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Managing Patients with Pain in Primary Care – Part 2

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This guideline is Part 2 of the **Managing Patients with Pain in Primary Care** Guideline. For Pain Assessment and Management Approaches see **Managing Patients with Pain in Primary Care – Part 1**.

Preamble

The intent of this guideline (Part 1 and Part 2) is to provide practical, accessible, and B.C. specific guidance. In essence, this is more of a **Clinical Guidance Document** and not a formal guideline. It's a distillation of many guidelines, expert recommendations, and standards of care. There are few overall pain guidelines for direct comparison. The guideline development working group members were made aware of the Appraisal of Guidelines for Research and Evaluation (AGREE) process that helped inform their appraisal of these guidelines. There is no clear or absolute clinical pathway to managing pain and many controversies persist, especially in the use of opioid and cannabis. The working group recommends reasonable clinical judgement, clear documentation, and frequent reassessment.

Pharmacological Treatment

For many patients with acute, subacute, or chronic pain, pharmacological management is part of overall care. Indeed, it is imperative to get acute pain under control early and effectively but with a clear goal of reassessing its effectiveness and presenting a well-articulated anticipated plan to taper and stop medications. The benefits of long-term medications, especially opioids, are less well understood. For longer term non-cancer pain, ensure that non-opioid and non-pharmacological therapies have been effectively optimized first.[1] The management of cancer and end-of-life pain usually requires a different strategy that may more appropriately include opioids.

Managing patients with most types of pain is not necessarily an "either/or" strategy but rather a layering of interventions including non-pharmacological management, self-management, and pharmacological management.

Considerations and Controversies of Care

- Many guidelines on pain management exist, including those from national, provincial, regulatory authority, advocacy, and academic institutions. They may not all completely align, and the levels of evidence and evidence review process used to create those guidelines may appear unclear in terms of clinical decision making. However, most have a consistent framework to guide clinicians while allowing for good individualized clinical judgement.
- Evidence may include large systematic reviews, randomized control trials, and expert opinion. Evidence may come from high quality studies, but the strength of the evidence may be described as poor, e.g., simply because of small study numbers. While an effect may be described as statistically significant, the magnitude of the clinical impact maybe small.
- Guidelines are generally considered to be based on strong clinical evidence, yet some recommendations clearly state the evidence is weak. However, weak evidence may be the only evidence available and is intended to give the clinician an option to consider.
- The number needed to treat (NNT), and the number needed to harm (NNH) are important concepts to help weigh the benefit and harm of a drug or treatment. They are used to inform a clinician about a specific condition response. However, an intervention may be used in several conditions but be more effective in one condition than another.

- **Pain is a symptom and not a specific condition** with clearly defined parameters like blood pressure and spirometry. Clinicians who need to treat patients with pain need information on how to do this as safely and effectively as possible for that patient.
- It is important to use medications with caution for any patient who may have reduced renal, hepatic, or cardiac function. Likewise, patients with reduced lean body mass (i.e., increased fat concentration), malnourishment (e.g., reduced albumin), concomitant disease, and multiple medications, may need dose adjustments. Consult product monographs for specific drugs and refer to Appendix A: Medication Table.

Non-Opioid Medications[2]

Acetaminophen

Indications: Consider for initial management of patients with mild to moderate pain.[3] Use the lowest effective dose and stop therapy if minimal or no effect.

Cautions: Higher doses, chronic use, increasing age, renal disfunction and alcohol use increase risk of hepatic toxicity.

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Indications: Consider for patients with mild to moderate musculoskeletal pain and inflammation. Use the lowest effective dose for the shortest duration to reduce adverse events and reassess effectiveness within the first few weeks.

Cautions:

- The risk of gastrointestinal (GI) complications is unlikely, but possible, within the first week. The risk increases with longer duration of therapy. Patients at high risk of GI complications may benefit from a COX-2 inhibitor (i.e., celecoxib), and/or the addition of a proton pump inhibitors (PPI) (i.e., rabeprazole) even for short term use.
- Patients at high risk or with established cardiovascular disease may be at increased risk of cardiovascular (CV) events with NSAIDs. Risk appears to be dose and duration dependent.
- Contraindicated in patients with a Creatinine Clearance (CrCl ≤30 ml/min. NSAIDs may cause further deterioration in renal function in patients with mild-moderate or declining renal function, use with caution.
- Older adults have a greater frequency of impaired renal function, existing electrolyte imbalances, comorbid conditions (including CV disease), and multiple medications including over the counter (OTC) products. Take a full history and assess individual patient's appropriateness for NSAIDs.

Combining Classes of Drugs and Combination Products

Indications: There is limited evidence comparing the combination of NSAIDs and acetaminophen to opioids, with some small trials suggesting no difference in pain during dental extractions, hip and knee osteoarthritis, and acute extremity pain.[4–7] A 2020 Cochrane review found low-quality evidence comparing an NSAID and acetaminophen to opioids in acute soft tissue injuries and was uncertain of the findings of no difference in pain at day 1, 3 or 7.[8]

Other small trials suggest lower opioid doses may be required after surgery when added to NSAIDs and acetaminophen.[6,7] A 2021 systematic review found NSAIDs to be associated with better pain scores at 6 and 12 hours postoperatively when compared to codeine with or without acetaminophen in outpatient surgery.[9]

A 2020 Cochrane Review comparing NSAIDs and opioids in acute soft tissue injuries, found moderate quality evidence of no difference in pain at 1 hour, and low certainty evidence of no difference in pain at 4 and 7 days.[8] NSAID participants were more likely to return to function in 7-10 days and experienced less GI and neurological adverse events.[8]

Topical NSAIDs

Indications: Consider for acute conditions such as when patients have sprains, strains and overuse injuries[10] and in some chronic conditions such as osteoarthritis, particularly of the hand or knee. Re-evaluate every 3 months and continue only in responders.[10]

Topical formulations with diclofenac (1-4%), ibuprofen (5-10%) or ketoprofen (1-5%) have the best evidence10 and are available OTC (diclofenac 1.16-2.32%) or through a compounding pharmacy (generally in the 5-10% range). These can be expensive and are not a PharmaCare benefit. While increased concentrations are seen in practice, they have not been studied extensively.

Cautions: Systemic absorption from topical NSAIDs is low (approximately 6-23%) compared to oral forms. However, systemic adverse events have been reported. Topical NSAIDs are generally well tolerated by all patients, including those over 65 years of age.

Skeletal Muscle Relaxants

Indications: For acute musculoskeletal pain only. There is insufficient evidence to support the use of cyclobenzaprine for chronic myofascial pain.[11]

Cautions: Due to the risk of long-term dependence and high incidence of adverse effects (e.g., sedation, dizziness, dry mouth), consider short term use only (1-2 weeks). Adverse effects may be more pronounced and may increase the risk of falls in frail older adults.

Gabapentinoids[12]

Indications: Consider for patients with neuropathic pain conditions such as post herpetic neuralgia or painful diabetic neuropathy. Benefits and harms can both often be seen and assessed as early as 1 week after initiation. Higher doses (gabapentin >1800 mg/d; pregabalin >300 mg/d) may not provide significant additional benefit relative to the increased risk of adverse events.[12] A good summary of gabapentinoids is provided by the B.C. Provincial Academic Detailing Service.

Cautions: Due to the risk of severe respiratory depression and sedation, use with caution when combined with opioids and/or other central nervous system (CNS) depressants.[13] Adverse effects (e.g. drowsiness, dizziness, etc.,) may be more pronounced and may increase risk of falls in frail older adults. Gabapentinoids have been identified as drugs of potential misuse.[14] These drugs are renally excreted, therefore use with caution in patients with renal impairment.

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

Indications: Consider for patients with neuropathic pain conditions (e.g. diabetic neuralgia, post herpetic neuralgia). Duloxetine has a larger evidence base for the treatment of neuropathic pain than venlafaxine.[15–17]

Benefits and harms can often be seen and assessed within 1 week. Higher doses (e.g. duloxetine >60 mg/d) do not produce better analgesia. SNRIs are better tolerated than tricyclic antidepressants (TCAs) in frail older adults.[18]

Tricyclic Antidepressants (TCAs)

Indications: Low quality evidence suggests TCAs may result in a 30% reduction in pain for some patients.

TCAs do not appear to be more effective than placebo in chronic low-back pain. There is a lack of evidence to evaluate the role of TCAs in fibromyalgia.[19]

Cautions: Due to high incidence of anticholinergic side effects (e.g., drowsiness, dry mouth, and constipation), consider alternatives in frail older adults. If a TCA is indicated, start with low doses and consider nortriptyline as it may have fewer anticholinergic effects and is often better tolerated.

Opioid Therapy

This section provides guidance for managing patients who are both opioid-naïve and those already on long-term opioid therapy. Indications for tapering and cessation of opioids are also included.

Controversies of Care

The use of opioids is one of the more controversial issues for many clinicians.

- There are national guidelines as well as regulatory authority directives that give clear guidance about the use of opioids. To some clinicians, these appear excessively harsh and restrictive while others may appreciate the specificity of the guidance. Some clinicians are concerned about disciplinary action if they prescribe opioids or exceed the recommended daily maximum.
- Virtually all guidelines distinguish between non-cancer and palliative end-of-life care, yet some clinicians fail to properly consider that distinction and restrict appropriate comfort measures.
- The 2017 Canadian Guideline for Opioids for Non-Cancer Pain (McMaster Michael G. DeGroote National Pain Centre) is the current standard, yet a follow-up review of those guidelines by the main author suggests that 1/3 of clinicians mistakenly believed the guideline suggested mandatory tapering and that 2/3 of respondents highlighted resistance by patients and lack of access to effective non-opioid treatment.[20]
- A 2018 review by the same author looking at 96 clinical trials, concluded "use of opioids was associated with significantly less pain and significantly improved physical functioning…but the magnitude of the association was small". The mean follow up period of the studies was 60 days.[21]

- As mentioned in the 2017 Canadian Medical Association Journal (CMAJ) article "No guideline can account for the unique features of patients and their clinical circumstances, and the new (2017) guideline is not meant to replace clinical judgement. Patients, prescribers and other stakeholders, including regulators and insurers, should not view its recommendations as absolute".[22]
- Consensual tapers may lead to improved or at least no worse pain management (though in a significant minority of patients this might not be the case), while forced tapers may increase risk of opioid use disorder (OUD), overdose, and suicide.[23]
- The 2017 National Pain Centre Guidelines that describe maximum daily doses, also suggest that some patients may benefit from higher doses.
- Clinicians may hesitate or avoid prescribing opioids to elderly patients, but age alone is not a reason to avoid opioids. Considerations for safely prescribing opioids for the elderly are described below.
- There are several screening tools available to identify the risk of developing OUD when initiating opioids, but evidence suggests these may not help identify those at low risk. Only the absence of a mood disorder was associated with low risk. Previous OUD, certain mental health conditions (e.g. personality disorder), and the use of certain psychiatric medications such as atypical anti-psychotics were associated with high risk of developing OUD.[24]
- The most commonly prescribed opioids in 2018/19, in BC, in order of most to least, are codeine, hydromorphone, tramadol, morphine, and oxycodone.[25] However, the analgesic activity of codeine (and to a lesser extent tramadol) is dependent on genetic polymorphisms, making them more difficult to dose adjust in patients requiring additional dose adjustments due to renal or hepatic impairment.
- **TRAMADOL**: There is a perception that tramadol is a safer opioid as it was not historically considered a Schedule 1 narcotic. However, effective March 31, 2022, Health Canada has added tramadol to the *Controlled Drugs and Substances Act* to reflect the fact it is an opioid with the same risks as others.[26] Tramadol's analgesic activity, much like codeine, is dependent on CYP2D6 metabolism which is altered in approximately 28% of patients.[27] In addition, tramadol acts as a serotonin and norepinephrine reuptake inhibitor (SNRI), increasing the risk of drug interactions and side effects (including serotonin syndrome and seizures) over that of other opioids.[28]

Considerations for Initiation of Opioid Therapy for Opioid-Naïve Patients

Indications for Opioid Medications:

- Moderate to severe acute pain (e.g., post-operative, injuries) expected to resolve.
- Palliative and life-limiting conditions (e.g., end-stage heart failure, chronic obstructive pulmonary disease (COPD), cancers) – for these situations, refer to Palliative Care Guideline as the benefits and risks are different in these patients who will need longer and likely escalating doses. **Palliative care patients should never be denied opioid medications when required.**

Opioids are a potent and useful class of medications for the treatment of pain and end-of-life symptoms when used appropriately. However, while supporting the patient with pain management, clinicians need to be aware of appropriate prescribing guidelines to mitigate the risks of opioid harms and dependence.

Despite previous practice, there is limited or weak evidence for the value of **initiating** opioids for patients with chronic non cancer pain (CNCP). In many instances, the risks of prescription OUD or adverse effects outweigh the potential benefits. The **long-term** use of opioids for managing pain has a potentially higher risk of harm and has limited evidence for benefit. A classic example of this type is a young patient with gradually worsening degenerative back or joint pain.

Prescribing Considerations:

- The initiation of an opioid should always be considered as a "therapeutic trial". Document well the initial discussion and rationale for use of opioids. Encourage patients to self-limit where possible.
- Limit prescriptions. Consider a trial for 7 days or less at a time. Increase interval as patient stabilizes on a dose that does not compromise function. An oral dose of morphine 5-10 mg, or hydromorphone 1-2 mg are common adult starting doses, especially in the immediate post-op period.
- Start patients, especially those who are opioid naïve, on lowest effective dose and titrate as needed with close monitoring of efficacy and side effects. A particularly useful tool is: Centre for Effective Practice 'Opioid Manager'. The Opioid Manager is a practical tool and checklist for opioid prescribing decisions including opioid therapy trials, maintenance, monitoring, switching, and tapering. Other tools include the Opioid Risk Tool, Current Opioid Misuse Measure (COMM)™.

- Consider and minimise drug interactions (e.g., CNS depressants, serotonin concerns with tramadol). See Appendix A: Medication Table for specific drug interactions.
- Be aware of the College of Physician and Surgeons of BC (CPSBC) Safe Prescribing Standards. The CPSBC also has a list of prescribing tools and resources on their website.
- Fully inform patients of the risks and benefits of using opioids and discuss plans for the possible tapering and/or discontinuation of the medication. Document this discussion.
- A patient handout is encouraged.
- Common side effects such as drowsiness and nausea often improve while constipation tends to persist and needs to be actively managed with diet, stool softeners and/or laxatives.
- Frail older adults with moderate to severe pain and functional impairment or poor quality of life should not be excluded from consideration of opioid therapy. See **Pharmacological Pain Management in the Older Adult** below.
- Patients on long-term opioids at stable doses (often referred to as legacy patients) may not be able to taper down to the recommended doses, but that doesn't preclude a conversation about their use and the potential to taper down to a lower dose.
- An additional resource is a detailed review on Opioid Metabolism by Howard Smith.[29]
- For B.C. specific information and coverage, see Appendix A: Medication Table.

Contraindications and Cautions

Absolute Contraindications	Relative Contraindications
Documented opioid allergy	Concurrent use of benzodiazepines and "z" drugs like zopiclone
Severe respiratory instability	Addition or increasing dose of methadone in a person with documented prolonged QTc interval
Acute psychiatric instability or increased risk of suicide	Documented history of diversion
Previously known opioid intolerance	

If considering prescribing opioids, assess for active and past substance use disorder (SUD) (including alcohol, opioids, marijuana) and psychiatric disorders. The presence of these disorders is not a reason to not prescribe but suggest a need to proceed with caution and to have a clear discussion with patient about risks. Indeed, the presence of any SUD is not an absolute contraindication to prescribe opioids, though it does increase risk of overdose and addiction to opioids. Thus, more safeguards, including enhanced monitoring, need to be put in place and clear documentation of risks and benefits for that particular patient outlined.

Use with Caution

- Concurrent use with CYP3A4 inhibitors/inducers (e.g., clarithromycin, diltiazem, "azoles" such as ketoconazole, certain ARV's such as ritonavir, phenobarbital, and phenytoin). See Appendix A: Medication Table.
- Codeine is metabolized by CYP2D6 to its active form, morphine. Up to 23% of the population may produce significantly more or less morphine than expected based on the dose.[30] Monitor for increased side effects, decreased efficacy or select alternative drug.
- Concurrent use of potentially sedating medications such as gabapentinoids[13] cyclobenzaprine, diphenhydramine and dimenhydrate.
- Hepatic and renal impairment may change the pharmacokinetics of medications, reducing elimination and increasing availability of that drug.
- Use of alcohol with opioids should be actively discouraged.
- When patients have co-existing mental health conditions such as mood or thought disorders, consider the extent to which they may be exacerbating or coexisting with the pain. Use caution when considering an opioid and reflect on the concomitant need to manage the mental health condition as well. The *Canadian National Guideline for Opioids for Chronic Non-Cancer Pain* recommends stabilizing an active psychiatric disorder before initiating a trial of opioids (weak recommendation).

Pandemic Considerations.

During the COVID-19 pandemic and concurrent opioid overdose epidemic, consideration may be needed to reduce the risk of harm from both. In an effort to reduce the spread of COVID-19, the BCCSU Risk Mitigation in the context of dual public health emergencies interim guidance document *outlines many related changes in* ***prescribing policy****. There are provincial policy changes that reduce risk of exposure such as phone orders and transferring scripts between pharmacies. Longer prescriptions and potentially delaying or slowing tapers may also be strategies to avoid destabilizing already vulnerable patients.*

Considerations for Patients Already on Opioid Therapy

Most primary care practitioners see patients who are already on long-term opioid therapy for chronic pain, regardless of initial indications. These considerations apply whether the patients are long established or new to the practice. Again, it is not appropriate to refuse to accept or continue to care for patients on opioids and it is not appropriate to abruptly stop prescribing.

Indications for Long-term Use of Opioid Medications:

- Palliative care and end-of-life conditions.
- Conditions not expected to improve and not well managed with non-opioid medications. Some examples may include worsening scoliosis, degenerative disc disease or vertebral fractures not amenable to other interventions.
- Some patients with chronic pain already on opioids may be stable and functional with minimal disability and side effects. Maintaining them on opioids may be appropriate and indicated. A forced taper may worsen pain and reduce stability.

Ongoing Management

- Reassess regularly to ensure that non-opioid and non-pharmacological therapies have been maximized. Document the reassessment.
- Self-Reflection: "If you are feeling pressured to prescribe opioids, ask yourself where this pressure is coming from and how you might respond".
- There is not a defined target morphine equivalent daily dose (MEDD), but clinicians should prescribe the lowest effective dose.
- The CPSBC Safe Prescribing Standards, suggests that doses above 90 MEDD require "substantive evidence of exceptional need and benefit". The standards do not say that higher doses cannot or should not be prescribed, just that the evidence and need for a higher dose must be documented. In addition, the guidelines do not suggest mandatory tapering.[20,31] Clinical examples may include patients with severe pain for which higher doses of opioids are needed and patients who present with existing prescription doses which exceed 90 MEDD for whom abrupt tapering or cessation would cause harm. Documentation is critical.
- Consider using long-acting opioids after stabilizing the patient on immediate release opioid. Even in this situation, be aware that there is poor evidence supporting long-term use of opioids and discuss and document the risk of long-acting opioids in advance.
- For anticipated longer term prescriptions, a written treatment agreement is encouraged. Sample agreement available at CPSBC Prescribing tools and resources.
- Divergence from the treatment agreement may suggest a need to re-evaluate the clinical situation and consider the biopsychosocial stressors that may be present. Agreements are not meant to be punitive so it does not necessarily indicate that opioids must be tapered or stopped. Breach of agreements should not be used as a method to justify termination of opioid therapy, nor should they be used to support discharging a patient from a practice. Instead, they should be used to support opening a conversation about appropriate and safe opioid use. Consider discussion with an addiction medicine specialist or pain specialist with experience in addictions.
- However, if there is clear evidence of prescription forgery or confirmed diversion (with a supportive urine drug test (UDT), you no longer have an obligation to prescribe.
- All patients on opioids for chronic pain could be considered for random UDT. However, there is uncertain evidence about the effect of urine drug screening on the risk of opioid overdose.[1] A urine drug test may be used in the context of patient education and safety to identify additional drugs (sometimes taken unknowingly) that may put patients at higher risk. Absence of the prescribed opioid in random urine testing should be a red flag for possible diversion. A respectful discussion of results may be useful before any action is taken. Refer to BCCSU's Opioid Use Disorder. See Urine Drug Testing for more information, but please note this is a document specific to the use of UDT in the management of OUD.

- Ideally, patients should be prescribed opioids by their primary care provider only. Where possible, only one consistent provider or team should be providing the prescriptions. However, the current reality in B.C. is that some patients may see multiple providers; therefore, make good use of documentation and electronic medical record (EMR) functions including ready access to patient agreements, current medications and any "cautions" or "flags" that are attached.
- **PharmaNet** provides an up-to-date list of filled prescriptions and should be used prior to every opioid prescription and refill. **CareConnect** provides recent clinical encounters including ER visits and prescriptions written.
- Consider blister-packs and controlled dispensing strategies if there is concern about use other than prescribed.
- Consider offering a naloxone kit and education to patient and family on how to administer and respond to overdose. Refer to towardtheheart.com produced by the BC Centre for Disease Control (BCCDC) for naloxone kit guidance.
- For safety of children, pets and opioid-naïve adults and prevention of theft, educate patients on safe storage and disposal of opioid medications.
- Reassess regularly and be vigilant for incipient or existing prescription OUD (e.g., escalating dosages, increasing pain complaints, multi-doctoring). Ask about alternate routes of use, including snorting, chewing, smoking, or injecting.

When to Taper and/or Stop Opioids

- For patients prescribed opioids for short-term, acute pain (e.g., post-operative or injuries), recommend a tapering and discontinuation plan including dosage, frequency and duration. Confirm the follow-up plan with the patient.
- Opioid tapering and discontinuation may be difficult for the patient who fears worsening of the pain and withdrawal symptoms. Patients should be actively engaged in a discussion about the merits of gradual dose reduction, including the potential for equivalent or better pain control with less opioid-associated risks (e.g., reduced risk of myocardial infarction [MI], motor vehicle accident (MVA), sleep apnea, sexual dysfunction, falls, depression, addiction, unintended overdose). However, a percentage of people will not experience these benefits and the taper may not be appropriate.
- Comments such as *'I think we can work towards giving you just as much pain control with less medication risks'* are a good start to conversations about the possibility of a dose reduction.

Indications for Tapering and/or Stopping

- When there is a loss of therapeutic effect on pain and function.
- When there are intolerable side effects such as sedation.
- Patient request.
- When there is non-adherence to the agreed plan or clear evidence of diversion. This is considered a breach of the opioid agreement and mitigation steps need to be taken such as daily witnessed dispensing or lowering the dose. With evidence of diversion and a supportive UDT confirming none of the prescribed opioid present, then you have no obligation to continue prescribing.
- When clear evidence of OUD is present or worsening it is appropriate to refer to addiction specialist instead of attempting to taper.

- Many guidelines suggest that a taper be considered for patients whose MEDD is above 90. This is not a strict limit and clinical judgement is always warranted. This does not apply to cancer/palliative patients.
- Patients on long-term opioids at stable doses may not be able to taper down to the recommended dose range. Again, it is never inappropriate to have a conversation about the continued use of these medications and the potential to slowly taper down to a lower dose.
- Opioid-induced hyperalgesia is an adverse effect that is characterized by decreasing efficacy that is not improved by increasing the dose of the opioid.[32] It is dose dependent and worse at higher doses but occurs at any opioid dose in patients with chronic non-cancer pain.[33] Symptoms include spreading or burning pain and allodynia (i.e. pain due to a stimulus such as light touch that does not usually provoke pain). It may also be accompanied by other signs of opioid toxicity such as myoclonus, delirium, and seizures. Symptoms improve by reducing or eliminating the drug. Consider opioid rotation in cases of opioid toxicity. See **Opioid Switching** section below.

Tapering Strategies

There is no evidence for any specific tapering strategy. However, a commonly described strategy is:

- A reduction of 5-10% of the daily dose.
- A dose reduction every 2-4 weeks.
- Tapering in the older adult may be slower (e.g., 5% every 2-8 weeks) and include rest periods. See the Canadian Guideline on OUD among older adults.
- Beginning with just a 2-3% drop can build confidence and allow the person to gain insight into any anticipatory anxiety-related pain symptoms.
- Patients habituated to high-dose, long-term opioids may need longer intervals between drops in dose (e.g., 5% every 1-3 months).
- Monitor the patient for withdrawal symptoms and consider withdrawal management medications such as clonidine, Imodium and NSAIDs.
- A good Canadian opioid reduction guide is Centre for Effective Practice 'Opioid' Manager-Opioid Tapering Template.

Cautions While Tapering / Discontinuing Long-Term Opioids:

- Never abruptly stop opioids with patients on chronic opioid therapy, especially if pregnant.
- Tapering (especially rapidly) can paradoxically increase the risk of overdose, OUD, and suicide if underlying pain is not well managed. Consider switching to an alternative opioid including methadone or partial agonist such as buprenorphine.
- A clinician needs to differentiate between worsening or non-responsive chronic pain, and untreated or unmasked OUD. The concomitant existence of OUD and chronic pain may require a referral to an addiction's specialist, whereas worsening chronic pain should prompt an overall evaluation of the pharmacologic and non-pharmacologic strategy.

Opioid Switching

For patients on opioids who have significant side effects or reduced effectiveness, consider switching to another opioid. See Appendix A: Medication Table for opioids medications profiles and the below resources:

- Centre for Effective Practice 'Opioid' Manager
- Opioid Manager (National Pain Centre) – Opioid Switching
- McMaster Opioid Manager

Opioid Use Disorder (OUD)

Prescribing opioids for pain is associated with a risk for developing prescription opioid use disorder.[34] Despite a number of screening tools available to identify patients at increased risk, there are few validated ways to identify those who can be safely prescribed opioid analgesics.[24]

This guideline is not intended to provide guidance on diagnosing and managing OUD. For full guidance, see BC Guidelines: Opioid Use Disorder and the British Columbia Centre on Substance Use (BCCSU).

Providing opioids for analgesia for patients with OUD is complex. Patients on opioid agonist therapy (OAT) may be prescribed opioids for severe acute pain but generally not for CNCP. Refer or request guidance from an addiction medicine specialist with pain experience.

- For patients already on long-acting opioids for years, consider whether they may have a prescription OUD, and, if evidence of OUD (versus increasing opioid tolerance), consider opioid agonist/partial agonist treatment (e.g., buprenorphine/naloxone or methadone).
- Managing patients with prescription opioid use disorder who also have complex chronic pain is challenging. Consider consulting with the Rapid Access to Consultative Expertise RACE line and BCCSU Provincial Guideline Opioid Use Disorder: Diagnosis and Management in Primary Care and The Canadian Guideline for Opioid Use Disorder in Older adults. Additional information and training on Opioid Use Disorder can be found at the BCCSU: www.bccsu.ca/about-the-addiction-care-and-treatment-online-certificate/, Provincial Opioid Addiction Treatment Support Program and their ECHO site on OUD: www.bccsu.ca/bcechoonsubstanceuse-oud/.
- Patients with active mental health issues (e.g. anxiety, depression, PTSD) may be at increased risk of prescription OUD.[34]

Cannabis

Cannabis and cannabinoid use for medical purposes can be another controversial topic. As with opioids, views and authorization practices may be influenced by media, social justice issues, personal experience and at times conflicting evidence. Complicating its use in a medical setting is the proportion of Canadians who indicated they had consumed cannabis within the last 12 months rose from 9.4% to 14.8% between 2004 and 2017, and in the year following legalization (2018-2019) that number increased to 17.5%.[35] Statistics Canada reported in 2018 that 45% of Canadians had tried cannabis at least once in the lifetime and that 50% of the people who self-reported using cannabis for medical reasons, did so for pain management.

The challenge for clinicians is weighing the evidence for medical use, managing the potential biases (including their own) from all sides of the debate, and being aware that many of their patients are and will be using it for managing pain. Be aware of simply switching one dependency (e.g. opioids) for another (e.g. cannabis) and be aware that evidence regarding cannabis use is still evolving.

The Canadian Public Health Association (CPHA) has produced *Cannabasics*, a document describing the basics of the plant and products but does not give treatment recommendations.

Cannabis for Chronic Pain

Recent guidance intended for the Canadian clinician highlights that more research is needed to determine the role of cannabis in managing chronic pain. However, the Simplified Guideline for Prescribing Medical Cannabinoids in Primary Care[36] suggests that cannabinoids may be useful for chronic neuropathic pain, chemotherapy induced nausea and vomiting, and spasticity of multiple sclerosis and spinal cord injury, but not as a first line therapy.

In contrast, a recent review by the National Academies of Sciences, Engineering and Medicine found there was conclusive or substantial evidence that cannabis or cannabinoids are effective for the treatment of chronic pain in adults.[37]

The *Canadian National Guideline for Opioids for Chronic Non-Cancer Pain* notes that nabilone may have similar effects on pain relief when compared to opioids, NSAIDs, or tricyclic antidepressants[34] (Low Quality Evidence). Evidence comparing opioids to nabilone was from a single study.[38]

Saskatchewan's Rx Files: Cannabinoids Overview provides a succinct overview of medical cannabis.

A recent 2021 BMJ review offered a "weak recommendation to offer a trial of non-inhaled medical cannabis … in addition to the standard care and management (if not sufficient), for people living with cancer and non-cancer pain". The review also describes the recommendation as "weak because of the close balance between benefits and harms … for chronic pain". Harms or adverse events in some cases are described as "mostly self-limited and transient" such as drowsiness and impaired attention, but that some patients place a high value on small to very small improvements in pain and physical functioning.[39]

More significant harms including risk of MI, stroke and atrial fibrillation have also been described.[40] Health effects of marijuana use is described by the Centers for Disease Control and Prevention (USA). It also warns that anxiety and depression may be aggravated and there are reports of interactions with blood thinners.[40]

Absolute risk is harder to quantify and there continues to be discussion about the effects of smoking cannabis verses edible forms, and what effect the THC:CBD ratio has on harms and adverse effects.

In summary, while cannabis is now legal, consumed by many patients and may prove effective for some conditions, it is difficult to provide broader evidence informed indications for its use. More clarity is needed for specific therapeutic products and dosing schedules.

The Lower-Risk Cannabis Use Guideline[41] provides 10 recommendations of modifiable behaviours to reduce the risk of adverse effects of cannabis use, including avoiding early age initiation, using lower potency THC products, avoiding synthetic cannabinoids, and preferring non-smoking methods.

Health care providers need to be knowledgeable and non-judgmental when informing patients about cannabis and cannabinoids.

The UBC Faculty of Medicine's Continuing Professional Development (CPD) eLearning has a free on-line module Cannabis Education for Health Care Providers as well as a Cannabis Education Toolkit.

Pharmacological Pain Management in the Older Adult

Managing 'older adults' with pain, especially the frail older adult, often requires modifications and adjustments in both approach and dosages. Many experts suggest that age greater than 70 and/or frailty require awareness of additional factors when assessing and managing pain. Frailty is a medical syndrome with multiple causes and contributors, characterized by diminished strength and endurance and reduced physiological function, leading to increased adverse health outcomes such as functional decline and early mortality. However, frailty is not inevitable in ageing and can be prevented or reversed. For more information see BCGuidelines: Frailty in Older Adults – Early Identification and Management. Information about Healthy Aging and Preventing Frailty, can also be found in the updated provincial healthy aging strategy.

The medication table found in Appendix A is provided for otherwise healthy adult patients. Dose adjustments for special populations (e.g., children, elderly, pregnancy, renal or hepatic dysfunction, polypharmacy) may be necessary. Please consult other resources for specific cases such as the product monograph, a pharmacist, primary literature and/or an interaction checker (e.g., Lexicomp) before prescribing.

Guiding principles when prescribing for frail/older patients:

- In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.
- Persistent pain in frail older adults increases morbidity and poor health outcomes, making treatment a priority.
- As cognition worsens, pain is less likely to be reported and may manifest as other distress behaviours (e.g., agitation, resisting care, insomnia, poor appetite).
- Risk of falls is elevated. However, pain, decreased attention or poor sleep due to chronic pain can also increase the risk of falls. For more information on preventing falls see BCGuidelines: Fall Prevention: Risk Assessment and Management for Community-Dwelling Older Adults.
- Multiple morbidity, cognitive impairment and altered pharmacokinetics mandate an individualized approach. Bloodwork as needed (e.g., renal function) in the initial assessment phase and intermittently if the use of medication persists.
- Opioid naive patients should be started at the lowest recommended dose and titrated as needed.
- Constipation is one of the most common side effects and may need to be actively managed, starting with diet and stool softeners.

Choices of Opioid for Frail Older Adults.

- The use of opioids is not contraindicated in frail older adults but starting doses should be at the low end of the dosing range reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy. Ongoing dosing, when needed, should be titrated slowly based on efficacy and adverse effects. Please consult product monographs for more information.
- The most commonly prescribed opioids in 2018/19, in BC, in order of most to least, are codeine, hydromorphone, tramadol, morphine, and oxycodone.[25]
- The analgesic activity of codeine (and to a lesser extent tramadol) is dependent on genetic polymorphisms, making them more difficult to dose adjust in patients requiring additional dose adjustments due to renal or hepatic impairment. See the cautionary note regarding Tramadol in the **Opioid Therapy: Controversies of Care** section above.
- In addition to starting at the low end of the dosing range for hydromorphone, morphine and oxycodone for all older adults, additional dose adjustments are needed for patients with impaired hepatic or renal function. Please consult product monographs for more information.
- Methadone, fentanyl, and buprenorphine are also used in managing pain, but less frequently and may require more experience or expert guidance.
- Gabapentinoids may have a higher rate of side effects including respiratory depression and sedation, and therefore should be used with caution in the older adult, especially in those with reduced renal function.

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Practitioner Resources

- **Pathways**: An online resource that allows GPs, nurse practitioners and their office staff to quickly access current and accurate referral information for specialists and specialty clinics, including wait times and areas of expertise. In addition, Pathways makes available hundreds of patient and physician resources that are categorized and searchable. Pain Management resource video at Pathways is available at vimeo.com/528999461.
- **PharmaNet**: PharmaNet, administered by the Ministry of Health, was developed in consultation with health professionals and the public to improve prescription safety and support prescription claim processing
- **CareConnect**: Secure, view-only Electronic Health Record (EHR) that delivers patient-centric information to support healthcare providers in their delivery of patient care.
- **Rapid Access to Consultative Expertise (RACE) line**: Pain is not listed as a specific speciality area, however, consider a RACE consult to a specialist if the pain is related to a specific specialty area. There is a provincial line for Addictions Medicine that can respond to questions related to co-occurring pain and opioid use disorder. Specialist Pain Clinics (Health Authority and Private clinics) can be found on Pathways.
- **Rural Coordination Centre of BC**: Real Time Virtual Support (RTVS) pathways enhance health equity in rural, remote, and First Nations communities across B.C. by connecting rural healthcare providers and patients to RTVS Virtual Physicians via Zoom or telephone. There are two types of pathways—those for healthcare providers, and those for patients. For support with myofascial pain: Quick Reply pathway for providers (myoLIVE) is available for rural and remote practitioners and clinicians who are challenged by a myofascial pain presentation.
- The **Centre for Effective Practice (CEP)**, is an excellent resource for primary care clinicians. There is a specific link to CNCP as well as mechanical back pain – Clinically Organized Relevant Exam (CORE) Back Tool.
- **First Nations Health Authority – Wellness**. This website lists the framework and resources to achieve a healthy lifestyle.
- **WorkSafeBC Physician's Hotline**: Call 1-855-476-3049 to speak with an agent about access to WorkSafeBC funded programs including the following: Occupational Rehabilitation (OR1 and 2); Pain and Medication Management Program (PMMP); Resiliency over perceived trauma (ROPT); Community Pain and Addiction Services (CPAS).
- **ICBC Claims**: Includes information and resources related to injuries from a car crash.
- **College of Physicians and Surgeons of British Columbia: Drug Programs**.
- **BC Centre on Substance Use**: a provincially networked organization with a mandate to develop, help implement, and evaluate evidence-based approaches to substance use and addiction.
- **Michael G. DeGroote Institute for Pain Research and Care**: Seeks to fund research and initiatives that will ultimately improve the quality of life for those living with Chronic Pain.
- **Canadian Family Physician: PEER simplified chronic pain guideline (2022)** - Management of chronic low back, osteoarthritic, and neuropathic pain in primary care: Provides a summary of treatment approaches and a patient handout.

- **Pain BC**: has several resources to support patients and caregivers, education for health professionals caring for those with pain. Some resources include Pain BC's Live Plan Be, Chronic Pain Road Map, support line.
- **Self-Management BC** is part of University of Victoria's Institute on Aging & Lifelong Health and is supported by the Patients as Partners Initiative (Primary Care Division, B.C. Ministry of Health). It offers three peer-delivered chronic pain programs free to B.C. residents.

Appendices

Appendix A: Medication Table

This guideline is based on scientific evidence current as of the effective date.

The guideline was developed by the Guidelines and Protocols Advisory Committee and adopted by the Medical Services Commission.

For more information about how BC Guidelines are developed, refer to the GPAC Handbook available at BCGuidelines.ca: GPAC Handbook.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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Disclaimer

The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. **We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.**

Appendix A: Medication Table[1-4]

This drug list includes examples of treatment options (commonly used drugs and/or a PharmaCare benefit) and is not a comprehensive list.

Information in this table is provided for otherwise healthy adult patients. Dose adjustments for special populations (e.g. children, elderly, pregnancy, renal or hepatic dysfunction, polypharmacy) may be necessary. Please consult other resources for specific cases such as the product monograph, a pharmacist, primary literature and/or an interaction checker (e.g., Lexicomp) before prescribing.

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
Analgesics						
Acetaminophen						
Acetaminophen *Tylenol, G* Tabs: 325, 500 mg XR tabs: 650 mg Suppositories: 325, 650 mg	*Mild-moderate pain:* 325-1000 mg every 4-6 hours *XR tabs:* 1300 mg TID *Low back pain:* 325-650 mg every 4 hours **Maximum**: 4000 mg per day	Hepatotoxicity in overdose or supratherapeutic dosing.	Chronic alcohol use increases the risk of hepatotoxicity. Acetaminophen has been reported to increase INR in warfarin-treated patients.	Regular benefit (Palliative Care, Plan W patients) Non-benefit (Other PharmaCare plans)	$10-20	Available OTC: 325, 500, 650 mg Maximum: 4000 mg/d
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)						
For treatment of Acute Pain: maximum duration of 7 days is recommended Use the lowest dose for the shortest duration to reduce risk of serious adverse effects (i.e., GI complications, CV events, renal toxicity) To reduce GI complications, use a COX-2 inhibitor or add a PPI even for short term use. Studies show CV risk is similar between naproxen (≤ 750 mg/d), ibuprofen (≤1200mg/d), and celecoxib (≤ 200 mg/d)[5,6]						
ibuprofen *Advil, Motrin, G* Caps/tabs: 200, 400, 600, 800 mg *Advil XR* XR tabs: 600 mg	*Anti-inflammatory:* 400-600 mg TID *Low back pain:* 300-600 mg TID-QID *Mild-moderate pain:* 200-800 mg every 6-8 hours *Dysmenorrhea*: 200-600 mg q6h *Headache:* 400-800 mg q6h x1-2 doses *Gout*: 800 mg TID for 5-7 days **Maximum:** 2400mg per day	GI: dyspepsia, epigastric pain, nausea/vomiting, diarrhea, gastric and duodenal ulcers, GI bleeding. Cardiovascular: MI, stroke, heart failure, fluid retention, hypertension. Nephrotoxicity may occur; avoid NSAIDs in patients with severe renal impairment (CrCl <30 mL/min). CNS: dizziness, drowsiness, headache, tinnitus, confusion (especially in the elderly); CNS effects may be dose related and respond to decreased dosage. Minor or serious skin rashes, pruritus.	Warfarin: increased anticoagulant effect. Antihypertensives (diuretics, beta-blockers, ACE inhibitors, alpha-blockers): possible reduction in antihypertensive effect. Increased risk of GI bleeding with SSRIs. Lithium: monitor lithium levels when NSAID added. Lithium may interfere with sodium/water balance.	Regular benefit, RDP Reference Drug	$15-30	Available OTC: 200, 400 mg Maximum: 1200 mg/d
naproxen *Naprosyn, G* Tabs: 250, 375, 500 mg EC Tabs: 250, 375, 500 mg	*Anti-inflammatory*: 375-500 mg BID *Mild-moderate pain*: 250-500 mg BID *Dysmenorrhea:* 500 mg STAT, then 500 mg BID or 250 mg TID-QID *Low back pain*: 250-375 mg BID-TID *Migraine*: 750 mg STAT, then 250-500 mg if needed *Gout*: 750 mg STAT, then 500 mg BID for 5-7 days **Maximum:** 1250-1500 mg per day			Regular benefit, RDP Reference Drug	$10-20	

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
naproxen sodium *Aleve, Anaprox, Motrin, G* Tabs: 220, 275, 550 mg	*Anti-inflammatory:* 440-550 mg BID *Mild-moderate pain*: 220-550 mg BID **Maximum**: 1375 mg per day *Naproxen sodium 220 mg= Naproxen 200 mg	GI: dyspepsia, epigastric pain, nausea/vomiting, diarrhea, gastric and duodenal ulcers, GI bleeding. Cardiovascular: MI, stroke, heart failure, fluid retention, hypertension. Nephrotoxicity may occur; avoid NSAIDs in patients with severe renal impairment (CrCl <30 mL/min). CNS: dizziness, drowsiness, headache, tinnitus, confusion (especially in the elderly); CNS effects may be dose related and respond to decreased dosage. Minor or serious skin rashes, pruritus.	Warfarin: increased anticoagulant effect. Antihypertensives (diuretics, beta-blockers, ACE inhibitors, alpha-blockers): possible reduction in antihypertensive effect. Increased risk of GI bleeding with SSRIs. Lithium: monitor lithium levels when NSAID added. Lithium may interfere with sodium/water balance.	Non-benefit	$25-40	Available OTC: 220 mg Maximum: 440 mg/d
celcoxib *Celebrex, G* Caps: 100, 200 mg	*Anti-inflammatory*: 200 mg once daily or BID *Mild-moderate pain:* 200 mg once daily or divided BID *Gout (off-label)*: 200 mg BID for 5-7 days **Maximum**: 400 mg per day			Limited coverage	$10-20	COX-2 selective inhibitor at therapeutic doses
diclofenac potassium *Voltaren Rapide, G* Tabs: 50 mg	*Anti-inflammatory*: 50 mg BID *Osteoarthritis*: 25 mg BID-TID or 50 mg BID *Dysmenorrhea (off-label):* 100 mg STAT then 50 mg q6-8h prn (max day 1: 200 mg; day 2+: 100 mg/d) **Maximum:** 100 mg per day			Limited Coverage, RDP	$25-30	
diclofenac sodium *Voltaren, G* EC tabs: 25, 50 mg SR tabs: 75, 100 mg Suppository: 50, 100 mg	*Anti-inflammatory*: EC: 50 mg BID SR: 75-100 mg SR once daily *Osteoarthritis*: EC: 25 mg BID-TID or 50 mg BID SR: 75-100 mg once daily *Dysmenorrhea (off-label):* EC: 100 mg STAT then 50 mg q6-7h (max day 1: 200 mg; day 2+: 100 mg/d) SR: 75 mg BID **Maximum:** 100 mg per day			Limited Coverage, RDP	$10-20	
indomethacin *Indocid, G* Caps: 25, 50 mg Suppository: 50, 100 mg	*Anti-inflammatory*: 25 mg TID *Gout:* 75 mg STAT; Day 1-2: 50 mg q6h; Day 3:50 mg q8h; Day 4: 25 mg q8h *Mild-moderate pain:* 25-50 mg TID **Maximum:** 200 mg per day			Limited Coverage, RDP	$20-30	
ketorolac *Toradol, G* Tabs: 10 mg	*Anti-inflammatory:* 10 mg QID *Mild-moderate pain*: 10 mg QID **Maximum:** 40 mg per day for 7 days (5 days in combination with IM/IV)			Non-benefit	$20/ 1 week	Maximum duration of 7 days.
meloxicam *Mobicox, G* Tabs: 7.5, 15 mg	*Anti-inflammatory*: 7.5 mg once daily *Mild-moderate pain*: 7.5-15 mg once daily *Gout:* 15 mg once daily **Maximum:** 15 mg per day			Limited Coverage	$10	COX-2 preferential at low dose, selectivity lost at high doses

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
Opioids						
codeine *Codeine, Codeine Contin, G* IR: 15, 30 mg CR (12h): 50, 100, 150, 200 mg	IR: 15-30 mg every 4 hours as required CR: 50 mg BID 50 mg ME = 334 mg/d 90 mg ME = 600 mg/d	All opioids: nausea, constipation, sedation or drowsiness, confusion, urinary retention, dry mouth, respiratory depression, risk of addiction; allergic reactions, e.g., rash.	All opioids: additive sedation with other CNS depressants such as alcohol; potential enhancement of opioid effects with lidocaine.	Regular benefit	$25-30	Codeine is metabolized by CYP2D6 to its active form, morphine. Up to 23% of the population may produce significantly more or less morphine than expected based on the dose. Monitor for increased side effects/ decreased efficacy or select alternative drug.
codeine/ acetaminophen with or without caffeine *Tylenol #1, 2, 3, 4, Emtec -30, G* Tabs: 8/300 mg, 15/300 mg, 30/300 mg, 60/300 mg with or without 15 mg caffeine	Codeine(mg)/tablet: 8-30 mg/tab: 1-2 tabs every 4-6 hours as required 60 mg/tab: 1 tab every 4-6 hours as required **Maximum:** 13 tablets per day (3900 mg acetaminophen)			Codeine ≥15 mg: Regular benefit Codeine <15 mg: Non-benefit	OTC: $25-35 Rx: $35-65	Products containing codeine 8 mg and 2 other medicinal ingredients are available without a prescription. See attached combination product table
hydromorphone *Dilaudid, Hydromorph-contin, G* IR: 1, 2, 4, 8 mg CR (12h): 3, 4.5, 6, 9, 12, 18, 24, 30 mg Syrup: 1 mg/ml	IR: 1-2 mg every 4 hours as required CR: 3 mg BID 50 mg ME = 10 mg/d 90 mg ME = 18 mg/d			IR: Regular benefit CR: Regular benefit (Plan P) Non-benefit (Other plans)	IR: $20-30 CR: $45-150 Syrup:	
morphine *MS-IR, Statex, M-Ediat* IR: 5, 10, 20, 25, 30, 50 mg *MS Contin, M-eslon* SR (12h): 10, 15, 30, 60, 100, 200 mg *Kadian* SR (24h): 10, 20, 50, 100 mg *Doloral* Syrup: 1 mg/ml, 5 mg/ml	IR: 5-10 mg every 4 to 6 hours as required SR (12h): 15 mg BID SR (24h): 20-30 mg once daily 50 mg ME = 50 mg/d 90 mg ME = 90 mg/d			Regular benefit	IR: $25 SR (12h): $15 SR (24h): $45 Syrup: $10-20 Inj: $300	
oxycodone *Oxy-IR, Supeudol, OxyNEO, G* IR: 5, 10, 20 mg CR (12h): 5, 10, 15, 20, 30, 40, 60, 80 mg Suppository: 10, 20 mg	IR: 5-10 mg every 4 to 6 hours as required CR: 10-15 mg BID 50 mg ME = 33 mg/d 90 mg ME = 60 mg/d			IR: Regular benefit CR: Regular benefit (Plan P) Non-benefit (Other plans)	IR: $35 CR (12h): $30-75	
oxycodone/ acetaminophen *Percocet, G* IR: 5/325 mg	1 tablet every 4-6 hours **Maximum:** 12 tablets per day (3900 mg acetaminophen)			Regular benefit	$25	*Also available in combination with 325 mg ASA

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
oxycodone/naloxone *Targin, G* Tabs: 5/2.5, 10/5, 20/10, 40/20 mg	10/5 mg every 12 hours **Maximum:** 80/40 mg per day			Non-benefit	$70-180	*naloxone is indicated for the relief of opioid-induced constipation
tramadol *Ultram, G* IR: 50 mg *Durela, Ralivia (Peak 12-15h, duration 24h):* ER tabs: 100, 200, 300 mg *Tridural, G (Peak 4-8h, duration 24 h):* ER tabs: 100, 200, 300 mg *Zytram XL (Peak 4-8h, duration 24 h):* XL tabs: 75, 100, 150, 200, 300, 400 mg	IR: 50 mg every 4 to 6 hours **Maximum:** 400 mg per day ER: 100 mg once daily **Maximum:** 300 mg per day XL: 150 mg once daily **Maximum:** 400 mg per day 50 mg ME = 300 mg/d 90 mg ME = 540 mg/d	Respiratory depression, sedation, ataxia, constipation, seizures, nausea, orthostatic hypotension.	Do not use if MAOIs taken within past 14 days. Caution with drugs that lower seizure threshold, e.g., SSRIs, TCAs, bupropion. Additive effects with other CNS depressants (e.g., alcohol, opioids, hypnotics). Carbamazepine may decrease analgesic effect of tramadol. Clearance of tramadol (and conversion to its active M1 metabolite) may be decreased by inhibitors of CYP2D6 such as fluoxetine, paroxetine or quinidine, increasing the risk of seizures or serotonin syndrome. Clearance may also be reduced by inhibitors of CYP3A4 such as erythromycin, itraconazole or ketoconazole.	Non-benefit	IR: $85 ER: $25-100 XL: $35-160	Tramadol is metabolized by CYP2D6 to a more active metabolite. Up to 28% of the population may produce significantly more or less of the metabolite than expected based on the dose. Monitor for increased side effects/ decreased efficacy or select alternative drug.
tramadol/ acetaminophen *Tramacet, g* Tabs: 37.5/325 mg	1-2 tablets every 4 to 6 hours as required **Maximum:** 8 tablets per day			Non-benefit	$80-160	

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
Tricyclic Antidepressants (TCA)						
amitriptyline *G* Tabs: 10, 25, 50, 75 mg	*Chronic neuropathic pain, postherpetic neuralgia (Off-label)* Initial: 10-25 mg once daily Usual: 50-150 mg once daily *Fibromyalgia (Off-label)*: Initial: 5-10 mg once daily Usual: 20-30 mg once daily *Interstitial cystitis (Off-label)*: Initial: 10 mg once daily Usual: 75-100 mg once daily *Postherpetic neuralgia (Off-label):* Initial: 10-25 mg once daily Usual: up to 160 mg per day	All TCAs: dry mouth, constipation, drowsiness, blurred vision, urinary retention, weight gain, confusion, tachycardia (rare reversible idiosyncratic effect). Avoid in patients with prostatic hypertrophy (because TCAs may cause/exacerbate urinary retention), angle-closure glaucoma or in significant heart disease because of cardiac toxicity, e.g., arrhythmias. Amitriptyline is more sedating than other TCAs; preferable option if insomnia is an issue.	All TCAs: metabolized by cytochrome P450; potential interactions with other substrates, inhibitors (e.g., erythromycin, fluoxetine, fluvoxamine, isoniazid, itraconazole, ketoconazole, paroxetine, valproic acid) or inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifampin); increased sedation with other CNS depressants such as alcohol; increased anticholinergic effects with other anticholinergic agents.	Regular benefit	$5-15	Amitriptyline is metabolized by both CYP2D6 and CYP2C19. Up to 50% of the population may produce significantly more or less metabolite than expected based on the dose. Monitor for increased side effects/ decreased efficacy or select alternative drug.
desipramine *G* Tabs: 10, 25, 50, 75, 100 mg	*Chronic neuropathic pain (Off-label)* Initial: 10-25 mg once daily at bedtime Usual: 50-75 mg once daily at bedtime *Diabetic neuropathy (off-label):* Initial: 12.5 mg once daily Usual: up to 250 mg per day *Postherpetic neuralgia (Off-label):* Initial: 12.5-25 mg once daily Usual: up to 150 mg per day			Regular benefit	$5-30	Desipramine is metabolized by CYP2D6. Up to 30% of the population may produce significantly more or less metabolite than expected based on the dose. Monitor for increased side effects/ decreased efficacy or select alternative drug.
nortriptyline *G* Caps: 10, 25 mg	*Chronic neuropathic pain (Off-label)* Initial: 10-25 mg once daily at bedtime Usual: 50-75 mg once daily at bedtime *Diabetic neuropathy (Off-label):* Initial: 10-25 mg once daily Usual: 25-100 mg per day *Postherpetic neuralgia (Off-label):* Initial: 10-20 mg once daily Usual: up to 160 mg per day			Regular benefit	$15-60	Nortriptyline is metabolized by CYP2D6. Up to 30% of the population may produce significantly more or less metabolite than expected based on the dose. Monitor for increased side effects/ decreased efficacy or select alternative drug.
Antidepressants						
duloxetine *Cymbalta, G* Caps: 30, 60 mg	*Diabetic neuralgia, fibromyalgia, chronic low back pain, osteoarthritis of the knee:* Initial: 30-60 mg once daily **Maximum:** 120 mg per day	Nausea, headache, drowsiness, insomnia, dizziness, dry mouth. Do not use in patients with severe renal impairment (CrCl<30 mL/min).	Alcohol, CNS depressants. Avoid use with MAOIs or tramadol; may cause serotonin syndrome. Avoid use with potent CYP1A2 inhibitors (e.g., ciprofloxacin, fluvoxamine, ketoconazole). CYP2D6 inhibitors (e.g., SSRIs); may increase duloxetine levels.	Limited coverage (for doses ≤ 60 mg/d) Non-benefit (doses >60 mg/d)	$15-35	

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
venlafaxine *Effexor XR, G* Caps: 37.5, 75, 150 mg	*Neuropathic pain (Off-label):* Initial: 37.5 mg once daily Usual: 150-225 mg once daily **Maximum:** 375 mg per day	Hypertension, ataxia, sedation, insomnia, nausea, hyperhidrosis, dry mouth, constipation, anxiety, anorexia.	Clearance may be reduced by inhibitors of CYP2D6 such as cannabidiol, fluoxetine, paroxetine or quinidine, or by inhibitors of CYP3A4 such as erythromycin, itraconazole, ketoconazole or grapefruit juice. Contraindicated with MAOIs.	Regular benefit	$10-15	Duloxetine is preferred due to more evidence of efficacy for neuropathic pain.
Gabapentinoids and Anticonvulsants						
carbamazepine *Tegretol, G* Chew tabs: 100, 200 mg IR tabs: 200 mg CR tabs: 200, 400 mg Suspension: 100 mg/5 ml	*Trigeminal Neuralgia:* IR Tabs/Susp: Initial: IR tabs/Susp: 100 mg BID-QID CR tabs: 100 mg BID Usual: 400-800 mg per day in 2-4 divided doses **Maximum:** 1200 mg per day	Rash 5–10%, which rarely can be very serious; increased liver enzymes; transient neutropenia (common); aplastic anemia (extremely rare); hyponatremia.	Substrate of CYP3A4 and potent inducer of several cytochrome P450 enzymes; therefore, many potential drug interactions. May decrease efficacy of hormonal contraceptives; adjunctive nonhormonal birth control is recommended.	Regular benefit	$5-15 Susp: $50-100	
gabapentin *Neurontin, G* Caps: 100, 300, 400 mg Tabs: 600, 800 mg	*Neuropathic Pain/Diabetic neuropathy and other chronic pain conditions (Off-label):* Initial: 100-300 mg 1-3 times per day Usual: 900- 2400 mg/d in divided doses **Maximum**: 3600 mg per day *Postherpetic neuralgia (Off-label):* Day 1: 300 mg once daily Day 2: 300 mg BID Day 3: 300 mg TID Usual: 1800 – 3600 mg per day **Maximum**: 3600 mg per day *Fibromyalgia (Off-label):* Initial: 100 mg at bedtime Usual: 1200-2400 mg in 2-3 divided doses **Maximum:** 2700 mg per day	Sedation, ataxia, tremor; less commonly, GI upset, peripheral edema, vision changes, weight gain, respiratory depression.	Potentiates risk of respiratory depression and death when combined with opioids. Administration with aluminum/magnesium-containing antacids may decrease bioavailability.	Regular benefit	$10-30	In neuropathic pain, doses over 1800 mg/day do not produce better analgesia but do tend to increase harms.

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
pregabalin *Lyrica, G* Caps: 25, 50, 75, 150, 225, 300 mg	*Neuropathic Pain:* Initial: 50-150 mg once daily or in 2 divided doses Usual dose: 150-300 mg BID **Maximum**: 600 mg per day *Fibromyalgia:* Initial: 25-50 mg at bedtime Usual: 75-150 mg BID **Maximum**: 450 mg per day *Diabetic neuropathy*: Initial: 25-75 mg once daily or in 2 divided doses Usual: 150 mg BID-TID **Maximum**: 600 mg per day *Postherpetic neuralgia*: Initial: 75 mg once daily or 50 mg TID Usual: 150 mg BID **Maximum:** 600 mg per day	Sedation, ataxia, edema, diplopia, weight gain, dry mouth.	No known significant drug interactions; caution when used with opioids as it may potentiate risks of respiratory depression and death.	Regular benefit	$15-30	In neuropathic pain, doses over 300 mg/day do not produce better analgesia but do tend to increase harms.
Muscle Relaxants						
Usual duration of 1-2 weeks for muscle spasm associated with acute musculoskeletal conditions						
baclofen *Lioresal, G* Tabs: 10, 20 mg	5 mg BID-TID or 10 mg BID for 1-2 weeks **Maximum:** 80 mg/day	Sedation, muscle weakness, nausea, dizziness. Hepatotoxicity (very rare). Gradual withdrawal is important to minimize the potential for seizures. Not recommended in >65 y.	Potential additive CNS depression with benzodiazepines, opioids, TCAs and some antihypertensive agents.	Regular benefit	$3/ week	
cyclobenzaprine *Flexeril, G* Tabs: 10 mg	*Musculoskeletal spasm:* 5-10 mg TID for 1-2 weeks **Maximum:** 30 mg per day *Fibromyalgia (Off-label):* Initial: 10 mg at bedtime **Maximum:** 40 mg per day	Drowsiness, dry mouth, dizziness, fatigue, nausea, constipation. Not recommended in >65 y.	May increase risk of CNS effects when used with opioids or other CNS depressants. Increased risk of seizures with tramadol. SSRIs and CYP1A2 inhibitors (quinolones, ketoconazole) may decrease clearance. Do not use with MAOIs.	Regular benefit	$3/ week	5 mg may be as effective as 10 mg with less adverse effects.
methocarbamol Robaxin, G Tabs: 500, 750 mg	1000 mg QID for 1-2 weeks	Drowsiness, dry mouth, dizziness, fatigue, nausea, constipation. Not recommended in >65 y.	Combination with opioids or other CNS depressants may increase risk of CNS depression.	Non-benefit	$45/ week	Available without a prescription as a single agent and in combinations. See attached combination table.
Topical analgesics						
diclofenac diethylamine *Voltaren Emulgel* Gel: 1.16%, 2.32%	*Sprains, strains, muscle/tendon soreness:* Apply TID – QID for up to 7 days *Osteoarthritis:* Apply TID-QID	Skin dryness or irritation, hypersensitivity. Serious GI toxicity has not been seen to date in clinical trials.	With significantly lower amounts of medication in circulation following topical application (approximately 6% absorbed) vs. oral administration, drug interactions are unlikely with use of topical diclofenac. See diclofenac, oral for potential interactions.	Non-benefit	$20 per 100g tube	May also be compounded in higher strengths with a prescription.
diclofenac sodium *Pennsaid, G* Solution: 1.5%	*Osteoarthritis of the knee:* Apply 50 drops TID or Apply 40 drops QID for up to 3 months			Non-benefit	$250	

Generic Name *Trade Name* Dosage Forms and Strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per Month[D]	Comments
Cannabis/ Cannabinoids						
nabilone *Cesamet, G* Caps: 0.25, 0.5, 1 mg	*Neuropathic pain (off-label):* Initial: 0.25-0.5 mg at bedtime Usual: 1 mg BID Maximum: 6 mg per day	Sedation, dizziness, ataxia, psychotropic effects ("high"), tachycardia, orthostatic hypotension, dry mouth.	Additive sedation occurs with other sedating medications such as opioid analgesics, hypnotics, alcohol; avoid or minimize concurrent use if possible. Cannabidiols are metabolized by many CYP enzymes including 2C19 and 3A4 and may interact with other CYP substrates.	Regular benefit	$100	

ACE angiotensin converting enzyme; **BID** twice daily; **CAP** capsule/caplet; **CBD** cannabidiol; **COX-2** cyclooxygenase-2; **CNS** central nervous system; **CR** controlled release; **CrCl** creatinine clearance; **CV** cardiovascular; **CYP** cytochrome P450; **/d** per day; **ER** extended release; **G** generic; **GI** gastrointestinal; **INR** international normalized ratio; **IR** immediate release; **MAOI** monoamine oxidase inhibitor; **ME** morphine equivalent; **mg** milligrams; MI myocardial infarction; **MS** multiple sclerosis; **NSAID** Nonsteroidal anti-inflammatory drugs **ODT** orally disintegrating tablet; **OTC** over the counter; **QID** four times a day; **SL** sublingual; **SR** sustained released; **SSRI** selective serotonin reuptake inhibitor; **STAT** immediately; **SUPP** suppository; **SUSP** suspension; **TAB** tablet; **TCA** tricyclic antidepressant; **TID** three times a day; **THC** delta-9-tetrahydrocannabinol; **XL** controlled release; **XR** extended release

[A] **For normal renal and hepatic function. Consult product monograph for detailed dosing instructions and dose adjustments for special patient populations (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp) and/or an interaction checker (e.g., Lexicomp(c)) before prescribing.**

[B] Not an exhaustive list. Consult product monograph (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp) or an interaction checker (e.g., Lexicomp(c))

[C] PharmaCare coverage as of December 2019 (subject to revision). **Regular Benefit:** Eligible for full reimbursement*. **Limited Coverage:** Requires Special Authority to be eligible for reimbursement*. **RDP:** Reference Drug Program. Drugs included in the RDP are comparable agents of the same therapeutic class. **RDP Reference Drug:** Eligible for full reimbursement* within the therapeutic class, subject to benefit status of the therapeutic class. **Partial Benefit RDP:** Eligible for limited reimbursement* under the RDP program up to the price of the Reference Drug. **Non-benefit:** Not eligible for reimbursement. *Reimbursement is subject to the rules of a patient's PharmaCare plan, including any deductibles. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

[D] Drugs costs are average retail cost of the generic, when available. Current as of December 2019 and does not include retail markups or pharmacy fees.

Note: Information on which products PharmaCare covers can be obtained using the B.C. PharmaCare Formulary Search (www.health.gov.bc.ca/pharmacare/benefitslookup/).

Table 2: Morphine Equivalent Dosing Table[2]

	50 mg Morphine Equivalent	90 mg Morphine Equivalent
Codeine	334 mg/d	600 mg/d
Hydromorphone	10 mg/d	18 mg/d
Morphine	50 mg/d	90 mg/d
Oxycodone	33 mg/d	60 mg/d
Tramadol	300 mg/d	540 mg/d

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Table 3: Combination products

Opioid	Dose	Example Brands	Comments
Codeine/ acetaminophen/ caffeine	Codeine 8 mg Acetaminophen 300 mg Caffeine 15 mg	Tylenol #1 Generics	Available without a prescription
	Codeine 15 mg Acetaminophen 300 mg Caffeine 15-30 mg	Tylenol #2 Atasol 15 Generics	Prescription
	Codeine 30 mg Acetaminophen 300 mg Caffeine 15- 30 mg	Tylenol #3 Atasol 30 Generics	Prescription
Codeine/acetaminophen	Codeine 8 mg/5 ml Acetaminophen 160 mg/5 ml	Generics Elixir	
	Codeine 30 mg Acetaminophen 300 mg	Emtec-30 Generics	Prescription
	Codeine 60 mg Acetaminophen 300 mg	Tylenol #4 Generics	Prescription
Codeine/acetaminophen/ methocarbamol	Codeine 8 mg Acetaminophen 325 mg Methocarbamol 400 mg	Robaxacet 8 Generics	Available without a prescription
Codeine/acetaminophen/ doxylamine	Codeine 8 mg Acetaminophen 325 mg Doxylamine 5 mg	Mersyndol with codeine Generics	Available without a prescription
Codeine/ASA/ caffeine	Codeine 8 mg ASA 375 mg Caffeine 15 mg	222 Generics	Available without a prescription
Codeine/Butalbital/ASA combination	ASA 330 mg Butalbital 50 mg Caffeine 40 mg Codeine 30 mg	Fiorinal C1/2	Prescription
	ASA 330 mg Butalbital 50 mg Caffeine 40 mg Codeine 15 mg	Fiorinal C1/4	Prescription
Codeine/ASA/methocarbamol combinations	ASA 325 mg Codeine 32.5 mg Methocarbamol 400 mg	Robaxisal C1/2 Generics	Regular benefit
	ASA 325 mg Codeine 16.2 mg Methocarbamol 400 mg	Robaxisal C1/4 Generics	Regular benefit
Methocarbamol/ analgesic	Acetaminophen 325 mg Methocarbamol 400 mg	Robaxacet Generics	Available OTC
	Acetaminophen 500 mg Methocarbamol 400 mg	Robaxacet Extra Strength Generics	Available OTC
	ASA 500 mg Methocarbamol 400 mg	Robaxisal Extra Strength Generics	Available OTC
	Ibuprofen 200 mg Methocarbamol 400 mg	Robax Platinum Generics	Available OTC
	Ibuprofen 400 mg Methocarbamol 400 mg	Robax Platinum Extra Strength Generics	Available OTC

Note:
Available OTC: These products are Schedule 3 products which can be sold by a pharmacist to any person from the self-selection Professional Products Area of a Licensed pharmacy.
Available without a prescription: These products are Schedule 2 products which may be sold by a pharmacist on a non-prescription basis, and which must be retained within the Professional Service Area of the pharmacy where there is no public access and no opportunity for patient self-selection.