

B.C. INTER-PROFESSIONAL PALLIATIVE SYMPTOM MANAGEMENT GUIDELINES

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DEFINITION

Constipation is the difficult passage of stools, less frequent than normal for the individual.¹⁻³ It includes straining, a sensation of incomplete evacuation, and stool consistency that ranges from small, hard lumps to a large bulky mass. It may cause discomfort or pain.^{2, 4-6, 8} **Diarrhea** is the passage of 3 or more loose stools a day, with urgency. Careful clarification is required to determine diagnosis since reports of diarrhea may include: as a single loose stool, frequent small stools, fecal incontinence, or liquid bypassing due to impaction.⁹⁻¹³

PREVALENCE

Constipation is a significant problem in the palliative care population^{14, 15} affecting 41% of non-cancer patients,¹⁶ 30-50% of patients with cancer,¹⁷⁻¹⁹ and 35-70%, and as high as 87-90%^{6,20} of patients using opioids.²¹⁻²⁷ It is more common in women and affects 24-50% of the elderly.²⁸⁻⁴⁰ Constipation increases as normal overall function decreases and burden of disease increases.⁴¹ **Diarrhea** is not common in palliative care, affecting less than 10% of cancer patients admitted to hospice or hospital.¹⁰

IMPACT

Constipation causes significant suffering through physical symptoms such as abdominal distention, anorexia, nausea and vomiting, halitosis, abdominal and rectal pain, as well as psychological distress leading to headaches, agitation⁸⁰ and delirium.¹ Up to 1/3 of patients modify opioid use to avoid constipation.⁴²⁻⁴⁵ In older adults, constipation is associated with fecal impaction and/or fecal incontinence,⁴⁶ which may be mistaken as diarrhea. This is an embarrassing, distressing and exhausting symptom for both the patient and family, and impacts dignity, mood and relationships.^{6, 9, 10} Fecal impaction can also cause urinary retention,⁴⁷⁻⁴⁹ painful fissures, ulceration, bleeding and anemia.⁵



STANDARD OF CARE

Step 1 | Goals of care conversation

Determine goals of care in conversation with the patient, family and inter-disciplinary team. Refer to additional resources (<u>Additional resources for management of constipation</u>) for tools to guide conversations and required documentation. Goals of care may change over time and need to be reconsidered at times of transition, e.g., disease progression or transfer to another care setting.

Step 2 | Assessment

Constipation Assessment: Using Mnemonic O, P, Q, R, S, T, U and V⁵⁰

Mnemonic Letter	Assessment Questions ^{1, 3, 6, 9, 10, 14, 15, 50, 51} Whenever possible, ask the patient directly. Involve family as appropriate and desired by the patient.	
Onset	When did it begin? How long does it last? How often does it occur? When was your last bowel movement?	
Provoking /Palliating	What brings it on? What makes it better? What makes it worse? What is your appetite like? How is your daily intake of food and fluids? How is your mobility? Do you need help to the bathroom/commode? When toileting? Do you have enough privacy? Do you have pain or any other problems?	
Quality	What is your normal bowel pattern? Are your bowel movements (BM) less frequent than usual? What do the stools look like? Are they smaller or harder than usual? Do you have discomfort or strain when passing stool? Is there controllable urge or sensation, prior to BM? Are you able to empty you bowels completely when desired? Do you have stool leakage or incontinence?	
Region/Radiation	Not applicable	

Constipation assessment: using mnemonic O, P, Q, R, S, T, U and V continued on next page



Constipation Assessment: Using Mnemonic O, P, Q, R, S, T, U and V continued

Severity	How severe is this symptom? What would you rate it on a scale of 0-10 (0 being none and 10 being the worst possible)? Right now? At worst? On average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom?
Treatment	What medications and treatments are you currently using? Are you using any non-prescription treatments, herbal remedies, or traditional healing practices? How effective are these? Do you have any side effects from the medications and treatments? What have you tried in the past? Do you have concerns about side effects or cost of treatments?
Understanding	What do you believe is causing this symptom? How is it affecting you and/or your family? What is most concerning to you? Do you get any other symptoms: pain, nausea/vomiting, loss of appetite, bloating, gas, blood or mucous in stools, headaches or agitation? Do you have any urinary problems? Do you have any previous trauma which may impact how we manage your bowel movements (e.g., rectal interventions may re-traumatize people with past abuse)? How can we make sure you feel safe and respected? Are you worried about incontinence?
Values	What overall goals do we need to keep in mind as we manage this symptom? What is your acceptable level for this symptom (0-10)? Are there any beliefs, views or feelings about this symptom that are important to you and your family?

Symptom Assessment: Physical assessment as appropriate for symptom

Conduct a detailed history and physical examination, including a rectal or stomal exam.^{1, 10, 52-54} Review medications, medical/surgical conditions, psychosocial and physical environment.^{10, 50, 52} **Differentiate fecal impaction with liquid stool bypass from diarrhea.**¹⁰ Further investigations should be tailored to patient prognosis, goals of care, access to health-care resources, and the potential benefits of a precise diagnosis.¹⁴



Diagnostics: consider goals of care before ordering diagnostic testing

- Blood tests are rarely needed but, depending on clinical presentation, CBC, electrolytes, calcium and thyroid function should be evaluated.^{10, 55}
- If obstruction is suspected, X-ray to determine if partial or complete, high or low.^{10, 52, 56}

Step 3 | Determine possible causes and reverse as possible if in keeping with goals of care (For more details, see <u>Underlying causes of constipation in palliative care</u>)

Constipation is often multifactorial in persons with advanced disease. 10, 14, 46, 57

Predisposing risk factors are many (see <u>Underlying causes of constipation in palliative care</u>); most common include: older age, reduced intake, immobility, advanced disease, and use of anticholinergic and/or opioid medications. 10, 57, 58 Opioids are a significant, but not exclusive, cause of constipation 11; therefore, focus should be broader than this single cause. 57



PRINCIPLES OF MANAGEMENT



When considering a management approach, always balance burden of a possible intervention against the likely benefit (e.g., does the intervention require transfer to another care setting?)

- Prevention of constipation is key when risk factors exist (e.g., opioids, decreased intake, decreased physical activity).
- Increase and monitor fluids, dietary fibre, and physical activity, as tolerated. 6, 10, 50
- Identify and correct modifiable risk factors.^{6, 7, 10, 59}
- Discontinue fiber in debilitated patients if unable to maintain hydration, or when bowel obstruction is suspected.^{3,52}
- Anticipate constipating effects of opioids and ensure a prophylactic laxative^{15, 60} unless bowel obstruction or diarrhea.^{1, 41, 55, 59-61}
- Oral measures are preferred and reduce need for rectal interventions.^{2,10}
- Regularly monitor bowel pattern and patient satisfaction to adjust to desired effect.^{1,7}
- Use practice tools to improve management: checklists, laxative protocols, audits.^{2, 3, 59, 62-64}
- Involve interdisciplinary team.⁵⁹ Consider personal, psychosocial and cultural perspectives.⁶
- Constipation is often progressively more challenging over time in end-of-life patients.



Step 4 | Interventions

LEGEND FOR USE OF BULLETS

Bullets are used to identify the type or strength of recommendation that is being made, based on a review of available evidence, using a modified GRADE process.

⊘	Use with confidence: recommendations are supported by moderate to high levels of empirical evidence.
	Use if benefits outweigh potential harm: recommendations are supported by clinical practice experience, anecdotal, observational or case study evidence providing low level empirical evidence.
\triangle	Use with caution: Evidence for recommendations is conflicting or insufficient, requiring further study
X	Not recommended: high level empirical evidence of no benefit or potential harm

Non-pharmacological interventions

Interventions available in the home and residential care facilities

It may be possible to manage constipation in the home or residential care facility with appropriate planning and support for the patient, family and staff; all of these interventions do not necessarily require additional equipment or admission to acute care.



Encourage hydration, fibre intake and mobility, as tolerated^{3, 14, 52, 82}



Wheat bran and prunes improve bowel function, 64 as tolerated.



Refer to **physiotherapy and/or OT** for appropriate exercise and mobility supports¹⁰ as immobility may be more constipating than opioids.^{14, 59, 83}

Non-pharmacological interventions continued on <u>next page</u>



Non-pharmacological interventions continued



Biofeedback training with physiotherapist may also benefit. 65



Avoid use of bedpans. ^{14, 84} Ensure privacy, personal preference, promote independence and convenience during toileting. ^{3, 52, 69, 85, 86}



There is little or no empirical evidence for other complementary approaches. 10

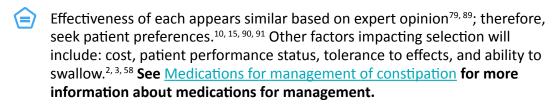


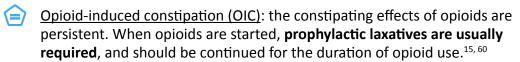
Probiotics, have some evidence of benefit in constipation,⁸⁰ but may also harm.⁸⁷ Avoid use in severely ill or immunocompromised patients.⁸⁸

Pharmacological interventions

ORAL LAXATIVES ARE FIRST-LINE THERAPY FOR CONSTIPATION

Recommended first-line oral laxatives: Sennosides, Lactulose, Polyethylene Glycol





- Sennosides may be the most useful single laxative when an opioid is prescribed. 6, 10, 52, 63, 90, 92, 93
- A combination of a stimulant (e.g., sennosides), plus an osmotic laxative to moisturize and to soften stool (e.g., lactulose or polyethylene glycol (PEG)) may be required, particularly for opioid-induced constipation.^{2, 6, 15, 60, 62}
- Use a stepwise approach, starting with simple, economical laxatives.

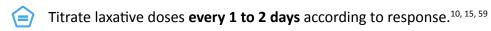
 See the Constipation and bowel obstruction management algorithm.

Pharmacological interventions continued on <u>next page</u>



Pharmacological interventions continued

Titration of Oral Laxatives



Once current regimen satisfactory and well tolerated, continue with it, reviewing regularly with the patient; explain importance of preventing constipation.¹

As the dose of opioids increases, the dose of laxatives often needs to increase, with dosing twice daily (breakfast/bedtime) or even three times daily, 6, 90 up to the maximum recommended or tolerable. 15, 90, 94, 95

The proportional dose of stimulant versus osmotic laxative is guided by stool consistency and tolerance.

<u>If faecal leakage</u>: reduce the dose of the osmotic laxative.^{2, 90} <u>If colic</u> (usually alongside hard stools): increase the osmotic laxative relative to the stimulant,² and/or divide the total stimulant daily dose into smaller, more frequent doses.⁶³

- Evaluate patient tolerance and adverse effects from laxatives. **Refer to**Constipation and bowel obstruction management algorithm.
- Resolve diarrhea from laxatives by holding drugs for 1 to 2 days; restart at a lower dose. 96
- Stop oral laxatives in the last few days of life when patients are no longer able to receive medication and their level of consciousness diminishes. Rectal care then is rare.^{2,59,96}

Use of Rectal Measures: When Standard Oral Laxatives are Unsuccessful

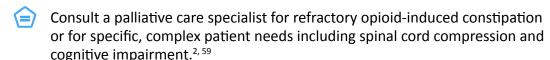
Rectal Interventions (suppository, enema, manual extraction) should be used infrequently. See Constipation and bowel obstruction management algorithm and Constipation and bowel obstructions extra resources or assessment tools for further rectal measures information.

Pharmacological interventions continued on next page



Pharmacological interventions continued

Refractory Constipation: When Standard Optimum Oral and Rectal Measures are Unsuccessful



When OIC suspected, and response to other standard measures is inadequate, opioid antagonists (e.g., methylnaltrexone, naloxegol) may be suitable with specialist advice.² Use only after failure of standard laxative therapy, to augment, not replace laxatives.⁶³ See Constipation and bowel obstruction management algorithm for more information.^{97,98}

Patient and family education

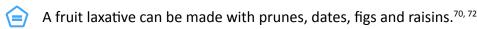
- Explain normal bowel function; this varies from person to person.⁶⁷
- A daily bowel movement is not necessary. As long as stools are soft and easy to pass, ^{68, 69} every 2 to 3 days is acceptable. ^{70,71}
- Don't ignore the urge to have a bowel movement. Try within 30 to 60 minutes following a meal, when the gastro colic reflex commonly occurs. 11, 72-74
- Avoid excess straining as this may be harmful in some medical conditions. 11, 64, 72
- Toilet in sitting position with use of a raised toilet seat, foot stool or bedside commode.
- Privacy during toileting^{11, 13, 22, 72, 73, 75, 76} helps reduce anxiety/aids relaxation.
- Advance pain control helps improve comfort and mobility. 11, 64, 72
- Teach how to differentiate between oozing stool and diarrhea.

Teach constipation prevention

- Increase fluids, dietary fibre, and mobility as tolerated; this is less possible over time.
- Nutritional liquids, milkshakes, cream soups, fruit juices may aid appetite/activity.⁶⁷



Patient and family education continued



When oral intake and mobility are reduced, avoid extra fibre.^{3, 11, 13, 22, 73, 75, 77, 78}
A laxative may be needed.

Patients on opioids for symptom control will need a stimulant laxative from the start of opioids to prevent ongoing constipating effects. 10, 14, 25, 57, 79, 80 (Medications for management of constipation)

Healthcare providers can help choose the laxative type most suited to individual needs.

Explain in advanced illness

Since the body continues to produce 1 to 2 ounces of stool per day, even if no oral intake, ⁸¹ a laxative may still be needed. It can be stopped in the last days of life.

ADDITIONAL RESOURCES FOR MANAGEMENT OF CONSTIPATION

Resources specific to constipation

- ALS of Canada fact sheet on constipation
 - → https://www.als.ca/wp-content/uploads/2017/04/ALSCAN-Constipation.pdf
- BC Guidelines: Constipation
 - http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/palliative2_constipation.pdf
- BC Cancer Agency: Constipation
 - → http://www.bccancer.bc.ca/nursing-site/Documents/3.%20Constipation.pdf
- HealthLink BC: Managing Constipation in Adults with Diet
 - → https://www.healthlinkbc.ca/healthlinkbc-files/constipation-adults

Additional resources for management of constipation continued on next-page



ADDITIONAL RESOURCES FOR MANAGEMENT OF CONSTIPATION CONTINUED

- BC Cancer Agency: Patient handout with suggestions for dealing with constipation
 - → http://www.bccancer.bc.ca/family-oncology-network-site/Documents/ SuggestionsforDealingwithConstipation.pdf

General Resources

- Provincial Palliative Care Line for physician advice or support, call 1877 711-5757 In ongoing partnership with the Doctors of BC, the toll-free Provincial Palliative Care Consultation Phone Line is staffed by Vancouver Home Hospice Palliative Care physicians 24 hours per day, 7 days per week to assist physicians in B.C. with advice about symptom management, psychosocial issues, or difficult end-of-life decision making.
- BC Centre for Palliative Care: Serious Illness Conversation Guide
 - → http://www.bc-cpc.ca/cpc/
- BC Guidelines: Palliative Care for the Patient with Incurable Cancer or Advanced Disease
 - → http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care
- BC Palliative Care Benefits: Information for prescribers
 - http://www2.gov.bc.ca/gov/content/health/practitioner-professionalresources/pharmacare/prescribers/plan-p-bc-palliative-care-benefitsprogram
- National Centre for Complementary and Alternative Medicine (NCCAM)
 for additional information on the use of non-pharmacological interventions
 - → https://nccih.nih.gov/
- Canadian Association of Psychosocial Oncology: Pan-Canadian Practice Guideline: Screening, Assessment and Management of Psychosocial Distress, Depression and Anxiety in Adults with Cancer
 - → http://www.capo.ca/wp-content/uploads/2015/11/FINAL_Distress_
 Guideline1.pdf



ADDITIONAL RESOURCES FOR MANAGEMENT OF CONSTIPATION CONTINUED

- Fraser Health psychosocial care guideline
 - → https://www.fraserhealth.ca/media/psychosocial%20care.pdf

Resources specific to health organization/region

- Fraser Health
 - http://www.fraserhealth.ca/health-professionals/professional-resources/ hospice-palliative-care/
- First Nations Health Authority
 - → http://www.fnha.ca/
- Interior Health
 - → https://www.interiorhealth.ca/YourCare/PalliativeCare/Pages/default.aspx
- Island Health
 - → http://www.viha.ca/pal_eol/
- Northern Health
 - → https://www.northernhealth.ca/Professionals/PalliativeCareEndofLifeCare.aspx
- Providence Health
 - → http://hpc.providencehealthcare.org/
- Vancouver Coastal Health
 - → http://www.vch.ca/your-care/home-community-care/care-options/hospice-palliative-care

Resources specific to patient population

- ALS Society of Canada: A Guide to ALS patient care for primary care physicians
 - → https://als.ca/wp-content/uploads/2017/02/A-Guide-to-ALS-Patient-Care-For-Primary-Care-Physicians-English.pdf
- ALS Society of British Columbia 1-800-708-3228
 - → www.alsbc.ca

Additional resources for management of constipation continued on next page



ADDITIONAL RESOURCES FOR MANAGEMENT OF CONSTIPATION CONTINUED

- BC Cancer Agency: Symptom management guidelines
 - → http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/symptom-management
- BC Renal Agency: Conservative care pathway and symptom management
 - → http://www.bcrenalagency.ca/health-professionals/clinical-resources/ palliative-care
- BC's Heart Failure Network: Clinical practice guidelines for heart failure symptom management
 - → http://www.bcheartfailure.ca/for-bc-healthcare-providers/end-of-life-tools/
- Canuck Place Children's Hospice
 - → https://www.canuckplace.org/resources/for-health-professionals/
 - 24 hr line 1.877.882.2288
 - Page a Pediatric Palliative care physician 1-604-875-2161 (request palliative physician on call)
- Together for short lives: Basic symptom control in pediatric palliative care
 - → http://www.togetherforshortlives.org.uk/professionals/resources/2434 basic symptom control in paediatric palliative care free download

UNDERLYING CAUSES OF CONSTIPATION IN PALLIATIVE CARE^{5, 6, 10, 11, 14, 39, 67, 77}

1. Primary	
Advanced age	Decreased intake
Inactivity	Low fiber diet
• Depression	Poor fluid intake
Sedation	Physical or social impediments

Underlying causes of constipation in palliative care continued on next page



UNDERLYING CAUSES OF CONSTIPATION IN PALLIATIVE CARE^{5, 6, 10, 11, 14, 39, 67, 77} CONTINUED

2.	Secondary		
Meta	abolic disturbances		
•	Dehydration	•	Uremia
•	Hyperglycemia	•	Hypothyroidism
•	Hypokalemia or Hypercalcemia		
Conc	current Disease		
•	Diabetes	•	Anal fissure
•	Hernia	•	Anterior mucosal prolapse
•	Diverticular disease	•	Hemorrhoids
•	Colitis	•	Spinal cord injury
•	Rectocele	•	Multiple Sclerosis, ALS
Neui	rological disorders		
•	Cerebral tumors	•	Sacral nerve infiltration
•	Autonomic failure	•	Spinal cord involvement/compression
Struc	ctural abnormalities		
•	GI obstruction	•	Radiation fibrosis
•	Pelvic tumor mass	•	Painful anorectal conditions (anal fissure, hemorrhoids, perianal abscess)

Underlying causes of constipation in palliative care continued on next-page



UNDERLYING CAUSES OF CONSTIPATION IN PALLIATIVE CARE^{5, 6, 10, 11, 14, 39, 67, 77} CONTINUED

3. latrogenic		
Drugs - Drug Classes	Specific Causative Examples	
5HT3 Antagonists	Ondansetron	
 Antacids 	 Aluminum, bismuth, calcium containing 	
 Anticholinergics 	Atropine, Glycopyrrolate, Hyoscine	
 Anticonvulsants 	Gabapentin, Phenytoin	
 Antidepressants 	 Amitriptyline, Mirtazapine, Nortriptyline, Paroxetine, Sertraline 	
Anti-diarrheal agents	Loperamide, Kaolin/Pectin	
 Antihypertensives 	 Clonidine, Diltiazem, Nifedipine, Verapamil 	
Antiparkinsonian agents	 Levodopa, Pramipexole, Selegiline 	
Antipsychotics	 Haloperidol, Olanzapine, Quetiapine, Risperidone 	
Chemotherapy	Capecitabine, Temozolomide, Vincristine	
Diuretics	 Furosemide, Hydrochlorothiazide when result in dehydration 	
Gastrointestinal agents	Cholestyramine, Sodium Polystyrene Sulfonate	
Hormonal agents	Octreotide	
Opioids	All. Fentanyl, Methadone may be least constipating	
Psyllium/Fiber	Occurs if insufficient fluid co-administered	
Supplements	Iron or calcium	

There are many medications that are reported to cause constipation. ⁹⁹ This table above provides some examples. Consult pharmacist if additional assistance is required.



MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

Avoid laxatives, especially stimulants, if intestine is fully obstructed; seek consult.

Drug, Action	Dose, Therapeutic	Onset, Adverse Effects, Precautions
	Range	and Dosing Concerns
Sennosides / Senna stimulant	Starting dose: 1 to 2 tablets PO at bedtime or 10 mL syrup. Maximum daily tablet dose: 36 mg PO TID ^{95,100}	6 to 12 hours. ^{6, 90} Intestinal colic is principal adverse effect ⁹² and may be similar to the cramping of severe constipation. Contraindicated in abdominal pain, nausea and vomiting, intestinal obstruction. ⁶⁹ Long term use considered safe. ^{10, 14} Start at bedtime, if dose increases required, add next dosing time at breakfast. This timing best matches drug onset to natural gastro-colic peristalsis.
		Irritable bowel syndrome patients may experience painful cramps; osmotic laxatives are often preferred. ⁹⁵
Lactulose osmotic	Starting dose: 15 mL PO daily with food. Maximum daily dose: 30 mL PO BID ^{55, 101}	1 to 2 days. 52, 69 Abdominal bloating, flatulence (20% for the first few days), nausea (may be reduced if diluted or taken with meals), intestinal colic. 90 Rarely causes serious electrolyte disorders or volume overload. 10, 52, 69 Contraindicated in galactosemia, intestinal obstruction. 69 Avoid in lactose-intolerant patients. 52 Use with hot tea, hot water or juices to improve unpalatable sweet taste. 6, 10 Lactulose does not affect diabetes mellitus management. 90
		Effectiveness requires a sufficiently high fluid intake.1



MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

CONTINUED

Drug, Action	Dose, Therapeutic Range	Onset, Adverse Effects, Precautions and Dosing Concerns
Polyethylene Glycol "PEG" osmotic	Starting dose: 17 g PO daily. Maximum daily dose: 2 17 g PO BID ⁹⁰ to TID ⁶⁹ 2 PCF5- BID, OB 139TID	1 to 3 days. 69 Nausea, bloating, occasional vomiting, stomach cramps. 69 Requires 125 to 250 mL fluid intake daily per 17 g dose. 69, 102 Contraindicated in intestinal obstruction or perforation, inflammatory bowel conditions (Crohn's disease, ulcerative colitis). 69 Adverse effect profile may be better than other oral laxatives. 62, 91 Use cautiously in patients unable to tolerate the fluid volume needed, e.g., if nauseated or frail. Used safely up to 6 to 12 months. 51
Glycerin Suppositories osmotic, lubricant	Dose: 1 supp PR x 1	15 to 30 min. ^{1, 90} Adverse effects rare but may include mild rectal irritation. ^{51, 103} Avoid suppositories in patients with severely reduced white cell or platelet counts due the risk of bleeding or infection. ⁶ Suppositories should be retained for 15 minutes. ^{6, 103, 104}
Drug, Action	Dose, Therapeutic Range	Onset, Adverse Effects, Precautions and Dosing Concerns
Bisacodyl Suppositories stimulant	Dose: 1 supp PR x 1	20 to 60 min, up to 3 hours. 90 Side effects rare but can cause occasional abdominal cramps and diarrhea or local rectal inflammation. 90 Can worsen pre-existing rectal tears and anal fissures. 55 Occasionally causes faecal leakage. Avoid suppositories in patients with severely reduced white cell or platelet counts due the risk of bleeding or infection. 6 Place suppository against rectal wall, not into faeces, to ensure effectiveness. 90



MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

CONTINUED

Drug, Action	Dose, Therapeutic Range	Onset, Adverse Effects, Precautions and Dosing Concerns
Micro-enema osmotic, softener	Starting dose: 5 mL PR x 1 Maximum dose: 10 mL PR daily	5 to 20 min, up to 60 min. ^{1, 90} Risk of intestinal necrosis: avoid use with sodium polystyrene sulfonate containing products. Do not use in the presence of abdominal pain, nausea, fever or vomiting.
		Contents include sodium citrate, sorbitol and sodium lauryl sulfoacetate ¹¹⁴
Mineral Oil Enema	Dose:	2 to 15 minutes
(stool softener)	130 mL PR x 1	Warm to room temperature before use.90
	Maximum dose: 1 enema PR daily	
Sodium-phosphate	Starting dose:	2 to 5 minutes, up to 30 minutes. 1, 90 Elderly
enema	130 mL PR x 1	patients (over 65) are particularly at risk of
osmotic		serious electrolyte disturbances. Fatalities have been reported. Contraindicated in
	Maximum dose:	renal failure. 100 Avoid multiple applications to
	1 enema PR daily	minimize risk of adverse effects. 103 If enemas are ever used regularly, must monitor for electrolyte, fluid imbalances, rectal trauma. 96 Warm to room or body temperature before use. 1,90



MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

CONTINUED

Drug, Action	Dose, Therapeutic Range	Onset, Adverse Effects, Precautions and Dosing Concerns
Methylnaltrexone peripheral opioid receptor antagonist	Subcutaneous injection every 2 days as needed. Dose is weight based:	24 minutes to 4 hours. 106, 107 Abdominal pain, diarrhea, nausea, flatulence. Rare: flushing, delirium, severe diarrhea leading to dehydration and subsequent cardiovascular collapse, extrasystoles. 98
	33-37 kg=6 mg 38-61 kg= 8 mg 62-114 kg=12 mg 115-126 kg=18 mg Outside these ranges, dose 0.15 mg/kg. Reduce doses by 50% when creatinine clearance is less than 30 mL/min.	Caution: Gastrointestinal (GI) perforation is a risk of this medication for patients with advanced illness such as: cancer, GI malignancy, GI ulcer, and Ogilvie's syndrome and taking medications such as bevacizumab, non-steroidal anti-inflammatory drugs and steroids. 115 To be used in conjunction with ongoing laxative therapy when laxatives alone are insufficient for treatment of opioid-induced constipation for advanced illness palliative care patients. 106, 107 Stop if response inadequate after four doses. 107 No drug interactions with cytochrome P450 metabolized drugs. 107 Balance drug cost alongside staffing costs, patient outcomes. 97, 98

Medications for management of constipation continued on <u>next page</u>



MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

CONTINUED

Drug, Action	Dose, Therapeutic Range	Onset, Adverse Effects, Precautions and Dosing Concerns
Naloxegol peripheral opioid receptor antagonist	Usual dose: 12.5 to 25 mg PO daily Maximum daily dose: 25 mg PO daily	6 to 12 hours. 108 50% of people respond within 12 hours. 109 Naloxegol is indicated for the treatment of opioid-induced constipation in adult patients with non-cancer pain who have had an inadequate response to laxatives. 109 Usual starting dose is 25 mg daily. Reduce to 12.5 mg daily if moderate to end-stage renal impairment or if used concomitantly with weak CYP3A4 inhibitors (e.g., cimetidine, quinidine). Renal patients can increase dose to 25 mg daily if the 12.5 mg dose is well tolerated. 109 Abdominal pain, flatulence, headache, diarrhea, and nausea 109 Anticipate numerous significant CYP3A4 drug interactions. Contraindicated in patients concomitantly receiving strong CYP3A4 inhibitors (e.g., ketoconazole, voriconazole, clarithromycin, protease inhibitors such as ritonavir). Interactions also occur with P-glycoprotein transporters (P-gp) modulators. 109 Avoid grapefruit juice. 109



MEDICATIONS FOR MANAGEMENT OF CONSTIPATION

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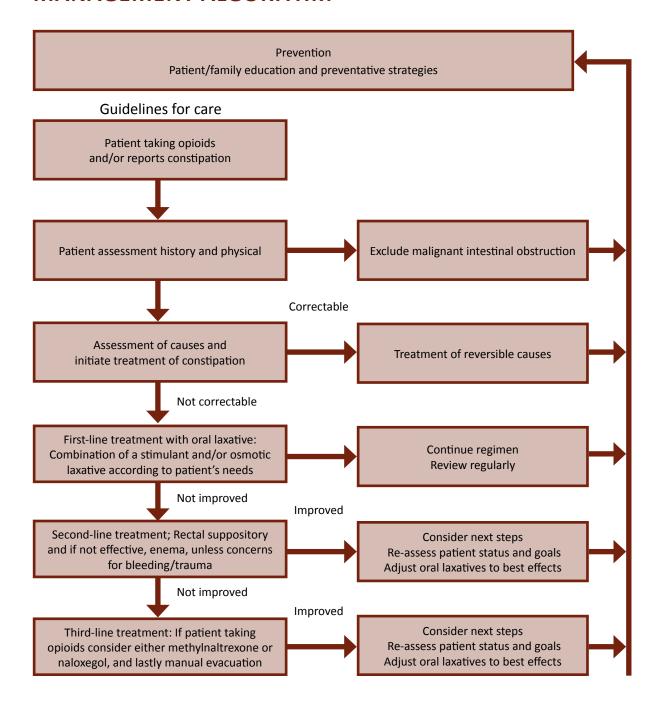
Drug, Action	Dose, Therapeutic Range	Onset, Adverse Effects, Precautions and Dosing Concerns
		Contraindicated in known or suspected GI obstruction or patients at risk of recurrent obstruction due to potential for GI perforation. Caution: if using in patients with any risk of impaired integrity of the gastrointestinal tract wall (e.g., severe peptic ulcer disease, Crohn's Disease, active or recurrent diverticulitis, infiltrative gastrointestinal tract malignancies or peritoneal metastases), consider the overall benefit/risk profile for a given patient. 109 When started, all current laxative therapy should be stopped until clinical effect of naloxegol is determined. 109 Does not cause systemic opioid withdrawal symptoms. Take in the morning on an empty stomach at least 1 hour prior to the first meal of the day or 2 hours post-meal. 109 Balance drug cost alongside staffing costs,
		patient outcomes. ^{97, 98}

[†] Off-label. PO = by mouth IV = Intravenous, SC = Subcutaneous, TID = three times daily, QID = four times daily ODT = oral dissolving tablet, CSCI = continuous subcutaneous infusion.

Prices for prescription drugs may be obtained from BC PharmaCare. The British Columbia Palliative Care Benefits Plan (http://www2.gov.bc.ca/assets/gov/health/health-drug-coverage/pharmacare/palliative-formulary.pdf) provides province-wide drug coverage for many of the recommended medications; check website to confirm coverage. **Consider price when choosing similarly beneficial medications, especially when the patient/family is covering the cost.**



CONSTIPATION AND BOWEL MANAGEMENT ALGORITHM^{3,4,7}



Refer to Medications for management of constipation for further drug details including precautions and contraindications. Refer to guideline sections for specifics for prevention and patient/family education and preventative strategies

Constipation and bowel obstruction references continued on next page

Algorithm adapted from Cancer Care Ontario – algorithm. 74



CONSTIPATION AND BOWEL OBSTRUCTIONS EXTRA RESOURCES OR ASSESSMENT TOOLS

- Victoria Bowel Performance Scale:¹¹⁰
 - http://www.victoriahospice.org/sites/default/ files/2bbbowelperformancescale.pdf
- Bristol Stool Form Scale and Stool Diary:^{111, 112}
 - → http://www.bowelcontrol.nih.gov/stool diary 508.pdf

CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES

- 1. Scotland N. Constipation in palliative care: NHS Scotland; 2014.
- 2. Larkin PJ, Sykes NP, Centeno C, Ellershaw JE, Elsner F, Eugene B, et al. The management of constipation in palliative care: clinical practice recommendations. Palliat Med. 2008;22(7):796-807.
- 3. Librach SL, Bouvette M, De Angelis C, Farley J, Oneschuk D, Pereira JL, et al. Consensus recommendations for the management of constipation in patients with advanced, progressive illness. J Pain Symptom Manage. 2010;40(5):761-73.
- 4. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology. 2006;130(5):1480-91.
- 5. Rao S. Constipation in the older adult: UpToDate; 2015 [
- 6. Caraccia Economou D. Bowel management: Constipation, diarrhea, obstruction, and ascites: Oxford University Press; 2015.
- 7. Algorithm WPCPCAM. WRHA Palliative Care Program Constipation Assessment & Management Algorithm. In: Algorithm WPC, editor.: Victoria Hospice Society; 2009.
- 8. Goodman M, Low J, Wilkinson S. Constipation management in palliative care: a survey of practices in the United kingdom. J Pain Symptom Manage. 2005;29(3):238-44.
- Scotland HI. Diarrhoea 2014.
- 10. Sykes NP. Constipation and diarrhoea: Oxford University Press; 2015.



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

- 11. Carter B, Black F, Downing G. Bowel Care Constipation and Diarrhea. In: Downing GM, Wainwright W, editors. Medical Care of the Dying. Victoria, B.C. Canada: Victoria Hospice Society Learning Centre for Palliative Care; 2006.
- 12. Waller A, Caroline N. Diarrhea. Boston, MA2000.
- 13. Waller A, Caroline N. Constipation. 2000. In: Handbook of Palliative Care in Cancer [Internet]. Woburn, MA: Butterworth-Heinemann. 2nd ed.
- 14. Prichard D, Bharucha A. Management of opioid-induced constipation for people in palliative care. Int J Palliat Nurs. 2015;21(6):272, 4-80.
- 15. Cheng CW, Kwok AO, Bian ZX, Tse DM. A cross-sectional study of constipation and laxative use in advanced cancer patients: insights for revision of current practice. Support Care Cancer. 2013;21(1):149-56.
- 16. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain. 2004;112(3):372-80.
- 17. de Groot JW, Peters FT, Reyners AK. [Treatment of constipation in the palliative care phase]. Ned Tijdschr Geneeskd. 2010;154:A2224.
- 18. Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients. Support Care Cancer. 2000;8(3):175-9.
- 19. Noguera A, Centeno C, Librada S, Nabal M. Screening for constipation in palliative care patients. J Palliat Med. 2009;12(10):915-20.
- 20. Sykes NP. The relationship between opioid use and laxative use in terminally ill cancer patients. Palliat Med. 1998;12(5):375-82.
- 21. Hellwig TR, Pottebaum AA. The role of methylnaltrexone in opioid-induced constipation. S D Med. 2013;66(10):425, 7.
- Tamayo AC, Diaz-Zuluaga PA. Management of opioid-induced bowel dysfunction in cancer patients. Support Care Cancer. 2004;12(9):613-8.



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

- 23. Choi YS, Billings JA. Opioid antagonists: a review of their role in palliative care, focusing on use in opioid-related constipation. J Pain Symptom Manage. 2002;24(1):71-90.
- 24. Panchal SJ, Müller-Schwefe P, Wurzelmann JI. Opioid-induced bowel dysfunction: prevalence, pathophysiology and burden. Int J Clin Pract. 2007;61(7):1181-7.
- 25. Pappagallo M. Incidence, prevalence, and management of opioid bowel dysfunction. Am J Surg. 2001;182(5A Suppl):11S-8S.
- 26. Klepstad P, Borchgrevink PC, Kaasa S. Effects on cancer patients' health-related quality of life after the start of morphine therapy. J Pain Symptom Manage. 2000;20(1):19-26.
- 27. Reid CM, Martin RM, Sterne JA, Davies AN, Hanks GW. Oxycodone for cancer-related pain: meta-analysis of randomized controlled trials. Arch Intern Med. 2006;166(8):837-43.
- 28. Talley NJ, O'Keefe EA, Zinsmeister AR, Melton LJ. Prevalence of gastrointestinal symptoms in the elderly: a population-based study. Gastroenterology. 1992;102(3):895-901.
- 29. Talley NJ, Fleming KC, Evans JM, O'Keefe EA, Weaver AL, Zinsmeister AR, et al. Constipation in an elderly community: a study of prevalence and potential risk factors. Am J Gastroenterol. 1996;91(1):19-25.
- 30. Wald A, Scarpignato C, Mueller-Lissner S, Kamm MA, Hinkel U, Helfrich I, et al. A multinational survey of prevalence and patterns of laxative use among adults with self-defined constipation. Aliment Pharmacol Ther. 2008;28(7):917-30.
- 31. Sandler RS, Jordan MC, Shelton BJ. Demographic and dietary determinants of constipation in the US population. Am J Public Health. 1990;80(2):185-9.
- 32. Everhart JE, Go VL, Johannes RS, Fitzsimmons SC, Roth HP, White LR. A longitudinal survey of self-reported bowel habits in the United States. Dig Dis Sci. 1989;34(8):1153-62.
- 33. Whitehead WE, Drinkwater D, Cheskin LJ, Heller BR, Schuster MM. Constipation in



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

the elderly living at home. Definition, prevalence, and relationship to lifestyle and health status. J Am Geriatr Soc. 1989;37(5):423-9.

- 34. Donald IP, Smith RG, Cruikshank JG, Elton RA, Stoddart ME. A study of constipation in the elderly living at home. Gerontology. 1985;31(2):112-8.
- 35. Harari D, Gurwitz JH, Avorn J, Bohn R, Minaker KL. Bowel habit in relation to age and gender. Findings from the National Health Interview Survey and clinical implications. Arch Intern Med. 1996;156(3):315-20.
- 36. Choung RS, Locke GR, Schleck CD, Zinsmeister AR, Talley NJ. Cumulative incidence of chronic constipation: a population-based study 1988-2003. Aliment Pharmacol Ther. 2007;26(11-12):1521-8.
- 37. Rosti G, Gatti A, Costantini A, Sabato AF, Zucco F. Opioid-related bowel dysfunction: prevalence and identification of predictive factors in a large sample of Italian patients on chronic treatment. Eur Rev Med Pharmacol Sci. 2010;14(12):1045-50.
- 38. Ishihara M, Ikesue H, Matsunaga H, Suemaru K, Kitaichi K, Suetsugu K, et al. A multi-institutional study analyzing effect of prophylactic medication for prevention of opioid-induced gastrointestinal dysfunction. Clin J Pain. 2012;28(5):373-81.
- 39. Sykes NP. An investigation of the ability of oral naloxone to correct opioid-related constipation in patients with advanced cancer. Palliat Med. 1996;10(2):135-44.
- 40. McCrea GL, Miaskowski C, Stotts NA, Macera L, Paul SM, Varma MG. Gender differences in self-reported constipation characteristics, symptoms, and bowel and dietary habits among patients attending a specialty clinic for constipation. Gend Med. 2009;6(1):259-71.
- 41. Mellar DP. Cancer constipation: are opioids really the culprit? Supportive Care in Cancer [Internet]. 2008; 16(5):[427-9 pp.].
- 42. Bell TJ, Panchal SJ, Miaskowski C, Bolge SC, Milanova T, Williamson R. The prevalence, severity, and impact of opioid-induced bowel dysfunction: results of a US and European Patient Survey (PROBE 1). Pain Med. 2009;10(1):35-42.
- 43. Thomas JR, Cooney GA, Slatkin NE. Palliative care and pain: new strategies for managing opioid bowel dysfunction. J Palliat Med. 2008;11 Suppl 1:S1-19; quiz S21-2.



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

- 44. Candrilli SD, Davis KL, Iyer S. Impact of constipation on opioid use patterns, health care resource utilization, and costs in cancer patients on opioid therapy. J Pain Palliat Care Pharmacother. 2009;23(3):231-41.
- 45. Bell T, Annunziata K, Leslie JB. Opioid-induced constipation negatively impacts pain management, productivity, and health-related quality of life: findings from the National Health and Wellness Survey. J Opioid Manag. 2009;5(3):137-44.
- 46. Candy B, Jones L, Goodman ML, Drake R, Tookman A. Laxatives or methylnaltrexone for the management of constipation in palliative care patients. Cochrane Database Syst Rev. 2011(1):CD003448.
- 47. Rao SS. Constipation: evaluation and treatment of colonic and anorectal motility disorders. Gastroenterol Clin North Am. 2007;36(3):687-711, x.
- 48. Sykes NP. The pathogenesis of constipation. J Support Oncol. 2006;4(5):213-8.
- 49. Twycross R, Sykes N, Mihalyo M, Wilcock A. Stimulant laxatives and opioid-induced constipation. J Pain Symptom Manage. 2012;43(2):306-13.
- 50. Health F. Symptom Guidelines: Hospice Palliative Care, Clinical Practice Committee; 2006 [Available from: http://www.fraserhealth.ca/health-professionals/ professional-resources/hospice-palliative-care/]
- 51. Fritz D, Pitlick M. Evidence about the prevention and management of constipation: implications for comfort part 1. Home Healthc Nurse. 2012;30(9):533-40; quiz 40-2.
- 52. Portenoy R, Mehta Z, Ahmed E. Cancer pain management with opioids: Prevention and management of side effects: UptoDate; 2017 [
- 53. Wald A. Etiology and evaluation of chronic constipation in adults: UpToDate; 2016 [
- 54. Bharucha AE, Pemberton JH, Locke GR. American Gastroenterological Association technical review on constipation. Gastroenterology. 2013;144(1):218-38.
- 55. Chai E, Meier D, Morris J, Goldhirsch S. Constipation: Oxford University Press; 2014.
- 56. Jashed N, Lee ZE, W. OK. Diagnostic approach to chronic constipation in adults; 84:[299-306 pp.].



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

- 57. Clark K, Lam LT, Agar M, Chye R, Currow DC. The impact of opioids, anticholinergic medications and disease progression on the prescription of laxatives in hospitalized palliative care patients: a retrospective analysis. Palliat Med. 2010;24(4):410-8.
- 58. Cayley WE. Management of constipation in patients receiving palliative care. Am Fam Physician. 2011;84(11):1227-8.
- 59. Committee NCE. Management of Constipation in Adult Patients Receiving Palliative Care. National Clinical Guideline: An Roinn Slainte Department of Health No. 10; 2015.
- 60. Clemens KE, Faust M, Jaspers B, Mikus G. Pharmacological treatment of constipation in palliative care. Curr Opin Support Palliat Care. 2013;7(2):183-91.
- 61. DeRegil ML, PenaRosas PJ, FernandezGaxiola AC, RaycoSolon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. Cochrane Database of Systematic Reviews [Internet]. 2015.
- 62. Caresearch. Constipation2017. Available from: https://www.caresearch.com.au/caresearch/tabid/744/Default.aspx.
- 63. Twycross R, Wilcock A. Palliative Care Formulary. In: Twycross R, Wilcock A, editors. Palliative Care Formulary. 4th ed ed: Palliativedrugs.com Ltd; 2011.
- 64. Clark K, Byfieldt N, Dawe M, Currow DC. Treating constipation in palliative care: the impact of other factors aside from opioids. Am J Hosp Palliat Care. 2012;29(2):122-5.
- 65. Staff MC. Constipation: Mayo Clinic; 1998-2017 [Available from: http://www.mayoclinic.org/diseases-conditions/constipation/diagnosis-treatment/treatment/txc-20252759?p=1.
- 66. Ontario CC. Bowel Care. Symptom Management Guide-to-Practice 2012.
- 67. Nursing BCAPP. Telephone Consultation Protocol: Constipation. 2006.
- 68. Scotland N. Scottish Palliative Care Guidelines2014 [cited 2016 12/15/2016]. Available from: http://www.palliativecareguidelines.scot.nhs.uk/guidelines/symptom-control/Nausea-and-Vomiting.aspx.



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

- 69. Connolly M, Larkin P. Managing constipation: a focus on care and treatment in the palliative setting. Br J Community Nurs. 2012;17(2):60, 2-4, 6-7.
- 70. Agency BCC. Management of Constipation draft. Suggestions for dealing with constipation draft: British Columbia Cancer Agency.
- 71. Ontario CC. How to manage your constipation. Cancer Care Ontario; 2016.
- 72. Paolini CA, Family Medicine DvoG. Symptoms management at the end of life. J Am Osteopath Assoc. 2001;101(10):609-15.
- 73. Beckwith C. Evidence Based Symptom Control in Palliative Care: Constipation in Palliative Care Patients. 2000.
- 74. Ontario CC. Constipation Symptoms in Adults with Cancer Algorithm. In: (Algorithm) BC-C, editor. 2012.
- 75. Esper P, Heidrich D. Symptom clusters in advanced illness. Semin Oncol Nurs. 2005;21(1):20-8.
- 76. Dean M, Harris J-D, Regnard C. Symptom Relief in Palliative Care. 2nd ed. Seattle: Radcliffe Publishing; 2006.
- 77. Fallon M, O'Neill B. ABC of palliative care. Constipation and diarrhoea. BMJ. 1997;315(7118):1293-6.
- 78. Cadd A, Keatinge D, Henssen M, O'Brien L, Parker D, Rohr Y, et al. Assessment and documentation of bowel care management in palliative care: incorporating patient preferences into the care regimen. J Clin Nurs. 2000;9(2):228-35.
- 79. Candy B, Jones L, Larkin PJ, Vickerstaff V, Tookman A, Stone P. Laxatives for the management of constipation in people receiving palliative care. Cochrane Database Syst Rev. 2015(5):CD003448.
- 80. Pitlick M, Fritz D. Evidence about the pharmacological management of constipation, part 2: implications for palliative care. Home Healthc Nurse. 2013;31(4):207-18.
- 81. Program CHRPC. Bowel Care Protocol for Palliative Care Patients. 2003.



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

- 82. Santucci G, Battista V. Methylnaltrexone for opioid-induced constipation in patients at the end of life. Int J Palliat Nurs. 2015;21(4):162, 4.
- 83. Fallon M. Constipation in cancer patients: prevalence, pathogenesis, and cost-related issues. Journal of Pain [Internet]. 1999; 3(1):[3-7 pp.].
- 84. Su Y, Zhang X, Zeng J, Pei Z, Cheung RT, Zhou QP, et al. New-onset constipation at acute stage after first stroke: incidence, risk factors, and impact on the stroke outcome. Stroke. 2009;40(4):1304-9.
- 85. Bouras EP, Tangalos EG. Chronic constipation in the elderly. Gastroenterol Clin North Am. 2009;38(3):463-80.
- 86. Iovino P, Chiarioni G, Bilancio G, Cirillo M, Mekjavic IB, Pisot R, et al. New onset of constipation during long-term physical inactivity: a proof-of-concept study on the immobility-induced bowel changes. PLoS One. 2013;8(8):e72608.
- 87. Doron S, Snydman DR. Risk and safety of probiotics. Clin Infect Dis. 2015;60 Suppl 2:S129-34.
- 88. Pham M, Lemberg DA, Day AS. Probiotics: sorting the evidence from the myths. Med J Aust. 2008;188(5):304-8.
- 89. Caresearch. Bowel Management2017. Available from: https://www.caresearch.com.au/caresearch/tabid/1738/Default.aspx.
- 90. palliativedrugs.com. Palliative Care Formulary 2014 [5th ed:[Available from: www.palliativedrugs.com.
- 91. Carsearch. Laxatives2017. Available from: https://www.caresearch.com.au/caresearch/tabid/744/Default.aspx.
- 92. Sykes N. Emerging evidence on docusate: commentary on Tarumi et al. J Pain Symptom Manage. 2013;45(1):1.
- 93. Committee NCE. Management of Constipation in Adult Patients Receiving Palliative Care: An Roinn Slainte Department of Health; Nov 2015 [10:[Available from: http://health.gov.ie/wp-content/uploads/2016/01/ConstipationV9forweb.pdf.
- 94. Droney J, Ross J, Gretton S, Welsh K, Sato H, Riley J. Constipation in cancer patients on morphine. Support Care Cancer. 2008;16(5):453-9.



CONSTIPATION AND BOWEL OBSTRUCTION REFERENCES CONTINUED

- 95. Committee A. Palliative Care for the Patient with Incurable Cancer or Advanced Disease. Guidelines & Protocols [Internet]. 2011.
- 96. Neron A. Constipation and Fecal Impaction: Apes; 2009.
- 97. Wee B, Adams A, Thompson K, Percival F, Burslem K, Jobanputra M. How much does it cost a specialist palliative care unit to manage constipation in patients receiving opioid therapy? J Pain Symptom Manage. 2010;39(4):644-54.
- 98. Siemens W, Gaertner J, Becker G. Advances in pharmacotherapy for opioid-induced constipation a systematic review. Expert Opin Pharmacother. 2015;16(4):515-32.
- 99. Micromedex. Drugs that cause constipation. Truven Health Analytics Inc; 2017.
- 100. Committee GPA. Part 2: Pain and Symptom Management Constipation 2017.
- 101. Drugdex. Lactulose. Truven Health Analytics; 2016.
- 102. Phendopharm. LAX-A-Day (polyethylene glycol 3350 powder for oral solution). 2011.
- 103. Ahmedzai SH, Boland J. Constipation in people prescribed opioids. BMJ Clin Evid. 2010;2010.
- 104. Clark K, Currow DC. Response to "A cross-sectional study of constipation and laxative use in advanced cancer patients: insights for revision of current practise". Support Care Cancer. 2012;20(12):3027-8; author reply 31.
- 105. Mendoza J, Legido J, Rubio S, Gisbert JP. Systematic review: the adverse effects of sodium phosphate enema. Aliment Pharmacol Ther. 2007;26(1):9-20.
- 106. Mehta N, O'Connell K, Giambrone GP, Baqai A, Diwan S. Efficacy of methylnaltrexone for the treatment of opiod-induced constipation: a meta-analysis and systematic review. Postgrad Med. 2016;128(3):282-9.
- 107. Pharmaceuticals S. Relistor2012:[66 p.].
- 108. Mehta S, Cook D, Devlin JW, Skrobik Y, Meade M, Fergusson D, et al. Prevalence, risk factors, and outcomes of delirium in mechanically ventilated adults. Crit Care Med. 2015;43(3):557-66.



- 109. AB A. Movantik2014:[29 p.].
- 110. Hospice V. Bowel Management Guide. In: Scale VBP, editor.: Victoria Hospice Society; 2006.
- 111. health NIo. Bristol Stool Form Scale. Informa Healthcare; 1997.
- 112. Health NIo. Stool Diary. Informa Health; 1997.
- 113. Health F. Symptom Guidelines: Hospice Palliative Care, Clinical Practice Committee; 2006 [Available from: http://www.fraserhealth.ca/health-professionals/ professional-resources/hospice-palliative-care/]
- 114. Microlax product information. Available from: https://www.microlax.ca/products/ microlax#active-ingredients-each-5ml-tube-contains
- 115. Health Canada: Recalls and safety alerts. Available at: http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2010/14087a-eng.php