily for 3 days | Ivermectin 200 μg/kg/day po for 3 days |

## ALBENDAZOLE

Brand name: Albenza
Manufacturer: GlaxoSmithKline

Dosages:
- ***Ancylostomiasis and necatoriasis: 400 mg po as a single dose***
- Ascariasis: 400 mg po as a single dose
- Clonorchiasis: 10 mg/kg po qd for 7 days
- Cutaneous larva migrans: 400 mg po qd for 3 days
- *Echinococcus granulosus* infection, hydatid disease: 60 kg or greater, 400 mg po bid for three 28-days cycles
- Enterobiasis: 400 mg po as a single dose; repeat in 2 weeks
- Enterocolitis, eosinophilic—Infection by *Ancyclostoma caninum*: 400 mg po as a single dose
- Infection by Gnathostoma: 400 mg po bid for 21 days
- Infection by Microsporidia: Intestinal due to *E. intestinalis*, 400 mg po bid for 21 days

Contraindications:
- ***Hypersensitivity to albendazole or benzimidazole products***
- Pregnancy
- Use with caution in impaired liver function

Adverse Effects:
- ***Gastrointestinal: Abdominal pain, nausea, vomiting, hepatotoxicity***
- Neurologic: Headache
- Renal: Acute renal failure (rare)
- Hematologic: Agranulocytosis, granulocytopenia, leukopenia, pancytopenia, thrombocytopenia (rare)

Drug Interactions:
- Increased risk of albendazole toxicity with praziquantel and dexamethasone

Pregnancy: C
Lactation: Safe
Relative cost: $$$

## MEBENDAZOLE

Brand name: Vermox
Manufacturer: McNeil Consumer Health

Dosages:
- Ancylostomiasis and necatoriasis: 100 mg po bid for 3 days.
- Ascariasis: 100 mg po bid for 3 days.
- Enterobiasis: 100 mg po qd dose.
- Trichuriasis: 100 mg po bid for 3 days. (Note: treatment may be repeated in 3 weeks in all above conditions)

Contraindications/cautions:
- Hypersensitivity to mebendazole products
- Caution in pts <2 years old.
- Pregnancy

Adverse Effects:
- Gastrointestinal: Abdominal pain, constipation, diarrhea, hepatitis
- Neurologic: Headache, seizure
- Dermatologic: Rash

Drug Interactions: No significant drug interactions
Pregnancy: C
Lactation: Safe
Relative cost: $$

## IVERMECTIN

Brand name: Stromectol
Manufacturer: Merck & Co., Inc

Dosages:
- Infection by *Onchocerca volvulus*: 150 μg/kg, single oral dose; retreatment interval between 3 and 12 months
- Intestinal strongyloidiasis: 200 μg/kg, single oral dose

Contraindications/cautions:
- Hypersensitivity to ivermectin or components
- Pregnancy

Adverse Effects:
- Gastrointestinal: Disease of gastrointestinal tract, nausea, vomiting, diarrhea
- Neurologic: Dizziness, headache
- Dermatologic: Pruritus

Drug Interactions: No significant drug interactions
Pregnancy: C
Lactation: Safety unknown
Relative cost: $$ (generic available: $$)

## PRAZIQUANTEL

Brand name: Biltricide
Manufacturer: Bayer

Indications:
- Schistosomiasis: 20 mg/kg po 3 times over 1 day
- Clonorchiasis: 25 mg/kg po 3 times over 1 day
- Tapeworms: 5–10 mg/kg po once
- Intestinal flukes: 25 mg/kg po 3 times over 1 day

Contraindications/cautions:
- Hypersensitivity to praziquantel
- Ocular cysticercosis

Adverse Effects:
- Gastrointestinal: Abdominal pain
- Cardiovascular: Cardiac dysrhythmia, heart block
- Neurologic: Dizziness, headache, seizure
- Other: Malaise

Drug Interactions:
- Chloroquine may decrease praziquantel levels
- Combination may increase albendazole levels

Pregnancy category: B
Lactation: Avoid breastfeeding for 3 days after last dose
Relative cost: $$$

## THIABENDAZOLE

Brand name: Mintezol
Manufacturer: Merck & Co., Inc

Dosages:
- Ascariasis: (not first line therapy): 50 mg/kg/day divided every 12 h po for 2 days.
- Cutaneous larva migrans—for 2 days
- Visceral larva migrans—for 7 days
- Trichinosis—for 2–3 days
- Dracunculosis—for 3 days

Contraindications/cautions:
- Hypersensitivity to thiabendazole products
- Prophylactic treatment of pinworm infestation

Adverse Effects:
- Gastrointestinal: Nausea, vomiting, anorexia, diarrhea, hepatotoxicity
- Neurologic: Central nervous system finding, dizziness, drowsiness
- Dermatologic: Erythema multiforme, Stevens–Johnson syndrome

Drug Interactions:
- Combination may increase theophylline levels and risk of toxicity

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $

## PYRANTEL PAMOATE

Brand name: Ascarel, Pamix, Pin-X
Manufacturer: Generic

Dosages:
- Enterobiasis: 11 mg/kg (up to maximum 1 g) po once
- Ascariasis: 11 mg/kg (up to maximum 1 g) po once

Contraindications/cautions:
- Hypersensitivity to drug
- Pregnancy
- Liver disease

Adverse Effects:
- Gastrointestinal: Abdominal discomfort, nausea, vomiting
- Neurologic: Dizziness, headache, somnolence

Drug Interactions: No major drug interactions
Pregnancy category: Generally regarded as unsafe
Lactation: Safety unknown
Relative cost: $ (generic available: $)

## TINIDAZOLE

Brand name: Tindamax
Manufacturer: Mission Pharmacal Company

Dosages:
- Intestinal amebiasis: 2000 mg po qd for 3 days
- Amebic liver abscess—2000 mg po qd for 3–5 days
- Giardiasis—2000 mg po once. Give with food

Contraindications/cautions:
- Hypersensitivity to drug or components
- Caution in impaired liver function
- Caution in disulfiram use, alcohol use, CNS disorder, blood dyscrasia

Adverse Effects:
- Gastrointestinal: Candidiasis, nausea, vomiting
- Neurologic: Seizures, peripheral neuropathy
- Pulmonary: Bronchospasm
- Hematologic: Thrombocytopenia
- Dermatologic: Stevens–Johnson syndrome, erythema multiforme
- Other: menorrhagia

Drug Interactions:
- Disulfiram like reaction with disulfiram, lopinavir/ritonavir, tipronavir, diazoxide, ethanol
- May increase levels of lithium, phenytoin, cyclosporine, tacrolimus

Pregnancy: C
Lactation: Unsafe
Relative cost: $$$ (Generic available: $$)

## PAROMOMYCIN

Brand name: Humatin
Manufacturer: King Pharmaceuticals, Inc.

Dosages:
- Intestinal amebiasis: 25–35 mg/kg/day po divided in 3 doses for 5–10 days
- Hepatic encephalopathy: 1000 mg po qid for 5–6 days.
- Cryptosporidial diarrhea in HIV: 1500–3000 mg po divided 3–6 times per day. Alternative—1000 mg po bid × 12 weeks in combination with azithromycin 600 mg po qd for 4 weeks. Give with food.

Contraindications/cautions:
- Hypersensitivity to drug or components
- Use with caution in impaired renal function.
- Use with caution in intestinal obstruction, inflammatory bowel disease neurotoxic agents, ototoxic agents, dehydration, neuromuscular disease, auditory or vestibular dysfunction.

Adverse Effects:
- Gastrointestinal: Enterocolitis, nausea, abdominal cramps, diarrhea
- Other: Nephrotoxicity, ototoxicity, neurotoxicity

Drug Interactions:
- Increased risk of nephrotoxicity with acyclovir, aminoglycoside, cyclosporine, flucytosine, foscarnet, ganciclovir, mitomycin, penicillamine, sirolimus, vancomycin

Pregnancy: C
Lactation: Probably safe
Relative cost: $$$ (generic available: $$$)

## IODOQUINOL

Brand name: Yodoxin
Manufacturer: Glenwood, LLC

Dosage:
- Intestinal amebiasis: 650 mg po tid for 20 days. Give after meals, repeat treatments should be performed in 2–3 weeks intervals

Contraindications/cautions:
- Hypersensitivity to drug or components
- Hypersensitivity to iodine
- Use with caution in hepatic dysfunction.
- Use with caution in thyroid disease.

Adverse Effects:
- Gastrointestinal: Nausea, vomiting, abdominal pain
- Dermatologic: Pruritus, skin discoloration
- Other: Optic neuritis, peripheral neuropathy, headache

Drug Interactions:
- Inadequate immunologic response to concomitant live oral typhoid vaccine
- May decrease levels of mycophenolate mofetil

Pregnancy: C
Lactation: Safety unknown
Relative cost: $$$$$

## DIETHYLCARBAMAZINE

Brand name: Hetrazan
Manufacturer: Wyeth

Dosage:
- See above

Contraindications/cautions:
- Hypersensitivity to drug or components

Adverse Effects:
- Neurologic: Encephalopathy
- Gastrointestinal: Nausea

Drug Interactions:
- Inadequate studies

Pregnancy: X
Lactation: Breast milk excretion unknown
Relative cost: $$$

## BENZNIDAZOLE

Brand name: Rochagan
Manufacturer: Brazilian Government (Not commercially available in the USA)

Dosage:
- See above

Contraindications/cautions:
- Hypersensitivity to drug or components

Adverse Effects:
- Neurologic: Convulsions, seizures, peripheral neuropathy

Drug Interactions:
- Inadequate studies

Pregnancy: Unknown
Lactation: Breast milk excretion unknown
Relative cost: $

## TRICLABENDAZOLE

Brand name: Egaten
Manufacturer: Novartis

Dosage:
- See above

Contraindications/cautions:
- Hypersensitivity to drug or components

Adverse Effects:
- Gastrointestinal: Self-limiting biliary obstruction, abdominal cramping

Drug Interactions:
- No known interactions

Pregnancy: B
Lactation: Safety unknown
Relative cost: $$$

## INFECTIVE ENDOCARDITIS PROPHYLAXIS FOR GI PROCEDURES

The administration of prophylactic antibiotics solely to prevent endocarditis is not recommended for patients who undergo GI tract procedures, including diagnostic esophagogastroduodenoscopy or colonoscopy as recommended by American Heart association 2007 guidelines.

## REFERENCES

1. Chey WD, Wong BC, Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology Guideline on the management of helicobacter pylori infection. Am J Gastroenterol. 2007;102(8):1808–25.
2. Feldman M, et al. Sleisenger & Fordtran's gastrointestinal and liver disease. 8th ed. Philadelphia: Saunders; 2006.
3. Johnson S, Schriever C, Galang M, et al. Interruption of recurrent Clostridium difficile-associated diarrhea episodes by serial therapy with vancomycin and rifaximin. Clin Infect Dis. 2007;44:846.
4. Louie TJ, Miller MA, et al. Fidaxomicin versus Vancomycin for C.Diff Infection. N Engl J Med. 2011;364:422–31.
5. Cohen S, et al. Clinical practice guidelines for clostridium difficile infection in adults: 2010 Update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) *Clinical Practice Guidelines*. JSTOR. 2010. http://www.cdc.gov/HAI/pdfs/cdiff/Cohen-IDSA-SHEA-CDI-guidelines-2010.pdf. Accessed 31 Dec 2015.

# II Liver Diseases

# 8 Hepatitis

*Roopjeet K. Bath and George Y. Wu*

***Contents***



## ABBREVIATIONS

| | |
|---|---|
| ADV | Adefovir |
| Alt | Alternative |
| cont | Continue |
| ETV | Entecavir |
| HCC | Hepatocellular carcinoma |
| LAM | Lamivudine |
| LdT | Telbivudine |
| mcg | Micrograms |
| mo | Month |
| Rx | Treat |
| TDF | Tenofovir disoproxil fumarate |
| ULN | Upper limit of normal |
| wk | Week |
| y | Year |

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## CHRONIC HEPATITIS B

### *Entecavir*

Brand name: Baraclude
Manufacturer: Bristol-Myers Squibb

Dosage: Chronic hepatitis B
- Nucleoside-naive: 0.5 mg po qd
- Lamivudine-refractory: 1 mg po qd
- Decompensated liver disease: 1 mg po qd

Contraindications:
- Hypersensitivity to drug

Adverse effects:
- Lactic acidosis/severe hepatomegaly
- Severe acute hepatitis upon discontinuation
- HIV resistance in untreated HIV-positive patients
- Nephrotoxicity
- Cardiovascular: Edema
- Hepatic: Ascites, increased liver enzymes, encephalopathy
- Gastrointestinal: Nausea, increased lipase, increased amylase
- Neurologic: Dizziness, headache, fatigue
- Dermatologic: Skin rash

Pregnancy Category: C
Relative cost: $$$$$ $$ (generic available $$)
Dosage Adjustments
Renal Impairment:

Nucleoside-naïve:
- CrCl >50: No adjustment
- CrCl 30–49: 50 % normal dose daily or normal dose every 48 h
- CrCl 10–29: 30 % normal dose daily or normal dose every 72 h
- CrCl <10: 10 % normal dose daily or normal dose every 7 days
- Hemodialysis: 10 % normal dose, give after hemodialysis

Hepatic impairment: No adjustment

### *Tenofovir*

Brand name: Viread
Manufacturer: Gilead Pharmaceuticals, Inc.
Dosage: Chronic hepatitis B: 300 mg po qd

Contraindications:
- Hypersensitivity to drug

Adverse effects:
- Lactic acidosis/severe hepatomegaly
- Severe acute hepatitis upon discontinuation
- Neurologic: Insomnia, headaches
- Gastrointestinal: Abdominal pain, diarrhea, nausea
- Hematological: Neutropenia
- Metabolic: Hypercholesterolemia
- Skeletal: Decreased bone density, back pain, arthralgias
- Dermatological: Rash

Drug interactions:
- Truvada, Atripla contains tenofovir, didanosine; atanazovir, and lopinavir/ritavir increase tenofovir concentrations. Co-administration with drugs that decrease renal function could increase tenofovir concentrations.

Pregnancy category: B
Relative cost: $$$$$ $$
Dosage Adjustments
Renal Impairment:
- CrCl 30–49: 300 mg po q48 h
- CrCl 10–29: 300 mg po q72–96 h
- CrCl <10: Not defined
- Hemodialysis: 300 mg po once weekly after hemodialysis

Hepatic impairment: No adjustment

## *Pegylated Interferon α-2a*

Brand name: Pegasys
Manufacturer: Roche

Dosage:
- 180 μg sc weekly for 48 weeks

Contraindications:
- Hypersensitivity to drug
- Autoimmune hepatitis, decompensated liver disease (Child-Pugh class B, C)
- Significant preexisting psychiatric disease
- Pregnancy (with ribavirin use)
- Neonates, Infants

Adverse effects:
- Neurologic: Fatigue, headache, insomnia, memory impairment, decreased concentration, peripheral neuropathy, stroke
- Hematologic: Neutropenia, thrombocytopenia, anemia
- Musculoskeletal: Fatigue, weakness, myalgia, arthralgia
- Dermatologic: Alopecia, pruritus, injection site inflammation, injection site reaction, dermatitis, xeroderma
- Psychiatric: Anxiety, irritability, depression, psychotic disorder, suicide
- Endocrine: Weight loss, hypothyroidism, hyperthyroidism, growth stunting
- Hepatic: Increased liver enzymes, hepatic decompensation
- Misc: Arrhythmias, MI, autoimmune disorders, cough, dyspnea, blurred vision

Pregnancy Category: C
Relative cost: $$$$$ $$

## *Dosage Adjustments for PEG-Interferon α-2a (Pegasys)*

Depression
- For mild depression: No dosage change necessary;
- For moderate depression: Decrease dose to 135 μg sc q1 week; if necessary, decrease to 90 μg. If symptoms improve or stable for ≥4 weeks, continue reduced dosing or return to normal dose.
- For severe depression: Discontinue treatment immediately and permanently; obtain immediate psychiatric consultation.

Hematological
- For neutrophil count <750/mm$^3$: Decrease dose to 135 μg sc q1 week
- For neutrophil count <500/mm$^3$: Suspend treatment until absolute neutrophil count (ANC) >1000/mm$^3$; reinstitute at 90 mcg sc q1week and monitor ANC
- For platelet count <50,000/mm$^3$: Decrease dose to 90 μg sc q1week
- For platelet count <25,000/mm$^3$: Discontinue treatment

Hepatic impairment:
- Decompensated hepatic disease (e.g., Child-Pugh class B or C) should not be treated with peginterferon α-2a.
- Progressive ALT increases above baseline: Decrease the dose to 135 μg sc q1week, resume after resolution of ALT flare.
- ALT increases up to 5 times upper normal limit: Decrease dose or temporary discontinuation of treatment.
- ALT increases up to 10 times upper normal limit: Discontinuation of therapy should be considered.

Renal impairment
- CrCl ≥30 mL/min: No dosage adjustment needed. (180 μg)
- CrCl <30 mL/min: 135 mcg sc weekly. Close monitoring for adverse reactions which may require dosage reduction to 90 μg until adverse reactions subside is recommended.
- Intermittent hemodialysis: 135 μg sc q1 week. Monitor patients closely.

## *Pegylated Interferon α-2b*

Brand name: Intron A
Manufacturer: Merck

Dosage:
- Chronic hepatitis B: 5 million IU sc daily or 10 million IU sc every 48 h for 16 weeks

Contraindications:
- Hypersensitivity to drug
- Decompensated liver disease (Child-Pugh B, C)
- Severe depression
- Significant preexisting psychiatric disease
- Autoimmune hepatitis

Adverse effects:
- Neurological: Confusion, insomnia, decreased concentration
- Hematologic: Neutropenia, anemia, autoimmune thrombocytopenia, myelosuppression
- Gastrointestinal: Colitis, pancreatitis, anorexia, nausea
- Hepatic: Increased liver enzymes
- Dermatologic: Injection site reaction, alopecia, pruritus
- Cardiovascular: Chest pain, edema, hypertension
- Psychiatric: Depression, irritability
- Endocrine: Weight loss, amenorrhea
- Other: Influenza-like illness, pulmonary toxicity, nephrotic syndrome

Pregnancy category: C
Relative cost: $$$$$ $$
Dosage adjustments for PEG-interferon α-2b

General:
- Severe adverse reactions: Modified dosage (50% reduction) or therapy should be temporarily discontinued until the adverse reactions resolve. If reaction persists, therapy should be discontinued.

Depression
- Clinical depression: Monitor closely during treatment and for 6 months after treatment.
- Severe depression: Discontinue immediately and seek psychiatric consult.

Hematological:
- ANC <500/mm$^3$ or platelets <50,000/mm$^3$: Discontinue treatment.

Hepatic:
- Liver function abnormality or hepatic decompensation (Child-Pugh B, C): Discontinue.

Renal:
- Creatinine clearance <50: Caution advised

Other:
- Pulmonary toxicity, pancreatitis, triglycerides >1000 mg/dL: Discontinue.

## *Lamivudine*

Brand name: Epivir HBV
Manufacturer: GlaxoSmithKline
Dosage: Chronic hepatitis B: 100 mg po qd for ≥1 year, and at least 6 months after HBeAg seroconversion or HBsAg clearance.

Contraindications:
- Hypersensitivity

Adverse effects:
- Gastrointestinal: Decreased appetite, nausea and vomiting, pancreatitis, hepatomegaly, relapsing type B viral hepatitis
- Neurologic: Headache, fatigue, insomnia, dizziness, neuropathy
- Hematologic: Neutropenia
- Endocrine metabolic: Lactic acidosis, lipodystrophy
- Other: Rash, increased CPK, arthralgias

Pregnancy Category: C
Relative cost: $$$$$ $ (generic available $$)
Dosage Adjustments for Lamivudine

Renal Impairment:
- CrCl >50: No adjustment
- CrCl 30–49: 100 mg po once then 50 mg po qd
- CrCl 15–29: 100 mg once then 25 mg po qd
- CrCl 5–14: 35 mg once then 15 mg po qd
- CrCl <5: 35 mg once then 10 mg po qd
- Hemodialysis/peritoneal dialysis: No supplement required

Hepatic Impairment: No adjustment

## *Adefovir Dipivoxil*

Brand name: Hepsera
Manufacturer: Gilead Sciences

Dosage: Chronic hepatitis B: 10 mg po qd

Contraindications:
- Hypersensitivity to drug

Adverse effects:
- Severe acute hepatitis upon discontinuation
- Nephrotoxicity
- HIV resistance in untreated HIV-positive patients
- Lactic acidosis/severe hepatomegaly
- Gastrointestinal: Abdominal pain, diarrhea, indigestion, nausea
- Neurologic: Headache, fatigue
- Dermatologic: Pruritus, rash
- Other: Hypophosphatemia, back pain

Pregnancy category: C
Relative cost: $$$$$ $$ (generic available $$)
Dosage Adjustments

Renal Impairment:
- CrCl >50: No adjustment
- CrCl 20–49: 10 mg po q48 h
- CrCl 10–19: 10 mg po q72 h
- CrCl <10: Not defined
- Hemodialysis: 10 mg po q7 days, no supplement after dialysis

Hepatic Impairment: No adjustment required

## *Telbivudine*

Brand name: Tyzeka
Manufacturer: Novartis

Dosage: Chronic hepatitis B: 600 mg po qd

Contraindications:
- Concurrent use with peginterferon α-2a
- Hypersensitivity to drug

Adverse effects:
- Lactic acidosis/severe hepatomegaly
- Severe acute hepatitis upon discontinuation
- HIV resistance in untreated HIV-positive patients

- Nephrotoxicity
- Neurologic: Headache, malaise, fatigue, peripheral neuropathy
- Musculoskeletal: Elevated creatine kinase level, myopathy
- Hematologic: Neutropenia
- Gastrointestinal: Abdominal pain, diarrhea
- Respiratory: Nasopharyngitis, upper respiratory infection

Pregnancy category: B
Relative cost: $$$$$ $$
Dosage Adjustments

Renal Impairment:
- CrCl >50: No adjustment
- CrCl 30–49: 600 mg po every 48 h
- CrCl <30: 600 mg po every 72 h
- End stage renal disease (ESRD)/hemodialysis: 600 mg po every 96 h; give after dialysis, no supplement required

Hepatic Impairment: No adjustment
For algorithms for the treatment of HBV in cirrhotics, see Fig. 8.1 and non-cirrhotics, see Fig. 8.2.

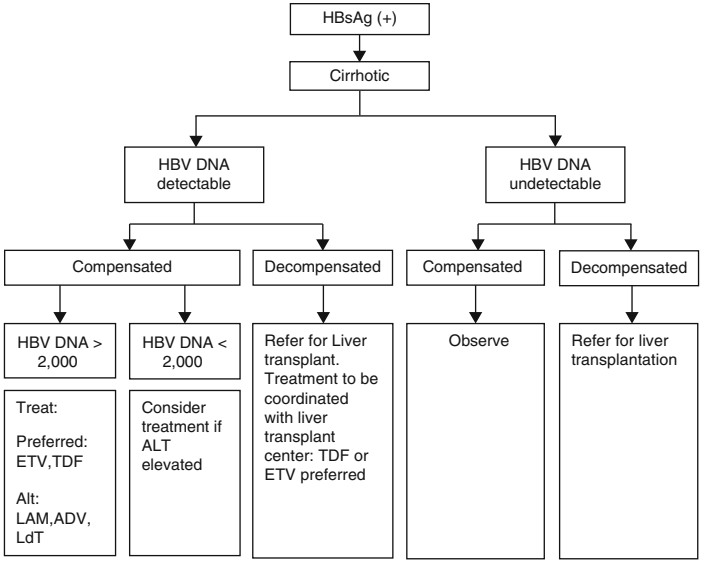


Fig. 8.1 An algorithm for the treatment of HBV in cirrhotics

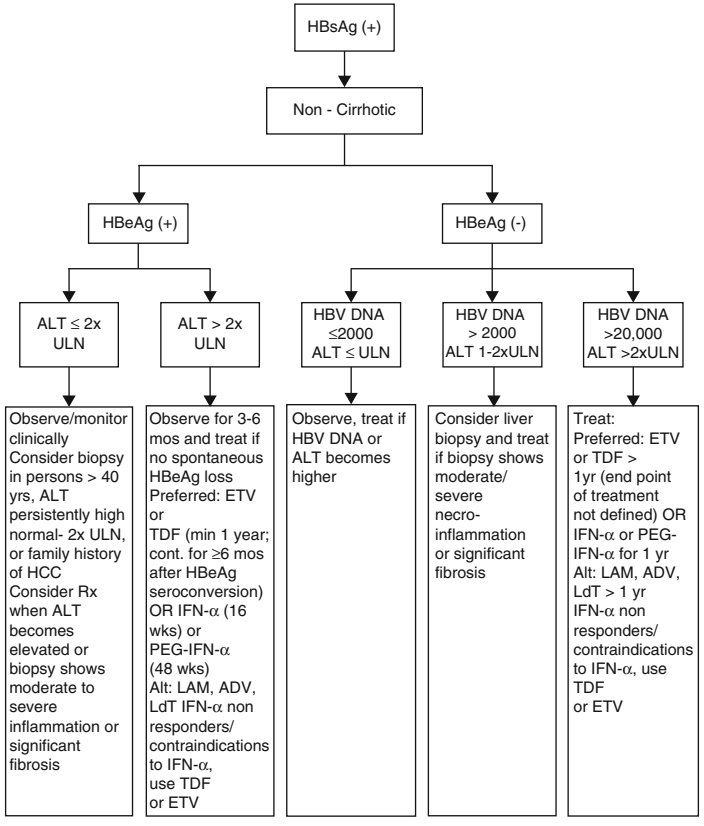


Fig. 8.2 An algorithm for the treatment of HBV in non-cirrhotics

## CHRONIC HEPATITIS C

### *Sofosbuvir*

Trade name: Sovaldi
Manufacturer: Gilead

Dosage: 400 mg po qd; used in combination with either ledipasvir, daclatisvir, simeprevir, ribavirin, or pegylated interferon for treatment of chronic hepatitis C

Indications: Genotypes 1, 4, 5, or 6 in combination with ledipasvir
No dosage adjustment required for mild or moderate renal impairment. No dosage recommendations available for patients with severe renal impairment

(eGFR <30) or with ESRD due to higher exposures of the predominant sofosbuvir metabolite.

Contraindications:
- Contraindications that apply to the combination therapy agent selected
- Not recommended for Child's B or C

Adverse effects:
- Serious, symptomatic bradycardia when co-administered with amiodarone and another HCV direct acting antiviral
- Fatigue
- Headache
- Elevations of bilirubin, lipase, and creatine kinase

Drug interactions:
- Drugs that are P-gp inducers in the intestine (rifampin, St. John's Wort) can decrease sofosbuvir plasma concentrations.

Pregnancy category: B
Relative cost: $$$$$ $$$$$

## *Ledipasvir*

Trade name: Used in combination with sofosbuvir: Harvoni
Manufacturer: Gilead

Dosage: Ledipasvir 90 mg/sofosbuvir 400 mg po qd; duration of therapy typically 12 weeks, but 24 weeks in treatment-experienced cirrhotic patients with genotype 1.

Indications: Genotypes 1, 4, 5, or 6
Contraindications: See sofosbuvir section

Adverse Effects:
- Serious, symptomatic bradycardia when co-administered with amiodarone
- Fatigue
- Headache
- Elevations of bilirubin, lipase, and creatine kinase

Drug interactions:
- Acid reducing agents: Can potentially decrease ledipasvir concentration
- Amiodarone: Risk of symptomatic bradycardia
- Digoxin: Increased digoxin level with co-administration
- Anticonvulsants (carbamazepine, phenytoin, phenobarbital, oxcarbazepine): Decrease concentrations of both ledipasvir and sofosuvir; co-administration not recommended
- Antimycobacterials (rifabutin, rifampin, rifapentine): Decreased ledipasvir and sofosbuvir concentrations

- HIV antiretrovirals: Regimens containing tenofovir (increased tenofovir concentrations); tipranavir/ritonavir: Decreased ledipasvir and sofosbuvir concentrations
- St. John's Wort (*Hypericum perforatum*): Decreased ledipasvir and sofosbuvir concentrations
- Rosuvastatin: Co-administration may increase rosuvastatin concentration

Pregnancy category: B
Relative cost: $$$$$ $$$$$

### *Simeprevir*

Trade name: Olysio
Manufacturer: Janssen

Dosage: 150 mg po qd (should be taken with food), given in combination with sofosbuvir +/− weight-based ribavirin. Duration of treatment: Non-cirrhotic: 12 weeks, cirrhotic: 24 weeks.

Indications: Chronic hepatitis C, genotype 1. Cirrhotic, genotype 1a patients should be negative for the Q80K variant on resistance testing
Not recommended for patients with moderate to severe hepatic impairment (Child-Pugh class B or C)

Contraindications:
- Contraindications that apply to co-administered medications

Adverse effects:
- Serious, symptomatic bradycardia when co-administered with sofosbuvir and amiodarone
- Fatigue
- Headache
- Nausea
- Pruritus, rash, and photosensivity

Drug interactions:
- Anti-arrhythmics: Amiodarone, digoxin, disopyramide, mexiletine, propafenone, quinidine
- Anticonvulsants: Carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- Antibiotics: Erythromycin, clarithromycin, telithromycin
- Antifungals: Intraconazole, ketoconazole, posaconazole, fluconazole, voriconazole
- Anti-mycobacterials: Rifampin, rifabutin, rifapentine
- Calcium channel blockers
- Herbal products: St. John's Wort, milk thistle
- HIV medications: Cobicistat-containing product, efavirenz, delavirdine, etravirine, nevirapine, darunavir, ritonavir

- HMG CO-A reductase inhibitors: Generally increases concentration of statin
- Immunosuppressants: Cyclosporine, sirolimus
- Phosphodiesterase-5 inhibitors
- Sedatives/anxiolytics: Midazolam, triazolam

Pregnancy category: C
Relative cost: $$$$$ $$$$$

## *Daclatasvir*

Trade name: Daklinza
Manufacturer: Bristol-Myers Squibb

Dosage: 60 mg po qd used in combination with sofosbuvir; FDA indication for treatment of HCV genotype 3. Duration of treatment: 12 weeks.

Dose modification: Reduce dosage to 30 mg/day with strong CYP3A inhibitors and increase dosage to 90 mg/day with moderate CYP3A inducers

Contraindications:
- Strong inducers of CYP3a, including phenytoin, carbamazepine, rifampin, and St. John's Wort

Adverse effects:
- Serious, symptomatic bradycardia when co-administered with sofosbuvir and amiodarone
- Fatigue
- Headache
- Nausea/diarrhea
- Elevation of lipase

Drug interactions:
- CYP 3A inhibitors and inducers
- Dabigatran (co-administration increases dabigatran concentration)
- Anti-arrhythmics: Amiodarone, digoxin
- HMG CO-A reductase inhibitors: Increases concentration of statin

Pregnancy category: FDA category not assigned
Relative cost: $$$$$ $$$$$

## *Paritaprevir/Ritonavir/Ombitasvir/Dasabuvir (PROD)*

Trade name: Viekira Pak
Manufacturer: Abbvie

Dosage: PRO: 2 tablets po qAM, D: 1 tablet po bid; can be given with or without ribavirin. Duration of therapy: 12 weeks. Genotype 1a with cirrhosis, 24 weeks.

Indication: FDA indication for treatment of HCV Genotype 1

Contraindications:
- Severe hepatic impairment due to risk of potential toxicity; contraindicated in Child-Pugh class B or C
- With drugs that are highly dependent on CYP3A for clearance and for which elevated plasma levels are associated with serious and/or life-threatening events; strong inducers of CYP3A or CYP2C8, which may lead to reduced efficacy of Viekira Pak; and strong CYP2C8 inhibitors, which may increase dasabuvir levels and the risk of QT prolongation
- With the following drugs: Alfuzosin HCL; carbamazepine, phenytoin, phenobarbital; gemfibrozil, rifampin, ergotamine, dihydroergotamine, ergonovine, methylergonovine; ethinyl estradiol-containing medicines, such as many oral contraceptives; St. John's Wort; lovastatin, simvastatin; pimozide; efavirenz; sildenafil (when dosed at Revatio for pulmonary arterial hypertension); triazololam and oral midazolam
- In patients with known hypersensitivity (e.g., toxic epidermal necrolysis or Stevens–Johnson syndrome) to ritonavir

Adverse effects:

In patients taking Viekira Pak with ribavirin:
- Fatigue
- Nausea
- Pruritus and other skin reaction
- Insomnia
- Asthenia

In patients taking Viekira alone:
- Nausea
- Pruritus
- Insomnia

Relative cost: $$$$$ $$$$$
Pregnancy category: B (X if combined with ribavirin)

### *Paritaprevir/Ritonavir/Ombitasvir (PRO)*

Trade name: Technivie
Manufacturer: Abbvie

Dosage: 75/50/12.5; 2 tablets po qd (paritaprevir 150 mg/ritonavir 100 mg/ombitasvir 25 mg) with weight-based ribavirin. Duration of therapy: 12 weeks.

Indication: FDA indication for treatment of patients with genotype 4 chronic hepatitis C without cirrhosis
Contraindications:
- Severe hepatic impairment due to risk of potential toxicity; contraindicated in Child-Pugh class B or C
- Hypersensitivity to drug/class/component
- Co-administration with drugs that are highly dependent on CYP3A for clearance; moderate and strong inducers of CYP3A
- Contraindications that apply to ribavirin

Adverse effects:
- Fatigue
- Nausea
- Pruritus and other skin reaction
- Insomnia
- Hepatic decompensation and hepatic failure in patients with cirrhosis
- Hyperbilirubinemia/ALT elevation, transient
- Anemia/decreased hemoglobin

Relative cost: $$$$$ $$$$$
Pregnancy category: B (X with ribavirin)

## *Elbasvir Plus Grazoprevir*

Trade name: Zepatier
Manufacturer: Merck

Dosage: Elbasvir 50 mg po qd plus grazoprevir 100 mg po qd +/– RBV

Indications: Genotypes 1, 4

Testing prior to initiation:
- Genotype 1a: Test for NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93
- Obtain hepatic laboratory testing prior to and during treatment with Zepatier

No dosage adjustment required for renal impairment; refer to ribavirin prescribing information when using ribavirin in patients with CrCl less than or equal to 50 mL/min

Contraindications:
- Not recommended for Child's B or C
- If Zepatier is administered with ribavirin, the contraindications to ribavirin also apply.

Adverse effects:

- AST, ALT elevations
- Elevations of bilirubin
- Fatigue
- Headache

Drug interactions:
- Drugs that are CYP3A inducers can decrease elbasvir plus grazoprevir plasma concentrations. Inhibitors can increase elbasvir plus grazoprevir levels.
- Drugs that inhibit organic anion transporter OATPB1/3 can increase grazoprevir levels.

Pregnancy category: B (X with ribavirin)
Relative cost: $$$$$

## *Ribavirin*

Trade name: Copegus; Rebetol; Ribasphere; Ribapak; Moderiba; ribavirin
Manufacturer: Genetech; Inc, Merck & Co. Inc; Kadmon Pharmaceuticals, LLC; generic

Dosage: Chronic hepatitis C (in combination with peginterferon α2a)
- <75 kg: 1000 mg po qd, in two divided doses
- ≥75 kg: 1200 mg po qd, in two divided doses

Contraindications:
- Hypersensitivity to drug
- Cardiac disease, significant or unstable; potential worsening due to drug-induced anemia
- Pregnancy or pregnant partner of male patient; may cause birth defects and/or death of the exposed fetus
- Hemoglobinopathy (such as thalassemia major and sickle-cell anemia)
- Decompensated liver disease
- Autoimmune hepatitis
- Significant renal function impairment (for rebetol, ribasphere)

Contraindications:
- Gastrointestinal: Abdominal pain, nausea, vomiting, pancreatitis
- Hematologic: Hemolytic anemia, cardiac and pulmonary events have occurred, thrombotic thrombocytopenic purpura (less than 1 %)
- Dermatologic: Pruritus, rash

Pregnancy category: X
Relative cost: $$$$$ $$ (generic available $$)

### *Ribavirin Dosage Adjustments*

- No cardiac history and hemoglobin <10 g/dL: Decrease dose to 600 mg po qd (200 mg po qam and 400 mg po qpm).
- No cardiac history and hemoglobin <8.5 g/dL: Permanently discontinue ribavirin therapy.
- History of cardiovascular disease with hemoglobin decreases by ≥2 g/dL during any 4 weeks period: Decrease ribavirin dose to 600 mg po qd. If the hemoglobin remains <12 g/dL after 4 weeks on the reduced dose, discontinue ribavirin therapy. Can restart ribavirin at 600 or 800 mg po qd.

Hepatic impairment: No specific guidelines are available.
Patients with renal impairment

Rebetol, Ribasphere:
- CrCl ≥50 mL/min: Closely monitor older patients (>50 years old) for development of anemia, especially if renal function impairment coexists.
- CrCl <50 mL/min: Oral ribavirin therapy should NOT be given.

Copegus, Moderiba:
- CrCl >50 mL/min: No dosage adjustment needed
- CrCl 30–50 mL/min: Alternate 200 mg and 400 mg every other day
- CrCl <30 mL/min: Including ESRD requiring hemodialysis: 200 mg once daily

### *Pegylated Interferon alfa-2a*

Trade name: Pegasys
Manufacturer: Roche

Dosage:
- Chronic hepatitis C—180 μg weekly sc for 12 weeks in conjunction with sofosbuvir and weight-based ribavirin

See drug under hepatitis B section for contraindications/adverse effects/pregnancy category and relative cost.
For a list FDA approved agents for the treatment of HCV, see Table 8.1. For a list of agents recommended by major society guidelines, see Table 8.2.

## AUTOIMMUNE HEPATITIS (AIH)

Treatment options for AIH:

**Table 8.1 Treatment options by Genotype (GT) According to FDA approval**

| *FDA Approved DAAs According to Genotype* | | | | | |
|---|---|---|---|---|---|
| *(Duration 12 weeks except as indicated)* | | | | | |
| *1* | *2* | *3* | *4* | *5* | *6* |
| Harvoni[a]<br>Zepatier[f,g,h]<br>Viekira +/− RBV[c]<br>IFN/Sovaldi/RBV | Sovaldi/RBV<br>PEG-IFN/RBV[d] | Sovaldi/Daklinza<br>Sovaldi/RBV[d]<br>PEG-IFN/RBV[e] | Zepatier[g,i,j]<br>Technivie[b]<br>PEG-IFN/Sovaldi/RBV<br>Harvoni[g] | Harvoni[g] | Harvoni[g] |

[a]Treatment-experienced cirrhotics for 24 weeks
[b]Contraindicated in cirrhotics
[c]GT 1a—add RBV for 12 weeks; genotype 1a cirrhotics, add RBV for 24 weeks
[d]24 weeks
[e]48 weeks
[f]GT 1a with polymorphisms (M28, Q30, L31, Y93)—add RBV for 16 weeks
[g]Contraindicated in Child's B or C
[h]Protease inhibitor-experienced—add RBV for 12 weeks
[i]IFN-RBV experienced—add RBV for 16 weeks
[j]PEG-IFN experienced—add RBV for 16 weeks
Harvoni—sofosbuvir plus ledipasvir
Sovaldi—sofosbuvir
Viekira (PROD)—paritaprevir/ritonavir/ombitasvir/dasabuvir
Technivie (PRO)—paritaprevir/ritonavir/ombitasvir
Daklinza—daclatasvir
Zepatier—elbasvir plus grazoprevir

**Table 8.2 Treatment options by genotype according to the AASLD-IDSA guidelines**

| **Genotype 1** | | |
|---|---|---|
| Therapy | Non-cirrhotic | Cirrhotic |
| Ledipasvir/Sofosbuvir | 12 weeks | Rx naïve: 12 weeks<br>Rx experienced:<br>– 24 weeks, or<br>– 12 weeks when combined with wt-based RBV |
| Daclatasvir/Sofosbuvir | 12 weeks | 24 weeks<br>+/− wt-based RBV |
| Elbasvir, plus Grazoprevir | 1a without NS5A polymorphisms: 12 weeks | 1a without NS5A polymorphisms: 12 weeks |
| | 1a with NS5A polymorphisms: 16 weeks + wt-based RBV | 1a with NS5A polymorphisms: 16 weeks + wt-based RBV |
| | 1b: 12 weeks | 1b: 12 weeks |
| PROD +/− weight-based ribavirin | 1a: + RBV; 12 weeks | 1a: + RBV; 24 weeks |
| | 1b: No RBV; 12 weeks | 1b: No RBV; 12 weeks |
| Sofosbuvir plus simeprevir +/− wt-based RBV | 12 weeks | 24 weeks<br>Genotype 1a patients must be negative for the Q80K variant |
| **Genotype 2** | | |
| Therapy | Non-cirrhotic | Cirrhotic |
| Sofosbuvir + | Rx naïve: 12 weeks | Rx naïve: 16 weeks |
| Weight-based RBV | Prior failure to PEG + RBV:<br>– 16–24 weeks, or:<br>– + PEG-IFN, 12 weeks | |

(continued)

**Table 8.2 (continued)**

| | | |
|---|---|---|
| Daclatasvir/Sofosbuvir | Rx naïve: use in patients that cannot tolerate RBV; 12 weeks<br>Prior failure to Sofosbuvir/RBV:<br>– 24 weeks +/− wt-based RBV<br>– Retreat with Sofosbuvir/RBV plus PEG-IFN, 12 weeks | 12 vs. 24 weeks |
| **Genotype 3** | | |
| Therapy | Non-cirrhotic | Cirrhotic |
| Daclatasvir/Sofosbuvir | 12 weeks | Rx naïve:<br>– 24 weeks +/− weight-based RBV<br>Prior IFN + RBV failure, or Sofosbuvir/RBV failure (& IFN ineligible):<br>– 24 weeks + weight-based RBV |
| Sofosbuvir + wt-based RBV + weekly PEG IFN (IFN-eligible patients) | 12 weeks | 12 weeks<br>– Same for prior IFN + RBV failure |
| Sofosbuvir + weight-based RBV x 24 weeks is an alternative regimen for Tx naive, IFN-ineligible pts | 24 weeks | 24 weeks |

(continued)

**Table 8.2 (continued)**

| **Genotype 4, 5, 6** | | |
|---|---|---|
| Therapy | Genotype 4 | Genotype 5 and 6 |
| Ledipasivir/Sofosbuvir | 12 weeks | 12 weeks |
| PRO + weight-based RBV | 12 weeks | N/A |
| Sofosbuvir + weight-based RBV | 24 weeks | N/A |
| Elbasvir/Grazoprevir | Treatment naïve: 12 weeks<br>PEGIFN/RBV-experienced: 16 weeks PLUS ribavirin | N/A |
| Alternate therapy: Sofosbuvir + wt-based RBV + weekly PEG IFN (IFN-eligible patients) | 12 weeks | 12 weeks |

*AASLD* American Association for the Study of Liver Diseases, *IDSA* Infectious Diseases Society of America, *PROD* Paritaprevir/Ritonavir/Ombitasvir/Dasabuvir, *PRO* Paritaprevir/Ritonavir/Ombitasvir

1. Combination therapy: Prednisone with azathioprine (preferred) OR
2. Prednisone monotherapy
3. Alternative therapy: Budesonide +/− azathioprine
4. Alternative adjunct therapy in place of azathioprine includes 6-MP

## *Azathioprine*

Refer to IBD Section 5 (Inflammatory Bowel Disease) for drug information

## *Prednisone*

**Refer to Section 5** (Inflammatory Bowel Disease) for drug information

Dosage:

1. Combination therapy [with azathioprine]: Start with 30 mg po qd and taper down to 10 mg po qd within 4 weeks in combination with azathioprine 50 mg po qd.
2. Prednisone monotherapy: 40–60 mg po qd for 2 weeks, and then decrease to 20 mg within 4 weeks.

### *Budesonide*

Refer to section 5 (Inflammatory Bowel Disease) for drug information
Dose for AIH: 9 mg po qd.

### *6-Mercaptopurine*

Trade name: Purinethol
Manufacturer: Gate pharmaceuticals

Dosage: Use as second line agent in steroid + azathioprine refractory cases. 75–125 mg po qd

Contraindications:
- Hypersensitivity to drug/class/component
- Caution if impaired renal function

Adverse Reactions:
- Gastrointestinal: Nausea, vomiting, diarrhea, hepatotoxicity, GI ulceration, pancreatitis, jaundice, abdominal pain
- Renal: Urate nephropathy, nephrolithiasis
- Hematological: Myelosuppression, anemia, leukopenia, thrombocytopenia, tumor lysis syndrome, immunosuppression
- Endocrine: Hyperuricemia
- Dermatological: Oral lesions
- Others: Anorexia, malaise, fever

Pregnancy category: D
Relative cost: $$$$ (generic available $)

## ALCOHOLIC HEPATITIS

### *Pentoxifylline**

Trade names: Pentoxil, Trental
Manufacturer: Upsher-Smith (Pentoxil), Trental Sanofi-Aventis (Trental)

Dosage: 400 mg po tid for 4 weeks

Indication: Patients with alcoholic hepatitis who have a Maddrey score of 32 or greater/hepatic encephalopathy or MELD 18 or higher AND in whom prednisone is contraindicated

Mechanism of action: Phosphodiesterase inhibitor, inhibits production of TNF alpha and other cytokines

Contraindications:
- Cerebral hemorrhage
- Retinal hemorrhage
- Hypersensitivity reaction to pentoxifylline or intolerance of xanthines (e.g., caffeine, theophylline, methylxanthine)
- Concomitant use of NSAIDS

Dose adjustments

Renal impairment
Creatinine clearance 10–50 mL/min: 400 mg po bid
Creatinine clearance <10 mL/min: 400 mg po qd, may need to reduce dose to 200 mg po qd or if using sustained release formulation, 400 mg po qod

Geriatric dosing: No adjustments, use in caution especially with concomitant renal failure

Pediatric dosing: Safety not yet established

Hepatic dosing: Not defined
Caution if using concomitant theophyllines or warfarin

Common adverse events:
- Gastrointestinal: Diarrhea, vomiting, nausea, epigastric pain
- Neurological: Headache, dizziness
- Skin: Rash
- Cardiovascular: Arrhythmias
- Respiratory: Dyspnea

Uncommon adverse events: Chest pain, hypotension anaphylaxis, angioedema, anxiety, edema, urticaria, bloating/flatus, constipation, cholecystitis, jaundice, liver enzyme elevations, xerostomia, anorexia, blurred vision, nasal congestion, sore throat, laryngitis aseptic meningitis, confusion, hallucinations, earache, scotoma, seizure, tremor, aplastic anemia, epistaxis, pancytopenia

Pregnancy category: C
Relative cost: $$$$ (generic available $)
*Note: pentoxifylline is not FDA approved nor recomended by AASLD guidelines for use in alcoholic hepatitis

## *Prednisolone**

Trade names: Millipred, Omnipred, Orapred, Orapred ODT, Prelone, Veripred 20, Pediapred, PredForte, Pred Mild, Prelone
Manufacturer: Generic

Dosage: 40 mg po qd for 4 weeks followed by 2–4 weeks taper

Indication: Patients with alcoholic hepatitis who have a Maddrey score of 32 or greater/hepatic encephalopathy or MELD 18 or higher

Contraindications:
- Known hypersensitivity reaction to prednisolone or its components
- Gastrointestinal bleeding
- Pancreatitis
- Active infection
- Opportunistic infections: e.g., latent or active tuberculosis, varicella, acute herpes simplex keratitis or ocular herpes simplex virus, systemic fungal infection
- Concomitant administration of live or attenuated viral vaccine
- Caution in: Renal failure, diabetes mellitus, osteoporosis, psychiatric disorder, recent surgery, hypertension, hypothyroidism, myasthenia gravis, coagulation or thromboembolic disorders

Dose adjustments
- Renal dosing: Caution in renal impairment
- Hepatic dosing: Not defined
- Geriatric dosing: Use at lowest effective dose
- Hyperthyroidism: May require higher dosing due to increased clearance

Adverse events
- General: Delayed wound healing, immunosuppression, opportunistic infections, growth suppression, anaphylaxis, insomnia, edema
- Gastrointestinal: Mucosal ulceration or perforation, pancreatitis
- Neurological: Psychosis, pseudotumor cerebri, seizures, headache, mood swings, vertigo
- Hematologic: Petechiae, ecchymoses
- Skin: Pigmentation abnormalities, thinning skin, facial erythema, urticaria
- Cardiovascular: Hypertension, congestive heart failure

- Endocrine: Adrenal insufficiency, Cushing's syndrome, hyperglycemia/diabetes mellitus, hypokalemic alkalosis, hirsutism
- Musculoskeletal: Myopathy, osteoporosis/osteopenia, tendon rupture
- Ocular: Cataract formation, exophthalmos, optic neuritis, glaucoma

Pregnancy category: C
Relative cost: $ (generic available)
*Note: Prednisolone is not FDA approved not recomended by AASLD guidelines for use in alcoholic hepatitis Fig. 8.3.

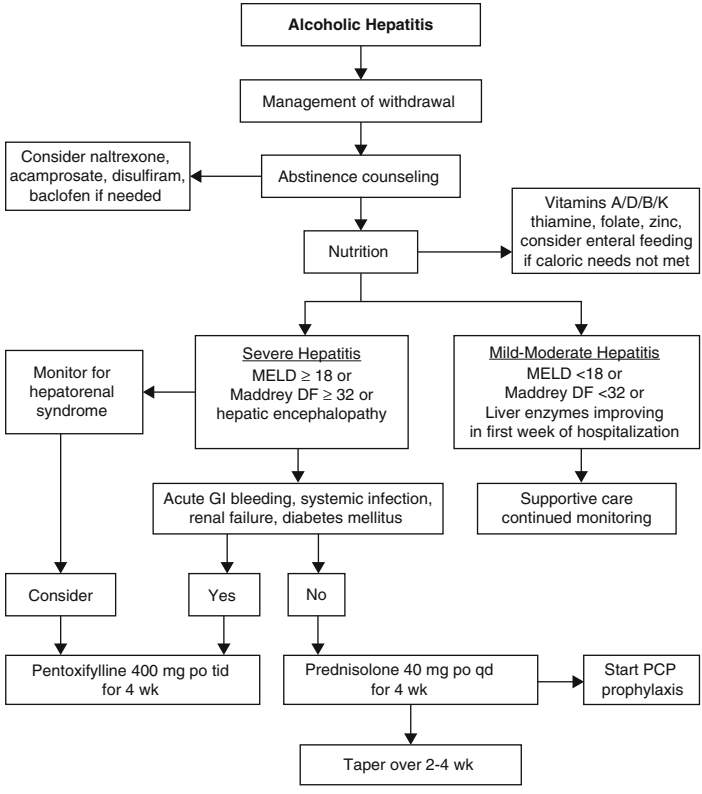


Fig. 8.3 An algorithm for the treatment of alcoholic hepatitis

## REFERENCES


1. Terrault NA, Bzowej NH, Chang K-M, Hwang JP, Jonas MM, Hassan Murad M. AASLD guidelines for treatment of chronic hepatitis B. Hepatology. 2015;63(1):261–83.
2. Lok ASF, Mcmahon BJ. AASLD Chronic hepatitis B: update 2009. Hepatology. 2009;50(3):661–2.
3. Lok ASF, Mcmahon BJ. AASLD Chronic hepatitis B: update 2009. Hepatology. 2009;50(3):661–2.
4. Manns MP, Czaja AJ, Gorham JD, Krawitt EL, Mieli-Vergani G, Vergani D, Vierling JM. Diagnosis and management of autoimmune hepatitis. Hepatology. 2010;51(6):2193–213.
5. Bath RK, Wu GY. Autoimmune Hepatitis. BMJ Best Practice. http://bestpractice.bmj.com/best-practice/monograph/130.html. Accessed 08 July 2015.
6. AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. Hepatology. 2015;62(3):932–54.
7. LexiComp
8. UpToDate Drug Information
9. Rambaldi A, et al. Systematic review: glucocorticosteroids for alcoholic hepatitis—a Cochran Hepato-Biliary Group systematic review with meta-analyses and trial sequential analyses of randomized clinical trials. Aliment Pharmacol Ther. 2008;27:1167–78.
10. Amini M, Runyon B. Alcoholic hepatitis 2010: a clinician's guide to diagnosis and therapy. World J Gastroenterol. 2010;16(39):4905–12.
11. Krishna B, et al. Pentoxifylline versus prednisolone for severe alcoholic hepatitis: a randomized controlled trial. World J Gastroenterol. 2009;15(13):1613–9.
12. Akriviadis E, et al. Pentoxifylline improves short-term survival in severe acute alcoholic hepatitis: a double-blind, placebo-controlled trial. Gastroenterology. 2000;119:1637–48.
13. Cohen SM, Ahn J. Review article: the diagnosis and management of alcoholic hepatitis. Aliment Pharmacol Ther. 2009;30:3–13.
14. Lucey MR, et al. Alcoholic hepatitis. N Engl J Med. 2009;360(26):2758–69.
15. O'Shea RS, et al. Alcoholic liver disease. AASLD practice guidelines. Hepatology. 2010;51(1):307–28.
16. Sovaldi [package insert]. Gilead Sciences Inc., Foster City, CA; 2015, Harvoni [package insert]. Gilead Sciences Inc., Foster City, CA; 2016, Olysio [package insert]. Janssen Therapeutics., Titusville, NJ; 2016, Daklinza [package insert]. Bristol-Myers Squibb Company., Princeton, NJ; 2016, ViekiraPak [package insert]. AbbVie Inc., North Chicago, IL; 2015, Technivie [package insert]. AbbVie Inc., North Chicago, IL; 2015
17. Feldman M (2010) Sleisenger & Fordtran's gastrointestinal and liver disease. 9th edn, vol 2, Section 9, Chapter 84, alcoholic liver disease.

# 9 Portal Hypertension

*Roopjeet K. Bath*

***Contents***



## PROPRANOLOL

Brand name: Inderal, Inderal LA, InnoPran XL
Class: Beta-adrenergic blockers, nonselective

## NADOLOL

Brand name: Corgard
Class: Beta-adrenergic blockers, nonselective
Manufacturer: Generic

## CARVEDILOL

Brand name: Coreg
Class: Beta-adrenergic blocker with alpha-blocking property
Manufacturer: Glaxo SmithKline

Dosage: Prevention of variceal bleeding (off-label use):

- Propranolol: Initiate 20 mg po q12 h, titrate to maximal dose tolerated or heart rate reduction by 25%, provided it does not drop below 55 beats per min.

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_9,

- Nadolol: Initiate 20–40 mg po qd, titrate to maximal dose tolerated or heart rate reduction by 25 %, provided it does not drop below 55 beats per min.
- Carvedilol: Initiate at 3.125 mg po bid and titrate to maximal dose tolerated; aim for HR 55-65

Contraindications/cautions:
- Bronchial asthma or chronic obstructive pulmonary disease
- Cardiogenic shock or hypotension
- Hypersensitivity to drug
- Overt cardiac failure
- Second- and third-degree AV block
- Severe sinus bradycardia
- Refractory ascites

Adverse effects:
- Gastrointestinal: Nausea, vomiting
- Neurologic: Fatigue, insomnia, paresthesias
- Cardiovascular: Bradyarrhythmias, hypotension
- Respiratory: Asthma, bronchospasm
- Dermatologic: Dermatitis, pruritus, urticaria
- Psychiatric: Depression, psychotic disorder

Drug interactions:
- Contraindicated with thioridazines due to risk of AV block, bradycardia, and hypotension
- Use with caution with haloperidol, amiodarone, digoxin, octreotide: Increased risk of hypotension, bradycardia, and cardiac conduction abnormalities

Pregnancy category: C
Lactation: Possibly safe
Relative cost: $$ (generic available: $–$$)
Octreotide
See Chap. 2.

## SUGGESTED READING

1. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Am J Gastroenterol. 2007;102:2086–102.

# 10 Cholestasis

*Roopjeet K. Bath*

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## PRIMARY BILIARY CIRRHOSIS

### *Ursodiol (UCDA)*

Brand names: URSO Forte, Actigall
Manufacturer: Generic; URSO Forte-Axcan Pharma; Actigall-Watson Pharmaceuticals

Dosage:
- Primary biliary cirrhosis: 13–15 mg/kg po qd
- Primary sclerosing cholangitis: ~20 mg/kg po qd (do NOT use doses >28 mg/kg po qd)
- Autoimmune hepatitis: Use with the initial therapy to induce remission as well as during continuation phase: 10 mg/kg po qd

Contraindications/cautions:
- Hypersensitivity to drug or bile acids
- Gallstones: Calcified cholesterol, radiopaque stones, radiolucent bile pigment stones
- Unremitting acute cholecystitis
- Acute cholangitis
- Biliary obstruction

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_10,

Adverse effects:
- Gastrointestinal: Diarrhea, nausea, vomiting
- Musculoskeletal: Backache

Drug interactions:
- Concomitant fibric acid derivatives, oral contraceptives, bile acid binding resins and antacids may decrease ursodiol efficacy

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$$ (generic available: $$–$$$)

## PRIMARY SCLEROSING CHOLANGITIS

### *UDCA*

See above.

## SUGGESTED READING

1. Lindor KD, Gershwin ME, Poupon R, Kaplan M, Bergasa NV, Heathcote J. Primary biliary cirrhosis. Hepatology. 2009;50(1):291–308.
2. Lindor KD, Kowdley KV, Harrison ME. ACG clinical guideline: primary sclerosing cholangitis. Am J Gastroenterol. 2015;110:646–59.

# 11 Hepatic Encephalopathy

*Roopjeet K. Bath*

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## GENERAL PRINCIPLES OF MANAGEMENT

- Identify and treat any precipitating cause of hepatic encephalopathy; this includes infections, gastrointestinal bleeding, electrolyte disorders, diuretic overdose, and constipation.
- Lactulose is the first choice for treatment.
- Rifaximin is an effective add-on therapy to lactulose for prevention of recurrent overt hepatic encephalopathy.
- Neomycin and metronidazole are alternative treatment choices; however, long-term use is associated with side effects such as ototoxicity and nephrotoxicity.
- The joint AASLD-EASL guidelines on hepatic encephalopathy note that oral branched-chain amino acids and intravenous l-ornithine l-aspartate can be used as alternative or additional therapies to treat patients nonresponsive to conventional therapy; however, these agents are not readily available for clinical use in the United States.

### *Lactulose*

Brand names: Cephulac, Cholac, Constulose
Class: Non-absorbed disaccharide
Manufacturer: Generic

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_11,

Dosages:
- Treatment and prophylaxis of hepatic encephalopathy: Start with 30–45 mL (20 g/30 mL) po 2–4 times po qd, then adjusted to achieve 2–3 soft formed stools/day or 300 mL (200 gm) mixed with 700 mL of water or saline rectally as a retention enema (retain for 30–60 min) every 4–6 h as needed
- Constipation: 15–30 mL po qd, or bid

Contraindications/cautions:
- Hypersensitivity to lactulose products
- Galactosemia

Adverse effects:
- Gastrointestinal: Bloating, diarrhea, epigastric pain, flatulence, nausea, vomiting, cramps
- Endocrine metabolic: Hypernatremia, hypokalemia

Drug Interactions:
- Increases anticoagulation effects of coumadin

Pregnancy category: B
Lactation: Safety unknown
Relative cost: $$ (generic available: $–$$)

## *Metronidazole*

Brand name: Flagyl; Metro
Class: Antibiotic, miscellaneous
Manufacturer: Generic

Dosage:
- Hepatic encephalopathy: 250 mg po bid

Contraindications/cautions:
- Hypersensitivity to metronidazole or any component of the formulation
- Pregnancy (single 2 g dose regimen)
- Alcohol use within 3 days
- Disulfiram use within 14 days
- Caution if blood dyscrasia, CNS disorder (e.g., seizure disorder)

Adverse effects:
- Central nervous system: Headache, metallic taste, dizziness, aseptic meningitis, ataxia, encephalopathy, disulfiram-like reaction (with alcohol), peripheral neuropathy, seizures
- Dermatologic: Stevens–Johnson syndrome, toxic epidermal necrolysis, urticaria
- Gastrointestinal: Nausea/vomiting, abdominal pain, diarrhea, xerostomia

- Genitourinary: Vaginitis, genital pruritus, dysmenorrhea, urine abnormality, urinary tract infection, vulvovaginal candidiasis
- Hematologic and oncologic: Leukopenia (reversible), thrombocytopenia (reversible, rare)
- Ophthalmic: Optic neuropathy
- Respiratory: Flu-like symptoms, upper respiratory tract infection, pharyngitis, nasal congestion, rhinitis, sinusitis
- Miscellaneous: Fever, lesion (central nervous system, reversible)

Pregnancy category: B
Relative cost: $$ (generic available: $–$$)

## *Neomycin*

Brand name: Neo-Fradin
Class: Non-absorbed antibiotic
Manufacturer: Generic

Dosage:
- Hepatic encephalopathy: 4–12 g po qd in divided doses for 5–6 days, maximum 12 g po qd; do not use longer than 2 weeks.

Contraindications/cautions:
- Hypersensitivity to neomycin/aminoglycosides
- Inflammatory/ulcerative gastrointestinal disease
- Intestinal obstruction

Adverse effects:
- Gastrointestinal: Diarrhea, nausea, vomiting
- Neurologic: Neuromuscular blockade finding
- Respiratory: Respiratory tract paralysis, concomitant anesthesia, muscle relaxants
- Renal: Nephrotoxicity
- Otic: Ototoxicity

Pregnancy category: D
Lactation: Safety unknown
Relative cost: $$$ (generic available: $$)

## *Rifaximin*

Brand name: Xifaxan
Class: Non-absorbed antibiotic
Manufacturer: Salix Pharmaceuticals

Dosage:
- Hepatic encephalopathy: 400 mg po tid
- Small intestinal bacterial overgrowth: 400 mg po tid for 2 weeks. Therapy may be repeated if required.

Contraindications/cautions:
- Hypersensitivity to rifaximin

Adverse effects:
- Gastrointestinal: Constipation, vomiting, abdominal pain
- Neurologic: Headache
- Immunologic: Immune hypersensitivity reaction

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$

## REFERENCES

1. American Association for the Study of Liver Diseases, European Association for the Study of the Liver. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. J Hepatol. 2014; 61(3):642–59.
2. Lexicomp/UpToDate drug information.

# 12 Overload Disorders

*Roopjeet K. Bath*

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## HEREDITARY HEMOCHROMATOSIS

### *Deferoxamine**

Brand name: Desferal
Manufacturer: Generic

Dosages:

- Acute iron toxicity:
  1000 mg im initially followed by 500 mg im q4 for up to 2 doses. Subsequent doses of 500 mg can be given q4–12 h. Maximum dose: 6 g/day.
  15 mg/kg/h IV for first 1000 mg, then 500 mg/4 h IV up to 2 doses.
- Chronic iron overload:
  20–40 mg/kg/day sc infusion for 1000–2000 mg over 8–24 h.
  40–50 mg/kg/day iv infusion over 8–12 h.
  Maximum 1 g qd in the absence of transfusions, 6 g qd if patient received transfusions.

Dose adjustments:
Renal impairment
Severe impairment/anuria: Contraindicated

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_12,

Contraindications/cautions:
- Hypersensitivity to deferoxamine or any component of the formulation, patients with severe renal disease or anuria
- CrCl 10–50 mL/min, CRRT: Administer 25–50 % of normal dose

Adverse effects:
- Cardiovascular: Flushing, hypotension, tachycardia, shock, edema
- CNS: Headache, fever, dizziness, neuropathy, seizure, exacerbation of aluminum-related encephalopathy (dialysis)
- Dermatologic: Angioedema, rash, urticaria
- Endocrine/metabolic: Growth retardation in children, hypocalcemia
- Gastrointestinal: Abdominal discomfort or pain, diarrhea, nausea, and vomiting
- Genitourinary: Dysuria
- Hematologic: Thrombocytopenia, leucopenia
- Local: Injection site burning, erythema, eschar, induration, irritation, pain, swelling, wheal or vesicle formation
- Neuromuscular and skeletal: Arthralgia, leg cramps, myalgia, paresthesias
- Ocular: Decreased acuity, blurred vision, dichromatopsia, maculopathy, night vision or peripheral vision impairment, visual loss, visual field defects, optic neuritis, cataracts, retinal pigmentary abnormalities
- Renal: Renal impairment, urine discoloration
- Respiratory: Acute/adult respiratory distress syndrome, asthma
- Miscellaneous: Anaphylaxis, hypersensitivity reaction, infections

Drug interactions: Ascorbic acid may enhance the adverse/toxic effect of deferoxamine
Pregnancy category: C

*not FDA approved for this indication

## *Deferasirox**

Brand names: Exjade, Jadenu
Manufacturer: Novartis

Dosages:
- Chronic iron overload due to blood transfusion:
  - Exjade:

    Initial 20 mg/kg po qd.
    Maintenance dose adjusted every 3–6 months based on serum ferritin levels 20–30 mg/kg po qd. Doses up to 40 mg/kg po qd for serum ferritin levels persistently >2500 μg/L

– Jadenu:
  Initial 14 mg/kg po qd, increase by 3.5–7 mg/kg po qd q3 months based on ferritin; maximum 28 mg/kg po qd

Dose adjustments

Renal impairment

Creatinine clearance >40 to <60 mL/min: Reduce initial dose by 50 %
Creatinine clearance <40 mL/min or serum creatinine >2 times age-appropriate ULN it is contraindicated

Hepatic impairment

Consider dose adjustment or discontinuation for severe or persistent elevations in liver function tests

Contraindications/cautions:
- Hypersensitivity to deferasirox or any component of the formulation
- Platelet count <50,000/$mm^3$
- Poor performance status and high-risk myelodysplastic syndromes or advanced malignancies
- Renal impairment as above

Adverse effects:
- CNS: Fever, headache, fatigue
- Dermatologic: Rash (dose related), urticaria
- Gastrointestinal: Abdominal pain, diarrhea, nausea, vomiting, (all dose related), aminotransferase elevations
- Renal: Increased serum creatinine (dose related), proteinuria
- Respiratory: Cough, nasopharyngitis, pharyngolaryngeal pain, bronchitis, tonsillitis, rhinitis
- Otic: Ear infection
- Neuromuscular and skeletal: Arthralgia, back pain
- Miscellaneous: Influenza

Drug interactions: Aluminum hydroxide, cholestyramine, CYP2C8 substrates, CYP3A4 substrates, phenobarbital, phenytoin, rifampin, ritonavir
Pregnancy category: C

*not FDA approved for this indication

For an algorithm for the treatment of hemochromatosis, see Fig. 12.1.

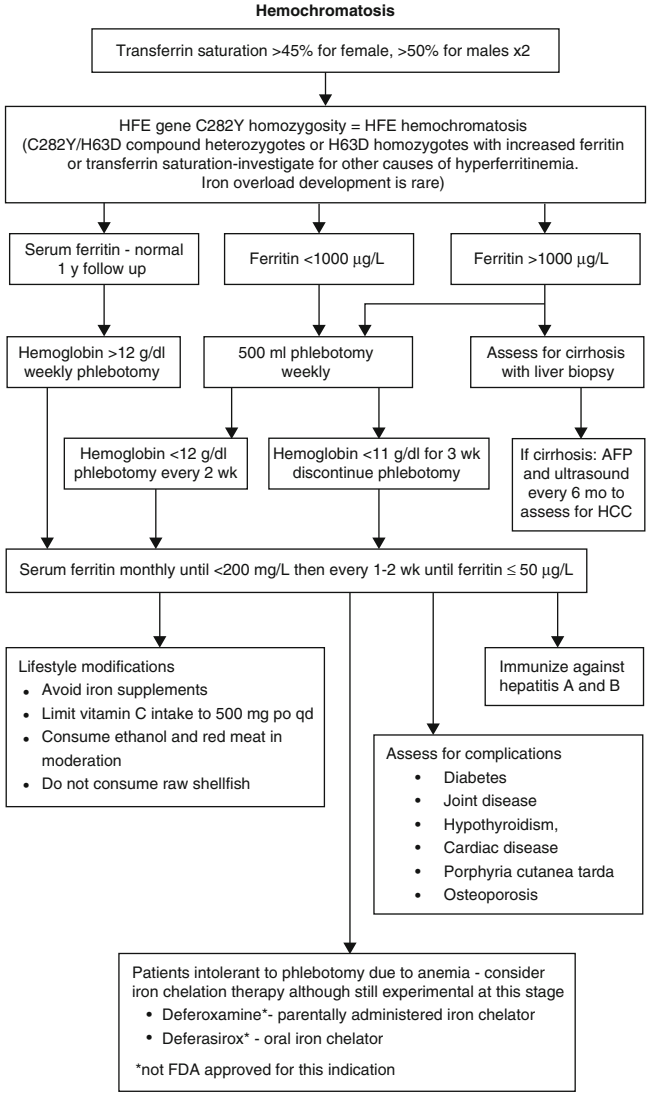


Fig. 12.1 An algorithm for the treatment of hemochromatosis

## *Penicillamine*

Brand name: Cuprimine
Manufacturer: Aton Pharma, Inc.
Dosage: 750–1500 mg po in divided doses po tid or qid.

Contraindications:
- Hypersensitivity to drug/class/component
- Pregnancy
- Breastfeeding
- History of penicillamine related aplastic anemia or agranulocytosis
- Renal impairment (RA patients)
- Hypersensitivity to penicillin

Common adverse effects:
- GI: Nausea, vomiting, epigastric pain, hepatic failure, pancreatitis
- Neurological: Myasthenia gravis
- Renal: Nephrotic syndrome, renal failure
- Hematological: Aplastic anemia, leukopenia, agranulocytosis, thrombocytopenia
- Immunological: Hypersensitivity reaction, SLE
- Dermatological: Exfoliative dermatitis, pemphigus

Uncommon adverse effects:
- Intrahepatic cholestasis (rare), hepatitis (rare), toxic epidermal necrolysis (rare)

Pregnancy category: D
Relative cost: $$

## *Trientine*

Brand name: Syprine
Manufacturer: Merck & Co., Inc.
Dosage: 250–500 mg po qid, maximum: 2 g po qd

Contraindications:
- Hypersensitivity to drug/class/component
- Rheumatoid arthritis
- Biliary cirrhosis
- Cystinuria

Adverse effects:
- Hematological: Iron deficiency anemia
- Immunological: Lupus, contact dermatitis

Pregnancy category: C
Relative cost: $$$

### *Zinc Sulfate*

Brand names: Orazinc, Zincate
Manufacturer: Mericon Industries Inc.
Dosage: 50 mg elemental zinc po tid (oral zinc sulfate is approximately 23 % elemental zinc)

Adverse reactions:
- GI: Nausea, stomach upset, heartburn
- Immunological: May have immunosuppressant effects

Pregnancy category: C
Relative cost: $

## GAUCHER'S DISEASE

### *Imiglucerase (Glucocerebrosidase)*

Brand name: Cerezyme
Manufacturer: Genzyme

Dosages:
- 30–60 units/kg iv q2 weeks, dosing individualized based on disease severity. Range: 2.5 units/kg iv 3 times/week-60 units/kg as frequently as once a week. Average dose 60 units/kg administered every 2 weeks.

Contraindications/cautions:
- Hypersensitivity to imiglucerase or any component of the formulation

Adverse effects:
- Miscellaneous: Hypersensitivity reaction including prurius, flushing, urticaria, angioedema, bronchospasm
- Cardiovascular: Tachycardia
- Central nervous system: Headache, dizziness, fatigue, fever
- Dermatologic: Rash, pruritus
- Gastrointestinal: Nausea, abdominal discomfort, vomiting, diarrhea
- Local injection site burning, swelling or sterile abscess
- Neuromuscular and skeletal: Backache
- Miscellaneous: Anaphylactoid reactions
- Antibody formation: Development of IgG antibodies has been reported in 15 % of patients and may increase the risk of hypersensitivity reactions

Drug interactions:
- No known significant interactions

Pregnancy category: C
Lactation: Excretion in breast milk unknown, use caution

## *Velaglucerase Alfa (Glucocerebrosidase)*

Brand name: VPRIV
Manufacturer: Shire

Dosages:
- 60 units/kg iv administered every other week based on disease severity/activity. Range of 15–60 units/kg has been evaluated in clinical trials.

Contraindications/cautions:
- None listed by manufacturer

Adverse effects:
- Central nervous system: Headache, fatigue, fever, dizziness
- Gastrointestinal: Abdominal pain, nausea
- Hematologic: aPTT prolonged
- Respiratory: Upper respiratory tract infections
- Miscellaneous: Infusion-related reactions, hypersensitivity reactions
- Cardiovascular: Flushing, hyper or hypotension, tachycardia
- Dermatologic: Rash, urticaria

Drug interactions:
- No known significant interactions

Pregnancy category: B
Lactation: Excretion in breast milk unknown, use caution

## *Miglustat*

Brand name: Zavesca
Manufacturer: Actelion

Dosages:
- 100 mg po tid; dose may be reduced to 100 mg po 1–2 times/day in patients with adverse effects

Contraindications/cautions:
- Hypersensitivity to miglustat or any component of the formulation, pregnancy

Adverse effects:
- Central nervous system: Headache, dizziness, memory impairment, migraine
- Gastrointestinal: Diarrhea, weight loss, abdominal pain, flatulence, nausea, vomiting, constipation, xerostomia, bloating, anorexia, dyspepsia, epigastric pain
- Neuromuscular and skeletal: Tremor, weakness, leg cramps, paresthesia
- Ocular: Visual disturbances
- Endocrine and Metabolic: Menstrual disorder
- Hematologic: Thrombocytopenia

Drug interactions: Imiglucerase. Miglustat increases the clearance of imiglucerase; combination therapy is not indicated.

Pregnancy category: X

- Decreased fetus weight, fetal loss, and difficult or delayed births observed in animal studies.
- Women of reproductive age should use contraception.
- Adverse effects on spermatogenesis and reduced fertility were observed in male animal studies.
- Manufacturer recommends male patients use reliable contraception during therapy and for 3 months following treatment.

Lactation: Excretion in breast milk unknown, but it is not recommended.
For an algorithm for the treatment of Gaucher's Disease, see Fig. 12.2.

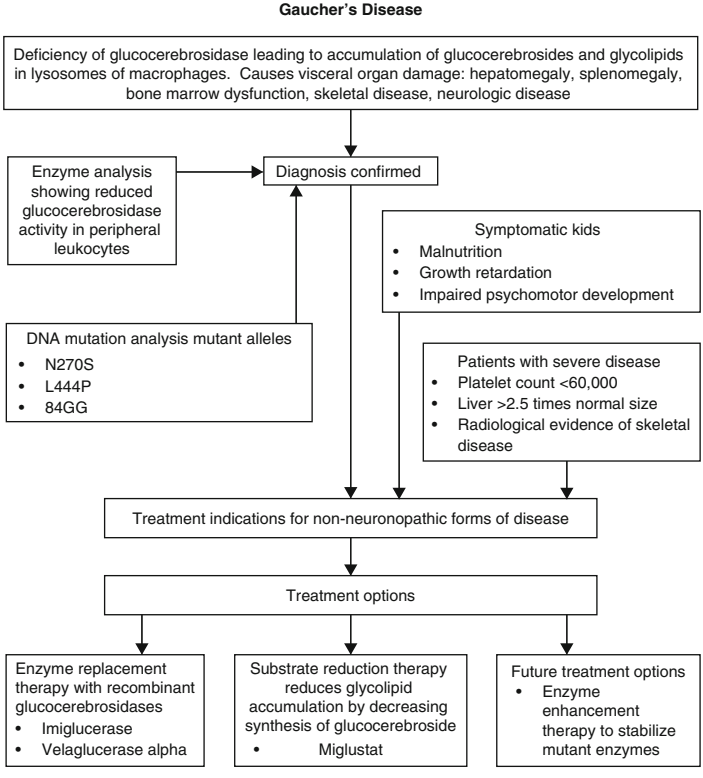


Fig. 12.2 An algorithm for the treatment of Gaucher's Disease

## REFERENCES

1. Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology. 2011;54(1):328–43.
2. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease: an update. Hepatology. 2008;47(6):2089–111.
3. Lexicomp/UpToDate drug information

# 13 Pruritus

*Marianna Mavilia and George Y. Wu*

***Contents***



## DIPHENHYDRAMINE

Brand names: Benadryl, Nytol, Sominex, Unisom, Banophen, Dicopanol, Diphenhist, Dytuss, Genahist, Geri-Dryl, Pharbedryl, QlearQuil, Quenalin, Relief, Siladryl, Triaminic, ZzzQuil

Manufacturers: Generic; Benadryl-Johnson & Johnson Consumer Inc.; Nytol-Omega Pharma; Sominex-Actavis; Unisom-Sanofi Pharamceuticals; Banophen- Major Pharmaceuticals; Dicopanol-Fusion Pharmaceuticals; Diphenhist-BIO-PHARM; Dytuss-Lunsco, Inc.; Genahist-Teva Pharmaceuticals; Geri-Dryl-Geri-Care Pharmaceutical Corp.; Pharbedryl-Pharbest Pharmaceuticals; QlearQuil-Procter & Gamble Manufacturing Company; Quenalin-Qualitest Pharm; Siladryl-Silarx Pharmaceuticals, Inc.; Triaminic-Novartis Consumer Health, Inc.; ZzzQuil-Procter & Gamble Manufacturing Company

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_13,

Dosage:
- 25–50 mg po qid

Contraindications/cautions:
- Caution in patients with breathing problems, glaucoma, and difficultly with urination.

Adverse effects:
- Drowsiness
- Excitability

Drug interactions:
- Alcohol, sedatives, tranquilizers

Pregnancy category: B
Lactation: Contraindicated
Relative cost: $ (generic available: $)

## HYDROXYZINE

Brand names: Vistaril
Manufacturer: Generic; Vistaril-Pfizer Pharmaceuticals

Dosage:
- 25 mg po tid

Contraindications/cautions:
- Hypersensitivity to the drug or its components.
- Elderly

Adverse effects:
- Neurological: Drowsiness, headache
- Psychiatric: Hallucinations
- Dermatologic: Pruritus, rash, urticarial
- Other: Dry mouth

Drug interactions:
- CNS depressants (including narcotics, non-narcotic analgesics, barbiturates, alcohol)

Pregnancy category: Contraindicated in early pregnancy
Lactation: Contraindicated
Relative cost: $$$$$ (generic available: $)

## CHOLESTYRAMINE

Brand names: Prevalite, Questran, Questran Light
Manufacturer: Generic; Prevalite-Upsher-Smith Laboratories, Inc.; Questran, Questran Light-Par Pharmaceuticals

Dosage:
- 4–6 g po 30 min before meals (or doses may be taken before and after breakfast without an evening dose)

Contraindications/cautions:
- Complete biliary obstruction
- Hypersensitivity to drug or its components

Adverse effects:
- Gastrointestinal: Constipation, abdominal pain, flatulence, nausea, vomiting, diarrhea, dyspepsia, eructation, anorexia, steatorrhea, bleeding tendencies, osteoporosis

Drug interactions:
- May inhibit absorption of fat-soluble vitamins
- Enhanced lipid-lowering effect with HMG-CoA reductase inhibitors
- Other interactions include spironolactone, oral phosphate supplements, phenylbutazone, warfarin, thiazide diuretics, propranolol, tetracycline, penicillin G, phenobarbital, thyroid and thyroxine preparations, estrogens and progestins, and digitalis.

Pregnancy category: C
Lactation: Caution
Relative cost: $$$$$ (generic available: $$$)

## RIFAMPIN

Brand names: Rifadin, Rimactane
Manufacturer: Generic; Rifadin-Aventis Pharmaceuticals; Rimactane-Sandoz Pharmaceuticals

Dosage:
- 300 mg po bid

Contraindications/cautions:
- Hypersensitivity to drug or its components
- Impaired liver function: Monitor LFTs every 2–4 weeks during therapy
- Diabetes mellitus
- Elderly

Adverse effects:
- Neurological: Dizziness, visual disturbances, drowsiness
- Gastrointestinal: Reflux, nausea, vomiting, hepatotoxicity
- Systemic: Fever, edema, red-orange discoloration of urine and secretions
- Musculoskeletal: Muscle weakness
- Endocrine: Menstrual disturbances
- Dermatologic: Flushing, urticarial, rash

Drug interactions:
- Anticonvulsants, digoxin, antiarrhythmics, oral anticoagulants, antifungals, barbiturates, β-blockers, calcium channel blockers, chloramphenicol, clarithromycin, corticosteroids, cyclosporine, cardiac glycoside preparations, clofibrate, oral or other systemic hormonal contraceptives, dapsone, diazepam, doxycycline, fluoroquinolones, haloperidol, oral hypoglycemic agents, levothyroxine, methadone, narcotic analgesics, progestins, quinine, tacrolimus, theophylline, TCAs, and zidovudine, atovaquone, isoniazid, ketoconazole, probenecid, cotrimoxazole, sulfasalazine, and antacids

Pregnancy category: C
Lactation: Contraindicated
Relative cost: $$$$$ (generic available: $$$$)

## URSODEOXYCHOLIC ACID

See Chap. 10 for details.

## NALTREXONE

Brand names: ReVia, Vivitrol, Depade
Manufacturer: ReVia-Teva Pharmaceuticals; Vivitrol-Alkermes, Inc.; Depade-Mallinckrodt Pharmaceuticals

Dosage:
- 50 mg po qd

Contraindications/cautions:
- Concomitant opioid analgesic use, current physiological opioid dependence, acute opioid withdrawal, or failure of naloxone challenge test
- Hypersensitivity to drug or its components

Adverse effects:
- Gastrointestinal: Nausea, vomiting, anorexia, appetite disorder, hepatic enzyme abnormalities, hepatoxicity
- Psychiatric: Depression, insomnia

- Neurological: Opioid withdrawal symptoms, dizziness, syncope, headache, somnolence
- Other: Nasopharyngitis, toothache, injection-site reactions

Drug interactions:
- Opioids

Pregnancy category: C
Lactation: Contraindicated
Relative cost: $$$$$ (generic available: $$$$)

## SERTRALINE

Brand names: Zoloft
Manufacturer: Generic; Zoloft-Pfizer Pharmaceuticals

Dosage:
- 75–100 mg po qd

Contraindications/cautions:
- Use of MAOI medication concomitantly or within 14 days.
- Hypersensitivity to drug or its components
- Bipolar disorder
- Seizure disorder

Adverse effects:
- Neurologic: Serotonin syndrome, mood changes, somnolence, tremor, dizziness, headache, agitation, insomnia
- Gastrointestinal: Diarrhea, dyspepsia, nausea, constipation, anorexia
- Reproductive: Sexual side effects
- Other: Dry mouth, fatigue

Drug interactions:
- Serotonergic drugs (including triptans, TCAs, fentanyl, lithium, tramadol, tryptophan, buspirone, St. John's wort) and with drugs that impair metabolism of serotonin (MAOIs), pimozide, disulfiram, warfarin, digoxin, sumatriptan, lithium, phenytoin, valproate, aspirin, NSAIDs, alcohol, cimetidine, diazepam, and tolbutamide

Pregnancy category: C
Lactation: Caution
Relative cost: $$$$$ (generic available: $$$)
A list of medications used for the treatment of pruritus is shown in Table 13.1.

**Table 13.1 Medications used to treat pruritus**

| *Drug* | *Regimen (po)* | *Efficacy* | *Adverse effects* |
|---|---|---|---|
| Antihistamines | | | |
| • Diphenhydramine<br>• Hydroxyzine | 25–50 mg qid<br>25 mg tid | Rarely provide significant relief apart from sedation | Drowsiness |
| Cholestyramine | 4–6 gm 30 min before meals (or doses may be taken before and after breakfast without an evening dose) | Beneficial in most patients | Fat malabsorption, decreased absorption of other medications, constipation |
| Rifampin | 300 mg bid | Beneficial in some controlled trials | Inducer of hepatic drug metabolizing enzymes, potential hepatotoxicity, red-orange discoloration of urine and secretions |
| Ursodeoxycholic acid | 13–15 mg/kg/day (~20 mg/kg/day for sclerosing cholangitis) | Beneficial in intrahepatic cholestasis of pregnancy | No major toxicity reported |
| Naltrexone | 50 mg qd | Beneficial in small controlled trials | Opiate withdrawal symptoms, rare hepatotoxicity |
| Sertraline | 75–100 mg qd | May be beneficial in cholestatic pruritus | Serotonin syndrome, mood changes, sexual side effects |

Pocket Handbook of GI Therapeutics, Ed. 1, Wu, Pappano eds, Humana Press, 2009

## REFERENCES

1. http://www.pdr.net/drug-summary/benadryl-allergy-ultratabs?druglabelid=3550. Accessed Feb 2016.
2. http://www.pdr.net/drug-summary/Benadryl-Allergy-Liqui-Gels-diphenhydramine-hydrochloride-3514. Accessed Feb 2016.
3. http://www.pdr.net/drug-information/vistaril?druglabelid=3067. Accessed Feb 2016.
4. http://www.pdr.net/drug-summary/Prevalite-cholestyramine-1938. Accessed Feb 2016.
5. http://www.pdr.net/drug-summary/Rifadin-rifampin-1036.2531. Accessed Feb 2016.
6. http://www.drugs.com/uk/rimactane-capsules-150mg-leaflet.html. Accessed Feb 2016.
7. http://www.pdr.net/drug-summary/Vivitrol-naltrexone-1199.2886. Accessed Feb 2016.
8. http://www.vivitrol.com/. Accessed Feb 2016.
9. http://www.pdr.net/drug-summary/Zoloft-sertraline-hydrochloride-474.3608. Accessed Feb 2016.

# III Pancreatic and Malabsorptive Diseases

# 14 Acute and Chronic Pancreatic Disease

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***Contents***



## ACUTE AND CHRONIC PANCREATITIS/PANCREATIC INSUFFICIENCY

For use of analgesic in acute and chronic pancreatitis, see algorithms on suspected chronic pancreatitis, Fig. 14.1, and acute pancreatitis, Fig. 14.2 at the end of the chapter.

## TRAMADOL

Brand names: Ultram, Ultram ER, Rybix, Ryzolt
Manufacturers: Ortho-McNeil-Janssen Pharmaceuticals, Inc; Victory Pharma; Purdue Pharma LP

From: *Clinical Gastroenterology: Pocket Handbook of GI Pharmacotherapeutics*
Edited by: G.Y. Wu, DOI 10.1007/978-3-319-33317-5_14,

Pharmacologic Category: Analgesic, Opioid
Dosage:
- Immediate-release formulation: 50–100 mg po q4–6 h (maximum 400 mg qd).
- Extended-release formulation

  Ultram ER
  Patients not currently on immediate-release (IR): 100 mg po qd; titrate up every 5 days (maximum dose 300 mg po qd).

  Patients currently on immediate-release: Calculate the 24 h immediate-release total dose and start the total extended-release daily dose (round dose to the next lowest 100 mg increment); titrate up (maximum dose 300 mg po qd).

  Ryzolt
  Patients not currently on immediate-release: 100 mg po qd; titrate up every 2–3 days by 100 mg/day (maximum dose 300 mg po qd).

  Patients currently on immediate-release: Calculate 24 h immediate-release total dose and start total extended-release daily dose (round dose to the next lowest 100 mg increment); titrate up (maximum: 300 mg po qd).

- Dosage patients >65 years old: Use caution and start at a lower dose.
- Immediate-release formulation: >75 years old: Do not exceed 300 mg/day.
- Extended-release (ER) formulation: >75 years old: Use with great caution.

Dose Adjustments:

Renal insufficiency
- Immediate-release: CrCl <30 mL/min: Give 50–100 mg po q12 h (maximum: 200 mg/day).
- Extended release: Should not be used in patients with CrCl <30 mL/min.

Hepatic impairment:
- Immediate-release: Cirrhosis: Recommended dose: 50 mg every 12 h.
- Extended release: Should not be used in patients with severe (Child-Pugh class C) hepatic dysfunction (Ryzolt should not be used in any degree of hepatic insufficiency).

Contraindications: Hypersensitivity to tramadol or opioids; opioid-dependent patients; acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids, or psychotropic drugs. Ryzolt is also contraindicated in severe or acute bronchial asthma, hypercapnia, or severe respiratory depression without a closely monitored setting. Tramadol is contraindicated while using or within 14 days of using MAO inhibitor therapy.

Adverse effects:
- Cardiovascular: Flushing
- Central nervous system: Dizziness, headache, somnolence, insomnia
- Dermatologic: Pruritus

- Gastrointestinal: Constipation, nausea, vomiting, dyspepsia
- Neuromuscular and skeletal: Weakness

Less common adverse effects:
Postural hypotension, vasodilation, sweating, fever, upper respiratory tract symptoms, flu-like syndrome, chest pain, anxiety, depression, confusion, impaired coordination, restlessness, malaise, fatigue, vertigo, rash, menopausal symptoms, diarrhea, dry mouth, abdominal pain, decreased appetite, weight loss, flatulence, urinary symptoms, joint pain, back pain, hypertonia, paresthesias, tremor, elevated creatine phosphokinase, visual disturbance.

Drug Interactions:
CNS depression: Ethanol, methotrimeprazine, valerian, St. John's Wort, kava kava, gotu kola
Serotonin syndrome: Tricyclic antidepressants (TCAs), monoamine oxidase (MAO) inhibitors, triptans, venlafaxine, trazodone, lithium, sibutramine, meperidine, dextromethorphan, St. John's wort, serotonin–norepinephrine reuptake inhibitors (SNRIs), and serotonin reuptake inhibitors (SSRIs).
Increased levels of tramadol: Conivaptan, dasatinib, CYP3A4 inhibitors
Decreased levels/therapeutic effects of tramadol: CYP2D6 inhibitors, CYP3A4 inducers, deferasirox

Increased seizure risk: TCAs, SSRIs, MAO inhibitors
Pregnancy category: C
Lactation: Not recommended
Relative cost: $$$ (generic available: $$)

## HYDROMORPHONE

Brand names: Dilaudid-HP; Dilaudid; Exalgo
Manufacturers: Purdue Pharma LP, Mallinckrodt Pharmaceuticals
Pharmacologic Category: Analgesic, Opioid

Dosage:
Acute pain (moderate-to-severe): When administered intravenously, one-fifth of the oral dose will provide similar analgesia.

Oral
Opiate-naive: 2–4 mg every 4–6 h as needed; elderly/debilitated patients may require lower doses; patients with prior opiate exposure may require higher doses. Usual dosage range: 2–8 mg every 3–4 h as needed.

I.V.
- Opiate-naive: 0.2–0.6 mg every 2–3 h as needed; patients with prior opiate exposure may tolerate higher initial doses. Critically ill patients (unlabeled

dose): 0.7–2 mg (based on 70 kg wt) every 1–2 h as needed. More frequent dosing may be required.
- Continuous infusion: Usual dosage range: 0.5–1 mg/h (based on 70 kg patient) or 7–15 mcg/kg/h. Patient-controlled analgesia (PCA): Opiate-naive: Consider lower end of dosing range: Usual concentration: 0.2 mg/mL; demand dose: Usual: 0.1–0.2 mg; range: 0.05–0.4 mg; lockout interval: 5–10 min. Epidural: bolus dose: 1–1.5 mg; infusion concentration: 0.05–0.075 mg/mL; infusion rate: 0.04–0.4 mg/h; demand dose: 0.15 mg; lockout interval: 30 min.
- I.M., sc. use may result in variable absorption and a lag time to peak effect.
  - Opiate-naive: 0.8–1 mg every 4–6 h as needed; patients with prior opiate exposure may require higher initial doses. Usual dosage range: 1–2 mg every 4–6 h as needed.
- Rectal: 3 mg every 4–8 h as needed.

Chronic pain:

Extended-release formulation (Exalgo)
Dosing range: 8–64 mg every 24 h. Only for use in opioid-tolerant patients; all other extended-release opioids should be stopped when beginning therapy. Start Exalgo at 50 % of the calculated total daily dose q24 h, not increased more often than every 3–4 days; titrate the dose with increases of 25–50 % of the current daily dose. If more than two extra doses are needed within 24 h for 2 consecutive days, consider increasing dose, but more often than every 24 h. When discontinuing Exalgo, gradually decrease the dose by 25–50 % every 2–3 days. If converting from transdermal fentanyl to Exalgo, start Exalgo 18 h after removal of the patch. Every 12 mg qd of Exalgo is equal to a fentanyl dose of 25 μg/h transdermally.

Dose Adjustments:

Dosing in elderly patients
- Oral: 1–2 mg every 4–6 h. Tolerance may develop requiring higher doses.
- Renal insufficiency: Exalgo: Moderate impairment: Start at a lower dose and monitor closely. Severe impairment: Consider using another analgesic.
- Hepatic impairment: Exalgo: In patients with moderate and severe hepatic impairment, start at a lower dose and monitor closely. Consider using another analgesic.

Contraindications: Hypersensitivity to hydromorphone or any component of the formulation; acute or severe asthma, severe respiratory depression (in absence of resuscitative equipment or ventilatory support); severe CNS depression.

Adverse effects:
- Cardiovascular: Dysrhythmia (bradycardia/tachycardia), extrasystoles, facial flushing, abnormal blood pressure, palpitations, peripheral edema, peripheral vasodilation, syncope

- Central nervous system: Sleep disturbance (abnormal dreams, insomnia), dizziness/lightheadedness, vertigo, drowsiness, encephalopathy, CNS depression, memory impairment, confusion, cognitive disorder, increased intracranial pressure, headache, seizure, attention disturbance, abnormal coordination, agitation/panic attacks/aggression/depression, suicidal ideation, dysphoria, hallucinations, fatigue, hyper-reflexia, paresthesias, hypothermia, malaise, chills
- Dermatologic: Excess sweating, pruritus, rash/urticaria
- Endocrine and metabolic: Decreased amylase, dehydration, hypokalemia, erectile dysfunction/hypogonadism/decreased libido/decreased testosterone, fluid retention, elevated serum uric acid
- Gastrointestinal: Constipation/diarrhea, abdominal distention, anal fissure, anorexia, bezoar (Exalgo), biliary tract spasm, diverticulosis/-itis, duodenitis, abnormal taste perception, dysphagia, burping, flatulence, abnormal gastric emptying/motility/ileus (Exalgo), gastroenteritis, hematochezia, intestinal obstruction (Exalgo), colonic perforation (Exalgo), nausea, pain with defecation, stomach cramps, vomiting, weight loss, dry mouth
- Genitourinary: Urinary complaints, ureteral spasm
- Hepatic: Abnormal liver function tests
- Local: Pain at injection site (I.M.), wheal/flare over vein (I.V.)
- Neuromuscular and skeletal: Joint pain, dyskinesia, muscle complaints, myoclonus, paresthesias, tremor, weakness
- Ocular: Blurred vision, diplopia, dry eyes, miosis, nystagmus
- Otic: Tinnitus
- Respiratory: Apnea, bronchospasm, dyspnea, hyperventilation, hypoxia, laryngospasm, rhinorrhea
- Miscellaneous: Antidiuretic effects, balance disorder, diaphoresis, difficulty ambulating, histamine release, physical and psychological dependence

Drug Interactions:
- CNS depression: Alcohol, valerian, St. John's Wort, kava kava, gotu kola
- Increase in adverse effects: Alvimopan, desmopressin, MAO inhibitors
- Hypotension/Orthostasis: Antipsychotics (phenothiazines), thiazide diuretics
- Decreased analgesic effect of hydromorphone: Mixed agonist/antagonist opioids, ammonium chloride
- Increased analgesic effect of hydromorphone: Amphetamines
- Serotonin syndrome: Serotonin reuptake inhibitors (SSRIs)
- Bradycardia: Succinylcholine
- Therapeutic effect decreased by hydromorphone: Pegvisomant

Pregnancy category: C
Lactation: Not recommended
Relative Cost: $$ (generic available: $-$$)
A list of equianalgesic agents is shown in Table 14.1.

**Table 14.1 Equianalgesic agents**

| *Drug* | *Injection (mg)* | *Oral (mg)* | *Duration of effect (h)* | *Onset of action (min)* | *Considerations* |
|---|---|---|---|---|---|
| Morphine | 10 | 30 | po 3–4 | iv 5–10<br>Oral 15–30 | Increased active metabolite in renal insufficiency |
| Fentanyl | 0.1 = 100 g | n/a | iv 0.5–1 | iv 1–2 | Safe in renal insufficiency |
| Hydrocodone | n/a | 30 | po 3–4 | po 10–20 | Caution in renal insufficiency |
| Hydromorphone | 1.5 | 6 | po and iv 3–4 | iv 5<br>po 15–30 | Caution in renal insufficiency |
| Oxycodone | n/a | 20 | IR 3–4 | IR 10–15 | CR oxycodone conversion to oral morphine is 1:2 or 2:3 (20 mg oxycodone = 30 mg morphine) |
| | | | ER 8–12 | ER 10–20 | Use clinical judgment when converting. Caution in renal insufficiency |
| Oxymorphone | 1 | 10 | iv 3–6<br>po IR 4–6<br>po ER 12 | iv 5–10<br>po 30 | Decrease initial dose by 50–60 % for CrCl <50 mL/min |
| Tapentadol | n/a | 100 | po 4–6 | po 40–60 | Caution in renal insufficiency. Avoid in patients taking MAOI |
| Hydrocodone bitartrate (Hysingla ER) | n/a | [a] | po 21–27 | po 10–20 | Decrease dosage in renal insufficiency |

*IR* immediate release, *ER* extended release

[a]Hydrocodone bitartrate 20 mg is equivalent to total daily dose (TDD) of hydrocodone (oral) 20 mg. For conversion of this drug from other opioid therapies, please refer to manufacturer website (http://www.hysinglaer.com)

**Table 14.1 (continued)**

Examples of analgesic conversions: hydromorphone iv to morphine po. (1) Total daily dose (TDD) of 100 mg iv hydromorphone. (2) 1.5 mg iv hydromorphone = 30 mg po morphine 3: 1.5 mg iv hydromorphone/30 mg po morphine = 100 mg iv hydromorphone/X mg po morphine
Correct Conversion: 2000 mg po morphine = 100 mg iv hydromorphone
Consultation with pharmacy or pain specialist should be considered when converting high-dose opioid therapies, especially in patients with special considerations or on prior long-acting analgesics such as methadone or suboxone
Table 14.1 adapted, with permission, from The University of Connecticut Health Department of Pharmacy and UptoDate 2015

## GABAPENTIN

Brand name: Neurontin
Manufacturer: Pfizer Inc.
Pharmacologic Category: Anticonvulsant
Mechanism of Action: It is structurally related to GABA, but it does not bind to GABAA or GABAB receptors, and it does not appear to affect the synthesis or uptake of GABA.

Dosage:
- Chronic pain: 300–1800 mg po qd given in three divided doses.
- Postoperative pain: 300–1200 mg po 1–2 h prior to surgery.

Dose reduction in elderly patients may be needed.

Dose Adjustments:

Renal insufficiency
Hemodialysis patients: Dialyzable. If the CrCl <15 mL/min, decrease the daily dose in proportion to creatinine clearance. If the CrCl ≥60 mL/min, give 300–1200 mg po tid; if the CrCl is >30–59 mL/min, give 200–700 mg po bid; if the CrCl is >15–29 mL/min, give 200–700 mg po qd.

Contraindications: Hypersensitivity to gabapentin.

Adverse effects:
- Central nervous system: Somnolence, dizziness, ataxia, fatigue
- Miscellaneous: Viral infections

Less common adverse effects:
Edema, vasodilatation, fever, emotional lability, fatigue/weakness, headache, memory impairment, depression/anxiety, abnormal speech, abnormal coordination, twitching, hyperesthesia, pruritus, rash, hyperglycemia, increased appetite, weight gain, diarrhea/constipation, nausea/vomiting, abdominal pain, dry mouth/throat, dyspepsia, flatulence, abnormal dentition, impotence, leukopenia, tremor, hyperkinesia, abnormal gait, back pain, muscle pain, fracture, nystagmus, diplopia, blurred vision, conjunctivitis, otitis media, rhinitis, respiratory infection, cough, pharyngitis, infection.

Uncommon adverse effects:
Acute renal failure/nephrosis, glycosuria, hematuria, renal stone, anemia, thrombocytopenia, coagulation defect, angina, pericardial rub, pericardial effusion, pericarditis, arrhythmias, palpitations, heart block, heart failure, myocardial infarction, abnormal blood pressure, peripheral vascular disorder, syncope, aspiration pneumonia, pulmonary thrombosis, pulmonary embolus, bronchospasm, dyspnea, irregular ventilation, stroke/intracranial hemorrhage, hemiplegia, CNS tumors, seizure, aphasia, encephalopathy, facial paralysis, glaucoma, retinopathy, blindness, hearing loss, hematemesis, fecal incontinence, colitis, gastroenteritis, pancreatitis, abnormal liver function tests/hepatitis/hepatomegaly, peptic ulcer, hemorrhage, hyperlipidemia, cushingoid appearance, abnormal thyroid function, leukocytosis/lymphocytosis, lymphadenopathy, non-Hodgkin's lymphoma, local myoclonus, meningismus, migraine, nerve palsy, ovarian failure, purpura, angioedema, paresthesias, psychosis, suicidal ideation, thrombophlebitis, skin necrosis.

Drug Interactions:
CNS depression: Alcohol, methotrimeprazine, valerian, St. John's Wort, kava kava, gotu kola
Decreased anticonvulsant effect: Ketorolac, mefloquine
Decreased seizure threshold: Evening primrose

Pregnancy category: C
Lactation: Caution
Relative Cost: $$$ (generic available: $$)

## AMITRIPTYLINE

Brand name: Elavil
Manufacturers: AstraZeneca Pharmaceuticals, LP
Pharmacologic Category: Tricyclic antidepressant, (tertiary amine)

Dosage:
- Depression: 50–150 mg po qd in a single dose at bedtime or in divided doses (maximum dose 300 mg po qd).

Mechanism of Action: Increases the synaptic concentration of serotonin and/or norepinephrine in the central nervous system by inhibition of their reuptake by the presynaptic neuronal membrane.

- Chronic pain (unlabeled use): Initial: 25 mg po qhs (maximum dose 100 mg/d).

Dose Adjustments:
- Dosage in elderly patients: Depression: Initial: 10–25 mg po at bedtime; dose should be increased in 10–25 mg increments every week if tolerated; dose range: 25–150 mg po qd.
- Renal insufficiency: Non-dialyzable.
- Hepatic impairment: Use with caution monitoring plasma levels and patient response.

Contraindications: Hypersensitivity to amitriptyline or any component of the formulation; use of MAO inhibitors within the past 14 days; acute recovery phase following myocardial infarction; concurrent use of cisapride.

Adverse effects: (anticholinergic effects)
- Cardiovascular: Orthostatic hypotension, hypertension, arrhythmia (nonspecific ECG changes), tachycardia, palpitations, AV conduction abnormalities/heart block, cardiomyopathy, myocardial infarction, stroke, syncope
- Central nervous system: Anxiety, insomnia, coma, fatigue, impaired cognitive function, seizure, extrapyramidal symptoms, hallucinations, dizziness, impaired coordination, ataxia, headache, nightmares, hyperpyrexia, suicidal ideation
- Dermatologic: Rash, urticaria, photosensitivity, alopecia
- Endocrine and metabolic: Syndrome of inappropriate antidiuretic hormone secretion, abnormal blood glucose
- Gastrointestinal: Nausea, vomiting, anorexia, weight gain, dry mouth, stomatitis, constipation/diarrhea, ileus, abnormal taste perception, black tongue
- Genitourinary: Urinary retention
- Hematologic: Bone marrow depression, eosinophilia, purpura
- Neuromuscular and skeletal: Paresthesias, peripheral neuropathy, numbness, tremor, weakness
- Ocular: Blurred vision, mydriasis, increased ocular pressure
- Otic: Tinnitus
- Miscellaneous: Withdrawal reaction, diaphoresis

Uncommon adverse effects: Neuroleptic malignant syndrome, serotonin syndrome Drug Interactions:

- CNS depression: Alcohol, propoxyphene, valerian, St. John's Wort, kava kava, gotu kola
- Increase neurotoxic effect: Lithium
- Serotonin syndrome: Monoamine oxidase (MAO) inhibitors, serotonin reuptake inhibitors (SSRIs), sibutramine
- Increased QTc-prolonging effect: Alfuzosin, artemether, chloroquine, ciprofloxacin, dronedarone, nilotinib, pimozide, quinidine, ziprasidone, thioridazine, tetrabenazine, gadobutrol, lumefantrine, quinine
- Increased vasopressor effect: Alpha-/beta-agonists (direct-acting)
- Increased orthostatic hypotension: Altretamine, MAO inhibitors
- Increased stimulatory and cardiovascular effect: Amphetamines
- Increased antiplatelet effect: Aspirin, NSAIDs (COX-2 Inhibitor)
- Increased anticoagulant effect: Vitamin K antagonists (e.g., warfarin)
- Decreased serum concentration: Barbiturates, carbamazepine, St. John's Wort, peginterferon alfa-2b
- Increased serum concentration: Bupropion, cimetidine, cinacalcet, conivaptan, divalproex, quinidine, terbinafine, valproic acid, grapefruit juice, duloxetine, protease inhibitors, SSRIs
- Increased adverse effects: Beta 2-agonists, desmopressin, dexmethylphenidate, methylphenidate, metoclopramide
- Increased seizure risk: Tramadol
- Decreased therapeutic effects/serum concentration: Iobenguane $I^{123}$, acetylcholinesterase inhibitors
- Increased therapeutic effect/serum concentration: Yohimbine
- Decreased antihypertensive effects: Alpha 2-agonists
- Increased anticholinergic effects: Pramlintide
- Increased hypoglycemic effects: Sulfonylureas

Pregnancy Category: C
Lactation: Not recommended
Relative Cost: $ (generic available: $)

## DULOXETINE

Brand name: Cymbalta
Manufacturer: Eli Lilly and Co.
Pharmacologic Category: Antidepressant, serotonin/norepinephrine reuptake inhibitor

Dosage:

Chronic pain syndromes (unlabeled use): Oral: 60 mg po qd.

Dose Adjustments:
- Renal insufficiency: Not recommended for use in CrCl <30 mL/min or end-stage renal disease. In mild-moderate impairment, lower starting doses can be considered with titration up based on response and tolerability.
- Hepatic impairment: Not recommended for use in hepatic impairment.

Contraindications: Current use or within 2 weeks of MAOI (monoamine oxidase inhibitor) use; uncontrolled narrow-angle glaucoma.

- Central nervous system: Somnolence, fatigue, headache, dizziness, insomnia
- Gastrointestinal: Nausea, dry mouth, constipation/diarrhea, decreased appetite

Less common adverse effects: Agitation/anxiety, lethargy, weakness, abnormal sleep/dreams, fever, yawning, hypoesthesia, vertigo, excess sweating, rash, pruritus, decreased libido/orgasm abnormality/erectile dysfunction/ejaculatory dysfunction, hot flushes, vomiting, dyspepsia, decreased appetite, loose stools, abnormal taste, weight gain/loss, flatulence, pollakiuria, abnormal liver function tests, muscle cramps/pain/spasms, tremor, paresthesias, rigors, blurred vision, nasopharyngitis, upper respiratory infection, cough, pharyngolaryngeal pain, seasonal allergies, palpitations

Uncommon adverse effects: Irritability, hallucinations, mania, suicide, mood swings, seizure, disorientation, dysarthria, diplopia, glaucoma, visual disturbance, retinal detachment, keratoconjunctivitis sicca, macular degeneration, dyskinesia, acne, eczema, dermatitis, alopecia, anaphylactic reaction, oropharyngeal edema, flushing, facial edema, angioneurotic edema, anemia, aphthous stomatitis, ataxia, atrial fibrillation, bundle branch block, heart failure, myocardial infarction, supraventricular arrhythmia, syncope, elevated systolic/diastolic blood pressure, hypertensive crisis, orthostatic hypotension, tachycardia, elevated CPK, dysphagia, impaired gastric emptying, gastric ulcer, irritable bowel syndrome, gastritis, gastroenteritis, GI bleeding, abnormal liver function tests, hepatic failure/jaundice, hepatic steatosis, hepatomegaly, esophageal stenosis, abdominal pain, colitis, diverticulitis, dehydration, dyslipidemia, dysuria, ecchymosis, peripheral edema, erythema, erythema multiforme, extrapyramidal syndrome, flu-like syndrome, flushing, gait instability, gingivitis, gynecological bleeding, poor diabetes control, hypersensitivity, hyponatremia, hypothyroidism, laryngitis, leukopenia, lymphadenopathy, malaise, urinary urgency, muscle spasm/tightness/twitching, nephropathy, night sweats, nocturia, polyuria, urinary

retention, phlebitis, photosensitivity, restless leg syndrome, serotonin syndrome, sexual dysfunction, SIADH, Stevens–Johnson syndrome, thirst, throat tightness, thrombocytopenia, tinnitus, trismus, urticaria, withdrawal syndrome

Drug Interactions:
CNS depression: Alcohol, methotrimeprazine, valerian, St. John's Wort, SAMe, kava kava, and gotu kola
Serotonin syndrome: Sibutramine, serotonin reuptake inhibitors (SSRIs), monoamine oxidase (MAO) inhibitors
Increased vasopressor and tachycardic effect: Alpha-/beta-agonists
Decreased antihypertensive effect: Alpha 2-agonists
Increased antiplatelet effect: Aspirin, NSAIDs (nonselective)
Increased serum concentration of drug or active metabolite: Fesoterodine, nebivolol
Decrease metabolism of duloxetine: Fluvoxamine, paroxetine
Decreased therapeutic effect: Iobenguane $I^{123}$, codeine
Increases risk of hepatotoxicity: Alcohol
Orthostatic hypotension: MAO inhibitors
Decreased metabolism: Tricyclic antidepressants, CYP2D6 substrates, tamoxifen, thioridazine
Decreased serum concentration of CYP2D6 substrates: Peginterferon α-2b
Increased serum concentration of CYP2D6 substrates: Darunavir
Increased metabolism of CYP1A2 substrates: CYP1A2 inducers
Decreased metabolism of CYP1A2 substrates: CYP1A2 inhibitors

Pregnancy category: C
Lactation: Not recommended
Relative Cost: $$$$ (generic available: $$$)

## OCTREOTIDE

Brand names: Sandostatin LAR; Sandostatin
Manufacturer: Novartis Pharmaceuticals Corp.
Pharmacologic Category: Antidiarrheal; Antidote; Somatostatin analog

Dosage:
- Diarrhea*
  iv: Initial: 50–100 μg q8 h; increase by 100 μg/dose at 48 h intervals; maximum dose: 500 μg qr h.
- Diarrhea associated with chemotherapy*
  Low grade or uncomplicated, 100–150 μg sc qr h.
  Severe, 100–150 g sc q8 h; may increase to 500–1500 g IV or sc q8 h. Complicated, 100–150 g IV or sc tid or iv infusion: 25–50 g/h; may increase to 500 g 3 tid until controlled.

- Diarrhea associated with graft versus host disease*
  500 g IV q8 h; discontinue within 24 h of resolution; maximum duration of therapy: 7 days.
- Esophageal variceal bleeding*
  25–50 g IV bolus followed by continuous iv infusion of 25–50 μg/h.
- Malignant bowel obstruction*
  150–300 μg sc bid
- Chronic pancreatitis*
  200 μg sc tid

**Octreotide LAR (depo-octreotide)** at a dose of 60 mg im q1 month for daily constant pain.

Dose Adjustments:
- Dosing in elderly patients should begin at the lower end of dosing range.
- Renal insufficiency: Non-dialysis-dependent renal impairment: No dosage adjustment required. Dialysis-dependent renal impairment: Depot injection: Initial dose: 10 mg im q4 weeks; adjust dose based on response (clearance is reduced by approximately 50 %).
- Hepatic impairment: Liver cirrhosis: Depot injection: Initial dose: 10 mg im q4 weeks; adjust dose based on response.

Contraindications: Hypersensitivity to octreotide or any component of the formulation.

Adverse effects:
- Cardiovascular: Bradycardia, chest pain
- Central nervous system: Headache, malaise, fatigue, fever, dizziness
- Dermatologic: Pruritus
- Endocrine and metabolic: Hyperglycemia
- Gastrointestinal: Abdominal pain, nausea, vomiting, diarrhea/constipation, flatulence, cholelithiasis/biliary sludge, biliary duct dilatation
- Local: Injection site pain
- Neuromuscular and skeletal: Back pain, arthropathy, myalgia
- Respiratory: Upper respiratory infection, dyspnea
- Miscellaneous: Antibodies to octreotide, flu-like symptoms

Less common adverse effects: Hypertension, cardiac conduction abnormalities, arrhythmia, palpitations, peripheral edema, angina, cardiac failure, pain, anxiety, depression, hallucinations, confusion, hypoesthesia, insomnia, rash, alopecia, hypothyroidism/goiter, decreased appetite, cramping, tenesmus, dyspepsia, fat malabsorption/steatorrhea, feces discoloration, anemia, joint/muscle pain, paresthesias, rigors, weakness, ear pain, renal stones, cough, pharyngitis, sinusitis, rhinitis, diaphoresis, flushing, hematoma, phlebitis,

abnormal gait, memory loss, dysphonia, neuralgia, somnolence, vertigo, acne, bruising, cellulitis, hypoglycemia, hypokalemia, hypoproteinemia, gout, cachexia, breast pain, impotence, colitis, diverticulitis, dysphagia, gastritis, gastroenteritis, melena, gingivitis, glossitis, stomatitis, abnormal taste perception, dry mouth, incontinence, pollakuria (non-depot formulations), urinary tract infection, injection site hematoma, hyperkinesia, hypertonia, neuropathy, tremor, visual disturbance, tinnitus, albuminuria, renal abscess, bronchitis, epistaxis, bacterial infection, cold symptoms, fungal infections

Uncommon adverse effects: Anaphylactic shock, wheal/erythema, aneurysm/cerebral vascular disorder, intracranial hemorrhage, pituitary apoplexy, increased intraocular pressure, ischemia, hemiparesis, neuritis, hyperesthesia, aphasia, Bell's palsy, migraine, myocardial infarction, atrial fibrillation, cardiac arrest, congestive heart failure, syncope, tachycardia, elevated CK, orthostatic hypotension, hypertensive reaction, pancreatitis, appendicitis, ascending cholangitis, biliary obstruction, fatty liver, hemorrhoids, hepatitis, cholecystitis, cholestatic hepatitis, abnormal liver function tests, jaundice, ascites, gallbladder polyp, gastrointestinal bleeding, peptic ulcer, intestinal obstruction, necrotizing enterocolitis, basal cell carcinoma, breast carcinoma, increased creatinine, deafness, diabetes insipidus/diabetes mellitus, facial edema, galactorrhea, glaucoma, gynecomastia, hematuria, hypoadrenalism, joint effusion, lactation, decreased libido, malignant hyperpyrexia, menstrual abnormalities, nephrolithiasis, renal failure/insufficiency, pancytopenia, petechiae, pleural effusion, hypoxia, status asthmaticus, pneumonia, pneumothorax, pulmonary embolism, pulmonary hypertension, pulmonary nodule, Raynaud's syndrome, retinal vein thrombosis, scotoma/visual field defect, seizure, suicide attempt, thrombophlebitis, thrombosis, urticaria, weight loss, arthritis

Drug Interactions:

- Increased QTc prolongation: Alfuzosin, artemether, chloroquine, ciprofloxacin, dronedarone, gadobutrol, lumefantrine, nilotinib, pimozide, quinine, tetrabenazine, thioridazine, ziprasidone
- Decreased metabolism: Codeine
- Decreased serum concentration: Cyclosporine
- Increased hypoglycemic effect: Hypoglycemic agents, alfalfa, aloe, bilberry, bitter melon, burdock, celery, damiana, fenugreek, garcinia, garlic, ginger, ginseng (American), gymnema, marshmallow, and stinging nettle

Increased adverse effects: Pegvisomant
Pregnancy category: B
Lactation: Caution
Relative Cost: $$$$$

## PANCREATIC INSUFFICIENCY

### *Pancrelipase*

Brand names: Creon, Pancreaze, Pancrelipase, Zenpep
Manufacturers: Abbott Products, Inc. (formerly Solvay Pharmaceuticals Inc.), McNeil Pediatrics, a Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., Eurand, X-gen
Pharmacologic category: Digestive enzymes with varying amounts of lipase, amylase, and protease.

Dosage:
- Pancreatic insufficiency
- Initial oral dose: Lipase 500 units/kg po per meal. Dosage range: Lipase 500–2500 units/kg po per meal. (maximum dose: Lipase 10,000 units/kg po qd or lipase 4000 units/g of fat per day).
- Adjust the dose based on body weight, clinical symptoms, and stool fat content. Allow several days before adjusting the dose. The total daily dose reflects approximately 3 meals per day and 2–3 snacks per day. Half the mealtime dose should be given with a snack. Doses of lipase greater than 2500 units/kg/meal (or lipase > 10,000 units/kg/day) should be used cautiously and only with documentation of 72 h fecal fat measurement. Doses of lipase greater than 6000 units/kg/meal are associated with colonic stricture. The enzyme supplement should be taken with meals or snacks and swallowed whole immediately without crushing or chewing, otherwise mucosal irritation can occur. If needed, the capsules can be opened and added to a small amount of an acidic food ($pH \leq 4$), which should be at room temperature and swallowed right after mixing.

Contraindications:
- Hypersensitivity to product, class, or pork protein; acute pancreatitis; Use caution if history of recurrent bowel obstruction, meconium ileus, Crohn's disease, short bowel syndrome, or prior intestinal surgery.

Adverse effects:
- Central nervous system: Headache
- Gastrointestinal: Abdominal pain

Less common adverse effects: Dizziness, hyper/hypoglycemia, flatulence, early satiety, weight loss, upper abdominal pain, abnormal defecation, cough, nasopharyngitis

Uncommon adverse effects: Allergic reaction/anaphylaxis, pruritis, urticaria, rash, asthma, carcinoma recurrence, constipation, nausea, intestinal obstruction,

fibrosing colonopathy, duodenitis, gastritis, abnormal liver function tests, hyperuricemia, muscle pain/spasm, transient neutropenia, blurred vision

Drug Interactions:
- $H_2$ blockers, proton pump inhibitors, antacids may cause premature dissolution of enteric-coated digestive enzyme products resulting in increased or decreased efficacy.
- May decrease oral iron absorption

Pregnancy category: C
Lactation: Caution
Relative cost: $$$
References: Lexi-comp
A list of pancreatic enzyme replacement preparations is shown in Table 14.2.

**Table 14.2 Pancreatic Enzyme Replacement Preparations**

| *Enteric-coated preparations (brand names)* | *Lipase content (USP units)* | *Protease content (units)* | *Amylase content (units)* |
|---|---|---|---|
| Pancrelipase | 5000 | 17,000 | 27,000 |
| Zenpep | 5000 | 17,000 | 27,000 |
| Zenpep | 10,000 | 34,000 | 55,000 |
| Zenpep | 15,000 | 51,000 | 82,000 |
| Zenpep | 20,000 | 68,000 | 109,000 |
| Creon | 6000 | 19,000 | 30,000 |
| Creon | 12,000 | 38,000 | 60,000 |
| Creon | 24,000 | 76,000 | 120,000 |
| Pancreaze | 4200 | 10,000 | 17,500 |
| Pancreaze | 10,500 | 25,000 | 43,750 |
| Pancreaze | 16,800 | 40,000 | 70,000 |
| Pancreaze | 21,000 | 37,000 | 61,000 |

Table 14.2 adapted from Pocket Handbook of GI Pharmacotherapeutics, ed. 1, Wu and Pappano, eds. Humana, 2000

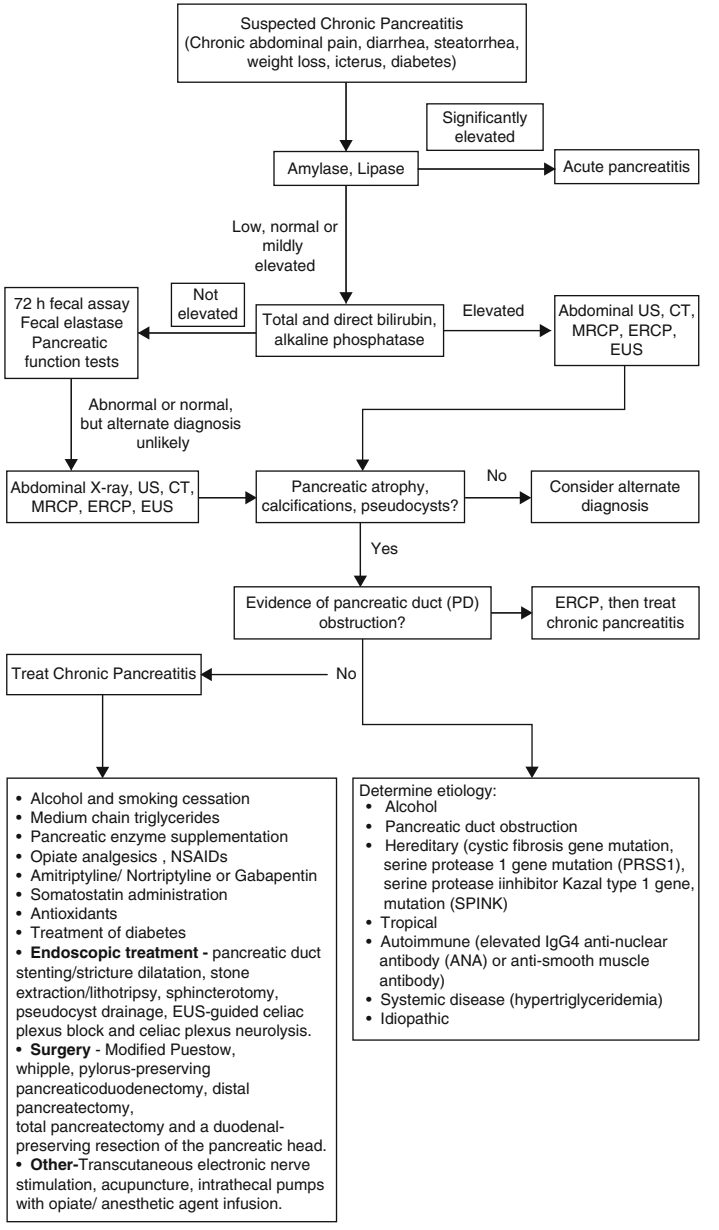


Fig. 14.1 An algorithm for the diagnosis and treatment of chronic pancreatitis with malabsorption

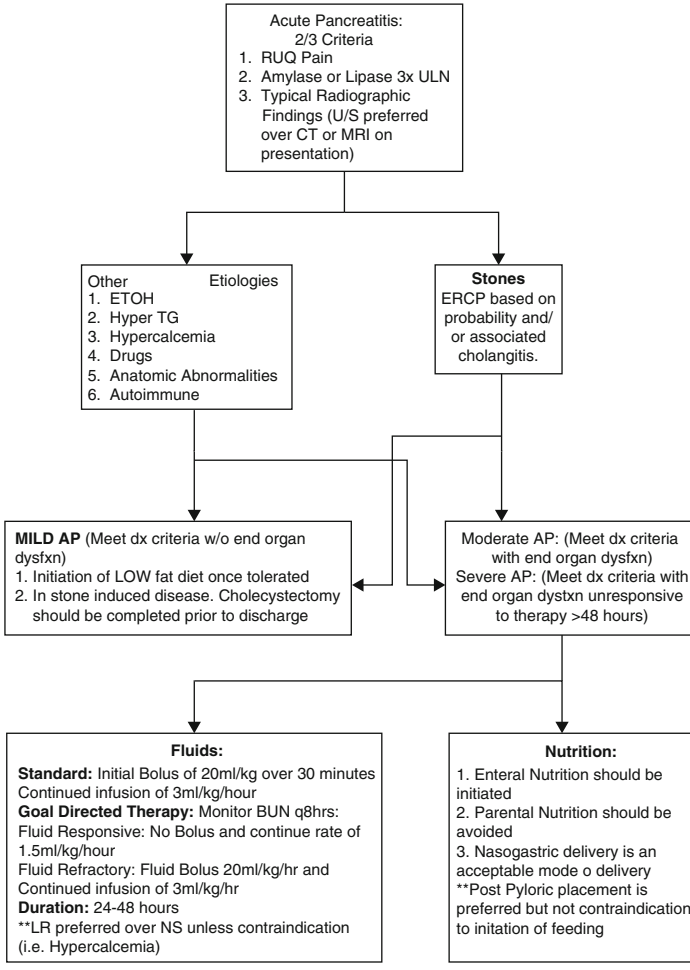


Fig. 14.2 An algorithm for the diagnosis and treatment of acute pancreatitis

## REFERENCES


1. Adeyemi EO, Savage AP, Bloom SR, et al. Somatostatin inhibits neutrophil elastase release in vitro. Peptides. 1990;11:869–71.
2. Aggarwal A. Fluid resuscitation in acute pancreatitis. World J Gastroenterol. 2014;20(48):18092–103.
3. Alkhawaja, Sana, Claudio Martin, Ronald J Butler, Femida Gwadry-Sridhar. Post-pyloric versus Gastric Tube Feeding for Preventing Pneumonia and Improving Nutritional Outcomes in Critically Ill Adults. Cochrane Database Syst Rev 2015;8:CD008875.
4. Fazel A, Li SC, Burton FR. Octreotide relaxes the hypertensive sphincter of Oddi: pathophysiological and therapeutic implications. Am J Gastroenterol. 2002;97:612–6.
5. Equianalgesic Chart. Department of Pharmacy Pocket Reference for Opioid Management. University of Connecticut Health. Department of Pharmacy. Web 10 Mar 2016. http://pharmacy.uchc.edu/references/docs/jdh_pocket_pain_guide.pdf
6. Hegyi P, Rakonczay Jr Z. The inhibitory pathways of pancreatic ductal bicarbonate secretion. Int J Biochem Cell Biol. 2007;39:25–30.
7. Kohler E, Beglinger C, Dettwiler S, et al. Effect of a new somatostatin analogue on pancreatic function in healthy volunteers. Pancreas. 1986;1:154–9.
8. Lexicomp
9. Lieb 2nd JG, Shuster JJ, Theriaque D, et al. A pilot study of Octreotide LAR vs. octreotide tid for pain and quality of life in chronic pancreatitis. JOP. 2009;10:518–22.
10. Linard C, Reyl-Desmars F, Lewin MJ. Somatostatin inhibition of phosphoinositides turnover in isolated rat acinar pancreatic cells: interaction with bombesin. Regul Pept. 1992;41:219–26.
11. Mulvihill SJ, Bunnett NW, Goto Y, et al. Somatostatin inhibits pancreatic exocrine secretion via a neural mechanism. Metabolism. 1990;9(Suppl2):143–8.
12. Petrov MS. Enteral nutrition and the risk of mortality and infectious complications in patients with severe acute pancreatitis. Arch Surg. 2008;143(11):1111–7.
13. Tenner S, Baillie J, Dewitt J, Vege SS, American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013;108(9):1400–15.
14. Toskes PP, Forsmark CE, DeMeo MT, et al. A multicenter controlled trial of octreotide for the pain of chronic pancreatitis. Pancreas. 1993;8:774.
15. Wu BU, Hwang JQ, Gardner TH, Repas K, Delee R, Yu S, Smith B, Banks PA, Conwell DL. Lactated Ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. Clin Gastroenterol Hepatol. 2011;9(8):710–717.e1.
16. UptoDate 2015

# 15 Nutrient and Enzyme Deficiencies

*Houman Rezaizadeh and Erik Olson*

***Contents***



## AMOXICILLIN-CLAVULANIC ACID

Brand name: Augmentin
Class: Penicillin
Manufacturer: GlaxoSmithKline

Dosage:
- 500–875 mg po bid or 250–500 mg po tid, usually for 2 weeks rotating with another antibiotic for 2 weeks

Contraindications/cautions:
- Hypersensitivity to drug or class
- Hepatic dysfunction or cholestatic jaundice with augmentin
- Caution if impaired liver function

Adverse reactions:
- Gastrointestinal: Cholestatic jaundice, hepatotoxicity, diarrhea, pseudomembranous colitis
- Neurological: Seizures
- Renal: Interstitial nephritis

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- Hematological: Anemia, leucopenia, thrombocytopenia
- Immunological: Hypersensitivity reaction, angioedema
- Dermatological: Rash, urticaria, contact dermatitis, erythema multiforme

Drug interactions:
- Avoid concomitant live oral typhoid vaccine due to inadequate vaccine response
- May increase methotrexate levels

Pregnancy category: B
Lactation: Probably safe
Relative cost: $$–$$$ (generic available: $–$$)
For an algorithm for the treatment of small bowel bacterial overgrowth, see Fig. 15.1.

## *Ciprofloxacin*

See Chap. 7.

## *Metronidazole*

See Chap. 6.

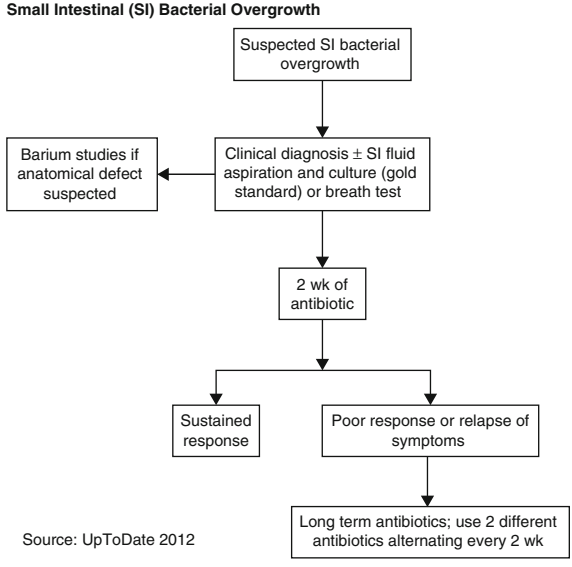


Fig. 15.1 An algorithm for the treatment of small bowel bacterial overgrowth

### *Rifaximin*

See Chap. 10.

### *Octreotide*

See Chap. 2.

## PANCRELIPASE

Brand names: Cotazym, Cotazym-S, Creon 5, Creon 10, Creon 20, Ilozyme, Ku-Zyme, Pancrease, Pancrease MT 10, Pancrease MT 16, Pancrease MT 20, Pancrease MT 4, Pancron D/R, Ultrase, Ultrase MT 12, Ultrase MT 18, Ultrase MT 20, Viokase, Zymase
Manufacturers: Axcan Pharma, Solvay Pharmaceuticals Inc., McNeil-PPC, Inc., Schwarz Pharma
Class: Digestive enzymes with varying amounts of lipase, amylase, and protease.

Dosing: Refer to Table 15.1 for dosing. Titrate dosing to response; take with meals (do not cut/crush/chew. May open caps and sprinkle on soft food with pH <5.5)

Contraindications:
- Hypersensitivity to product or class
- Acute pancreatitis
- Caution if history of recurrent bowel obstruction, meconium ileus, Crohn's disease, short bowel syndrome, or prior intestinal surgery

Adverse reactions:
- Gastrointestinal: Fibrosing colonopathy, bowel obstruction, nausea, vomiting, bloating, cramps, diarrhea, constipation
- Immunological: Allergic reaction, hypersensitivity reaction

Drug interactions:
- $H_2$ blockers, proton pump inhibitors, and antacids may cause premature dissolution of enteric coated digestive enzyme products resulting in increased or decreased efficacy
- Concomitant use of oral iron may decrease iron absorption

Pregnancy category: C
Lactation: Safety unknown
Relative cost: $$$

**Table 15.1 Enzyme preparations for the treatment of pancreatic insufficiency**

| *Brand names* | *Lipase content (USP units)* | *Minimum dose per meal needed to treat steatorrhea* |
|---|---|---|
| Non-enteric coated preparations | | |
| Viokase 8 | 8000 | 6 tabs |
| Viokase 16 | 16,000 | 3 tabs |
| llozyme | 11,000 | 4 tabs |
| Generic pancrelipase | 8000 | 6 tabs |
| Enteric coated preparations | | |
| Creon 5 | 5000 | 9 cap |
| Creon 10 | 10,000 | 5 caps |
| Creon 20 | 20,000 | 2 caps |
| Pancrease MT 4 | 4000 | 11 tabs |
| Pancrease MT 10 | 10,000 | 4 tabs |
| Pancrease MT 16 | 16,000 | 3 tabs |
| Pancrease MT 20 | 20,000 | 2 tabs |
| Ultrase MT 5 | 5000 | 10 tabs |
| Ultrase MT 12 | 12,000 | 4 tabs |
| Ultrase MT 18 | 18,000 | 3 tabs |
| Ultrase MT 20 | 20,000 | 2 tabs |
| Ku-Zyme HP | 8000 | 6 caps |
| Zymase | 12,000 | 4 caps |
| Cotazyme-S | 5000 | 9 caps |

Source: UpToDate 2012

## LACTASE DEFICIENCY

### *Lactase*

Brand name: Lactaid
Manufacturer: Generic

Dosage: Swallow or chew 3 caplets (original strength), 2 caplets (extra strength), or 1 caplet (ultra) po with first bite of dairy product. Adjust dose based on response

No significant adverse effects or drug interactions
Probably safe in pregnancy and lactation
Relative cost: $

## VITAMIN $B_{12}$ DEFICIENCY/PERNICIOUS ANEMIA

### *Vitamin $B_{12}$ (Cyanocobalamin)*

Dosage:
- Start 1000 μg sc/im qd for 1 week, then q week for 1 month, then q month for maintenance
- Poor oral absorption but 1000–2000 μg po may be used for maintenance; also may be given intranasally

Contraindications/caution:
- Hypersensitivity to drug, class or cobalt
- Hereditary optic atrophy
- Caution if uremia, myelosuppression, or folic acid deficiency

Adverse reactions:
- Gastrointestinal: Diarrhea, nausea
- Neurological: Ataxia, nervousness, headache
- Cardiovascular: Pulmonary edema, peripheral vascular thrombosis
- Renal: Hypokalemia
- Hematological: Thrombocytosis

Drug interactions:
- Impaired absorption of oral form with chloramphenicol, neomycin, $H_2$ antagonists, omeprazole, and colchicine

Pregnancy category: C
Lactation: Safe
Relative cost: $

## LYSOSOMAL ACID LIPASE DEFICIENCY (LAL-D)

### *Sebelipase Alfa*

Brand name: Kanuma
Manufacturer: Alexion Pharmaceuticals, Inc.
Mechanism of Action: Sebelipase alfa is internalized into lysosomes and catalyzes the lysosomal hydrolysis of cholesteryl esters and triglycerides to free cholesterol, glycerol, and free fatty acids.

Dosage:
- Lysosomal acid lipase deficiency: IV: 1 mg/kg every other week
- Rapidly progressive lysosomal acid lipase deficiency presenting within the first 6 months of life: Infants: IV: Initial: 1 mg/kg once weekly; if response not optimal, may increase to 3 mg/kg once weekly

Contraindications/cautions:
- None listed within the manufacturer's labeling

Adverse effects:
- CNS: Headache
- Dermatologic: Urticaria
- Endocrine and metabolic: Increase in LDL cholesterol, increase in serum triglycerides
- Gastrointestinal: Diarrhea, vomiting
- Immunologic: Immunogenicity/antibody formation
- Neuromuscular: Weakness
- Respiratory: Rhinitis, cough, nasopharyngitis
- Miscellaneous: Fever

Drug interactions:
- No known significant interactions

Pregnancy category: Not assigned
Lactation: Safety unknown
Relative cost: $$$$$

# INDEX




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