## Appendix A: Non-pharmacological treatments

### A) Physical activity/exercise therapies

<table>
<thead>
<tr>
<th>Type of activity/exercise</th>
<th>Benefits/role</th>
<th>Evidence level</th>
<th>Type of pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerobic exercise (e.g. walking)</td>
<td>Improved global well being and physical function, reduced pain FM (fibromyalgia)</td>
<td>**</td>
<td>Fibromyalgia</td>
</tr>
<tr>
<td>Strengthening exercise (e.g. lifting weights)</td>
<td>Global well being, pain and physical function (FM)</td>
<td>*</td>
<td>Fibromyalgia, non-specific LBP</td>
</tr>
<tr>
<td>Core stabilising exercises (e.g. pilates)</td>
<td>Reducing pain (non-specific low back pain [LBP(^2)], FM(^1))</td>
<td>Not reported in guideline</td>
<td>Non-specific LBP, Fibromyalgia</td>
</tr>
<tr>
<td>Tai Chi</td>
<td>Reducing pain, improving disability (arthritis(^1)), QoL (FM(^1))</td>
<td>Not reported in guideline</td>
<td>Chronic arthritis, Fibromyalgia</td>
</tr>
<tr>
<td>Yoga (any type)</td>
<td>Reducing pain and disability (headache, back pain, RA(^1)), Improved QoL, pain and function (FM(^1))</td>
<td>**</td>
<td>Fibromyalgia, Headache, LBP, RA</td>
</tr>
<tr>
<td>Therapeutic Aquatic Exercise</td>
<td>Improved pain, QoL, physical function, muscle strength (FM(^1), LBP(^2))</td>
<td>Not reported in guideline</td>
<td>Fibromyalgia, LBP</td>
</tr>
</tbody>
</table>

### B) Self-management programs

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Evidence level</th>
<th>Type of pain</th>
<th>Benefits/role</th>
<th>Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-management resources should be considered to compliment other therapies of patients with chronic pain</td>
<td>**</td>
<td>Chronic MSK pain (OA, RA, FM, LBP, neck pain, shoulder pain)</td>
<td>Reduced pain and disability (arthritis(^1))</td>
<td>Possible increased pain with exercise, resulting in drop out from programs: if this occurs, explore with the patient how best to help them cope.(^1)</td>
</tr>
</tbody>
</table>

### C) Psychological therapies

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Recommendations</th>
<th>Evidence level</th>
<th>Type of pain</th>
<th>Benefits/role</th>
<th>Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT</td>
<td>Cognitive behavioural therapy should be considered for the treatment of patients with chronic pain</td>
<td>**</td>
<td>Orofacial pain, LBP, neck pain, RA, FM</td>
<td>Reduced pain (orofacial, LBP, FM(^1), FM(^2))</td>
<td>Rarely may include worsening of co-existing mental disorders</td>
</tr>
<tr>
<td>Mindfulness based interventions</td>
<td>No recommendations given in guidelines</td>
<td>**</td>
<td>FM, LBP, RA, MSK pain</td>
<td>Reduced pain, reduced depression and anxiety, improved QoL</td>
<td>Not reported in guideline</td>
</tr>
<tr>
<td>Acceptance and Commitment Therapy</td>
<td>No recommendations given in guidelines</td>
<td>***</td>
<td>OA, Neuropathic pain, low back pain</td>
<td>Improved depression and anxiety</td>
<td>Not reported in guideline</td>
</tr>
<tr>
<td>Respondent behavioural therapies</td>
<td>Progressive relaxation or EMG biofeedback should be considered for the treatment of patients with chronic pain</td>
<td>**</td>
<td>LBP</td>
<td>Short term pain reduction, reduction in disability. No better than CBT</td>
<td>Not reported in guideline</td>
</tr>
</tbody>
</table>

### D) Physical therapies

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Type of pain</th>
<th>Evidence</th>
<th>Recommendations</th>
<th>Benefits/role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual Therapy</td>
<td>LBP, neck pain</td>
<td>***</td>
<td>Manual therapy should be considered for short term pain relief of patients with chronic low back pain</td>
<td>Short term: pain relief, functional improvement and cervicogenic headache(^2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Manual therapy in combination with exercise should be considered for the treatment of patients with chronic neck pain</td>
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</tr>
<tr>
<td>TENS</td>
<td>NP, LBP</td>
<td>***</td>
<td>TENS should be considered for the relief of chronic pain; either low or high frequency can be used</td>
<td>Pain (NP(^2)), improved function (LBP(^2))</td>
</tr>
<tr>
<td>Low Level Laser Therapy</td>
<td>LBP</td>
<td>***</td>
<td>Low level laser therapy should be considered as a treatment option for patients with chronic low back pain</td>
<td>Reduced pain(^2)</td>
</tr>
</tbody>
</table>
### Non-opioid Medications: General

<table>
<thead>
<tr>
<th>Drug/drug class</th>
<th>Pain type</th>
<th>Role in therapy</th>
<th>Potential harms</th>
<th>Dosage*</th>
<th>Tapering**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Osteoarthritis (hip or knee), in additional to non-pharmacological treatment</td>
<td>Should be considered for hip or knee osteoarthritis (alone or in combination with NSAIDs), in addition to non-pharmacological treatments</td>
<td>• Can be hepatotoxic at doses greater than 3–4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease</td>
<td>1000–4000 mg/day</td>
<td>Tapering not required</td>
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<td></td>
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<td></td>
<td>• Consider liver function tests (LFTs) if hepatic risk (history of liver problems or alcohol abuse, long-term use)</td>
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<td></td>
<td>• Reduce dose in liver insufficiency or alcohol dependence</td>
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<td></td>
<td>• Many medications (e.g., over the counter cough and cold and pain relief products) contain acetaminophen; read the label and avoid exceeding maximum dose</td>
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</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs (NSAIDs):</td>
<td>Low back pain</td>
<td>Should be considered for chronic non-specific low back pain</td>
<td>May have synergistic, dose-sparing effect when added to opioids</td>
<td>With all NSAIDs:</td>
<td>Tapering not required</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Risk of gastrointestinal (GI) bleeding/perforation, gastritis, and peptic ulcer disease</td>
<td>Allow 1–2 weeks for full effect.</td>
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<td></td>
<td></td>
<td></td>
<td>• Causes fluid retention</td>
<td>Consider lower doses in the elderly.</td>
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<td></td>
<td>• Avoid in severe renal dysfunction (CrCl &lt; 30 mL/min) or deteriorating renal disease; use caution if CrCl = 30–59 mL/min</td>
<td>Swallow whole, take with food.</td>
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<td></td>
<td>• Avoid in severe hepatic impairment</td>
<td>Avoid in the elderly (consider topicals instead)</td>
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<td></td>
<td>• Avoid during pregnancy (3rd trimester) or breastfeeding, severe uncontrolled heart failure, severe allergy to ASA or NSAIDs, active peptic ulcer disease, cerebrovascular disease, inflammatory bowel disease, or known hyperkalaemia</td>
<td>Monitor blood pressure (BP) and signs of heart failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Avoid in the elderly (consider topicals instead)</td>
<td>Avoid cardiovascular risks (heart attack and stroke)</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>• Ibuprofen (but not other NSAIDs) interacts with ASA to make it less effective for cardioprotection and stroke prevention.</td>
<td>Ibuprofen regular-release formulation: 200–400 mg q6–8h (max 1200 mg/day)</td>
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<td></td>
<td></td>
<td></td>
<td>• Naproxen (220 mg strength): 220 mg q8–12h (max 440 mg/day)</td>
<td>Naproxen (220 mg strength): 220 mg q8–12h (max 440 mg/day)</td>
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<td></td>
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<td></td>
<td>• Naproxen (125, 250, 375, and 500 mg strengths): Starting dose 250 mg BID may be increased to 375–500 mg BID.</td>
<td>Naproxen (125, 250, 375, and 500 mg strengths): Starting dose 250 mg BID may be increased to 375–500 mg BID.</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Naproxen (275 and 550 mg strengths): 275 mg q6–8h (max 1375 mg/day) or 550 mg BID.</td>
<td>Naproxen (275 and 550 mg strengths): 275 mg q6–8h (max 1375 mg/day) or 550 mg BID.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Naproxen (750 mg sustained-release strength): 750 mg once daily (max 750 mg/day)</td>
<td>Naproxen (750 mg sustained-release strength): 750 mg once daily (max 750 mg/day)</td>
<td></td>
</tr>
</tbody>
</table>

**LEGEND: CATEGORIES FOR LEVELS OF EVIDENCE** (according to original guidelines’ taxonomy)

- ***: Highest level of evidence (meta-analyses; systematic reviews of RCTs; RCTs with varying levels of bias)
- ••: Mid-level evidence (systematic reviews of case studies; high quality case control or cohort studies; experimental studies w/o randomization; case reports or studies)
- •: Low-level evidence (expert opinion and/or clinical experiences of respected authorities/guideline development group)
### Non-opioid medications: anticonvulsants

<table>
<thead>
<tr>
<th>Drug/drug class</th>
<th>Pain type</th>
<th>Evidence level</th>
<th>Role in therapy</th>
<th>Potential harms</th>
<th>Dosage*</th>
<th>Tapering**</th>
</tr>
</thead>
</table>
| **Carbamazepine** | Trigeminal neuralgia (may also be used for general neuropathic pain) | ••• | • Should be considered for neuropathic pain. | • May cause blood dyscrasias and liver toxicity.\(^\text{10}\)  
• Monitor blood counts and liver function tests\(^\text{11}\)  
• Enzyme inducer – may interfere with other drugs such as warfarin\(^\text{11}\) | • Starting dose: 100 mg – 200 mg daily  
• Titration: increase biweekly by 100-200 mg/day  
• Usual maintenance dose: 200-800 mg per day (in 2 to 4 divided doses). Doses of up to 1200-1600 mg/day have been used.\(^\text{2,21}\) | • Every 3 months, consider discontinuing or reducing the dose\(^\text{21}\)  
• Requires tapering: reduce dose by approximately 20% each week (faster if patient has reduced liver function)\(^\text{22}\) |
| **Gabapentin** | Neuropathic pain | ••• | • Should be considered (at doses titrated up to at least 1,200 mg/day) for neuropathic pain.  
• Normally the gabapentinoid of choice. | • May cause dizziness, drowsiness, or confusion\(^\text{10}\)  
• Potential for abuse - could lead to drug misuse or make the patient a target for drug abusers\(^\text{15}\) | • Starting dose: 300 mg once daily at night  
• Titration: Increase weekly by 300 mg/day  
• Usual maintenance dose: 1,200-3,600 mg/day (divided into 3 doses)\(^\text{2}\) | • Requires tapering: Reduce dose gradually over at least 1 week.\(^\text{23,24}\) |
| **Pregabalin** | Neuropathic pain | ••• | • Should be considered (at doses titrated up to at least 300 mg/day) for neuropathic pain if other 1st and 2nd line pharmacological treatments have failed. | • May cause sedation or dizziness\(^\text{10}\) | • Starting dose: 75 mg twice daily  
• Usual maintenance dose: 300 mg/day (150 mg twice daily).  
• Maximum: 600 mg/day (300 mg twice daily)\(^\text{2}\) | • Reduce dose gradually over at least 1 week.\(^\text{25}\) |
| Fibromyalgia | • Is recommended (at doses titrated up to at least 300 mg/day) for fibromyalgia. | ••• | | | |

**Anticonvulsants with insufficient evidence to support use in chronic pain:**
- Sodium valproate, lacosamide, lamotrigine, phenytoin, clonazepam, levetiracetam, topiramate

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**Legend: Categories for Levels of Evidence**

- ••• Highest level of evidence (meta-analyses; systematic reviews of RCTs; RCTs with varying levels of bias)
- •• Mid-level evidence (systematic reviews of case studies; high quality case control or cohort studies; experimental studies w/o randomization; case reports or studies)
- • Low-level evidence (expert opinion and/or clinical experiences of respected authorities/guideline development group)
### Appendix B: Non-Opioid Medications

#### Part 3 of 4

## Non-opioid medications: antidepressants[^2]

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Tricyclic Antidepressants (TCAs):</strong>&lt;br&gt;Amitriptyline, nortriptyline, imipramine</td>
<td>Neuropathic pain</td>
<td>***</td>
<td>Should be considered for neuropathic pain, except HIV-related neuropathic pain (imipramine or nortriptyline may be used if amitriptyline is ineffective)</td>
<td>• May cause sedation, dry mouth, confusion, constipation, urinary retention, prolonged QT interval, weight gain[^14][15]&lt;br&gt;• Many side effects may be tolerable with patient education, gradual dose titration and allowance for 1-2 weeks at a steady dose&lt;br&gt;• Caution in elderly (nortriptyline preferred)[^10]</td>
<td><strong>Amitriptyline:</strong>&lt;br&gt;• Starting dose: 10-25 mg/day&lt;br&gt;• Titration: increase weekly by 10 mg/day&lt;br&gt;• Usual maintenance dose: 25-125 mg/day[^9]&lt;br&gt;• Imipramine or nortriptyline: 25-75 mg/day[^4]&lt;br&gt;Requires tapering:&lt;br&gt;• Taper gradually over 4 weeks to 3 months or more (e.g., reduce dose by 25% every 4 weeks)[^16]&lt;br&gt;particular if patient has been on the drug for 6 weeks or more&lt;br&gt;• Doses should be decreased more slowly towards the end of the taper[^26][28][29]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibromyalgia</td>
<td>***</td>
<td>Should be considered for fibromyalgia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duloxetine</strong>&lt;br&gt;(a selective serotonin norepinephrine reuptake inhibitor; SNRI)</td>
<td>Neuropathic pain due to diabetes</td>
<td>***</td>
<td>Should be considered for diabetic neuropathic pain if other 1st or 2nd line pharmacological therapies have failed</td>
<td>• May cause headache, GI upset, insomnia, drowsiness, constipation, fatigue, dizziness[^10]&lt;br&gt;• Contraindicated in hepatic or severe renal impairment[^10]</td>
<td><strong>Starting dose:</strong> 60 mg once daily (30 mg starting dose may be used for tolerability reasons in some patients, with a goal of reaching 60 mg once daily within 1-2 weeks)[^10]&lt;br&gt;• Usual maintenance dose: 60 mg once daily (doses of up to 120 mg/day have been used)[^2]</td>
<td>Requires tapering if patient has been taking for more than 1 week[^10]&lt;br&gt;• Taper by switching to 30 mg strength or taking 60 mg on alternate days for at least 2 weeks.[^11]</td>
</tr>
<tr>
<td></td>
<td>Fibromyalgia</td>
<td>***</td>
<td>Should be considered for fibromyalgia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Osteoarthritis</td>
<td>***</td>
<td>Should be considered for osteoarthritis</td>
<td></td>
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</tr>
<tr>
<td><strong>Fluoxetine</strong>&lt;br&gt;(serotonin reuptake inhibitor; SSRI)</td>
<td>Fibromyalgia</td>
<td>***</td>
<td>Should be considered for fibromyalgia</td>
<td>• May cause nausea, dizziness, headache, anxiety, nervousness, drowsiness, weakness, diarrhea, upset stomach, dry mouth, loss of appetite, excessive sweating, sexual dysfunction&lt;br&gt;• May cause aggression or suicidal ideation/behaviour&lt;br&gt;• May prolong QT[^12]</td>
<td><strong>20 mg/day (up to 80 mg/day)[^2]</strong></td>
<td></td>
</tr>
</tbody>
</table>

## Non-opioid medications: topical[^2] (unless otherwise specified)

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>General</strong>&lt;br&gt;<strong>Topical NSAIDs:</strong> diclofenac solution[^25] or gel[^24]</td>
<td>Musculoskeletal pain[^1] and osteoarthritis[^15]</td>
<td>***</td>
<td>Should be considered for musculoskeletal pain[^1] or osteoarthritis,[^15] in patients who cannot tolerate oral NSAIDs (see below)&lt;br&gt;Manufactured and compounded NSAID products may vary in potency.</td>
<td>• Do not apply to skin with cuts or rashes.&lt;br&gt;• May cause skin blistering&lt;br&gt;• Increases sun sensitivity (rare)[^14]&lt;br&gt;<strong>Solution:</strong> 50 drops per knee 3 times a day, or 40 drops per knee 4 times a day[^31]&lt;br&gt;<strong>Gel:</strong> Apply twice daily (for lower strengths) or 3-4 times daily (for higher strengths)[^14]&lt;br&gt;Allow 1 week to reach full effects[^7]</td>
<td></td>
</tr>
<tr>
<td><strong>Topical rubefacients</strong>&lt;br&gt;(salicylate-containing; e.g. triethanolamine salicylate)</td>
<td>Postherpetic neuralgia (if 1st-line therapies ineffective)</td>
<td>***</td>
<td>Should be considered for musculoskeletal pain if other pharmacological therapies have been ineffective</td>
<td>Skin reddening and irritation at application site</td>
<td>1 to 3 plasters (12 hours on, 12 hours off). Try for up to 4 weeks, then discontinue if no improvement.</td>
</tr>
</tbody>
</table>

[^2]: Tapering recommendations are intended as general guidelines only. Monitor the patient’s response to dosage changes and use clinical judgment to base the pace of the taper on the patient’s response to prior dosage reductions.[^26]
## Non-opioid medications: Cannabinoids

<table>
<thead>
<tr>
<th>Drug/drug class</th>
<th>Pain type</th>
<th>Evidence level</th>
<th>Role in therapy</th>
<th>Potential harms</th>
<th>Dosage*</th>
<th>Tapering</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabinoids:</td>
<td>Neuropathic pain</td>
<td>Oral/buccal cannabinoids: Evidence is weaker than for other drug treatments</td>
<td>Oral/buccal cannabinoids: In general, other pharmacological and non-pharmacological neuropathic pain therapies should be tried first.</td>
<td>May cause drowsiness, euphoria, dry mouth, hallucinations</td>
<td>Nabilone: 1 or 2 mg BID; max 6 mg/day</td>
<td>Data not available on tapering.</td>
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<td>Even low doses of cannabis can cause cognitive impairment lasting up to 24 hours</td>
<td>Nabiximols: 4 to 8 sprays/day (divided BID); max 12 sprays/day</td>
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<td></td>
<td></td>
<td>May cause physical or psychological dependence</td>
<td>Dried cannabis: Dose is difficult to standardize due to limited dosing studies, differences in administration and cannabinoid content of different strains of cannabis, as well as interpatient variability. One study of vaporized cannabis used 800 mg placed in the vaporizer, with 8 to 12 inhalations taken over 2 hours. Inhale slowly over 3 seconds, hold breath for 10 seconds, then gently exhale.</td>
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<td></td>
<td>Dried cannabis is not appropriate for people:</td>
<td>For smoked cannabis (note: vaporization is generally preferred to smoking for safety reasons), the dose may range from 100-700 mg of no more than 9% THC cannabis daily. The upper safe level is approximately 3.0 g of dried cannabis per day (this upper limit would only be used for experienced cannabis users, not naïve patients, and would be gradually reached).</td>
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<td>under 25 years of age</td>
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<td>with personal or strong family history of psychosis</td>
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<td>with current or past cannabis use disorder</td>
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<td></td>
<td>with cardiovascular disease</td>
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<td></td>
<td>who are pregnant, planning to become pregnant, or breastfeeding</td>
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<td></td>
<td>Caution (for oral cannabis) in liver dysfunction</td>
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</tbody>
</table>

### General

- **Cannabinoids:**
  - Synthetic tetrahydrocannabinol (nabilone-oral)
  - Nabiximols (buccal cannabinoids)
  - Dried cannabis (taken by vaporizer or as an edible product)

### Non-Opioid Mediations

**Legend: Categories for Levels of Evidence** (according to original guidelines’ taxonomy)

- Highest level of evidence (meta-analyses; systematic reviews of RCTs; RCTs with varying levels of bias)
- Mid-level evidence (systematic reviews of case studies; high quality case control or cohort studies; experimental studies w/o randomization; case reports or studies)
- Low-level evidence (expert opinion and/or clinical experiences of respected authorities/guideline development group)
### Key points to discuss prior to an opioid trial

<table>
<thead>
<tr>
<th>Issue</th>
<th>Talking points[40,41]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Explaining an opioid trial</strong></td>
<td>• “Opioids may or may not help you, and they have some risks. This is why we usually do what is called a ‘trial’. We will start the medication slowly and gradually increase the dose to see if we can find a dose that improves your pain and function without causing side effects that you can’t live with.”</td>
</tr>
</tbody>
</table>
| **Establishing realistic goals of therapy for pain and function[3]** | • “What do you hope that the opioid treatment will do for you? How important is this benefit to you?”
  - • Goals may include reducing pain, improving function, or improving quality of life. Keep in mind that:
    - Opioids have a medium effect on pain (10–20% difference on pain scale)
    - Opioids have a small effect on function (<10% change on function scale)
    - Function can improve even when pain is still present.
    - However, there is no good evidence that opioids improve pain or function with long-term use.
    - “It can also be helpful to think about what coping skills you may use to manage the pain. We can discuss non-drug methods of managing pain in more detail.” |
| **Patient’s concerns about therapy** | • “Is there anything that worries you about starting opioid treatment? What difficulties do you think you might have?”
  - • See the relevant rows in this table for talking points to address common concerns. |
| **Possible risks of therapy** | • **Common side effects**: nausea (28%), constipation (26%), drowsiness (24%), dizziness (18%), dry skin/itching (15%), vomiting (15%).
  - • “The most common side effects are nausea and constipation. These can usually be managed by using anti-nausea drugs and anti-constipation drugs while on an opioid. Anti-nausea drugs are generally used short-term until the nausea side effect wears off. Anti-constipation drugs are generally used long-term while you are on the opioid.”
  - • **Accidents**: See “Driving” below
  - • **Overdose**: Avoid mixing opioids with alcohol or sleeping pills because this increase the risk of overdose. Signs of overdose include slurred or drawling speech, becoming upset or crying easily, poor balance, or “nodding off” during conversation or activity.
  - • **Addiction**: see “Addiction” row in this table.
  - • **Long-term risks**: Long-term use of opioids can lead to serious side effects such as sleep disorders, increased sensitivity to pain, and hormonal effects (low testosterone, loss of sex drive, decreased fertility).[4] |
| **Possible benefits of therapy** | • **Reduced pain**: “With treatment, we hope to reduce your pain by a couple of points on the pain scale, for example, from a 7 to a 5 (out of 10).”
  - • **Improved function**: “With treatment, we hope to improve your ability to do the activities that are important to you. However, the effect of the medication on function may be small. It’s important not to overuse the medication, or function may actually get worse.”
| **Safety** | “Opioids can help but they do have risks – these can be managed if we work together.”
  - • **Driving/operating machinery**: “Don’t drive while your dose is being gradually increased or if the medication is making you feel sleepy or confused.”
  - • **Withdrawal**: “If you stop taking your medication abruptly, you will experience withdrawal symptoms. This may feel like the flu: nausea, diarrhea, and chills. Withdrawal can be uncomfortable but it is not dangerous. It does not mean that you are addicted, just that you stopped the drug too quickly. If you stop your medication for 3 days or more, check with me before restarting it, because restarting opioids at your usual dose can have a significant risk of overdose and even death.”
  - • **Safe storage**: “Your body will get used to the dose that we set for you, but this same dose can be very dangerous for others. Store your medication safely at home; consider storing it in a lockbox, especially if there are children in the home. Do not store it in the medicine cabinet, as others will know to look for it there. Do not share your medication with others.”
  - • **Naloxone**: (particularly important for patients on doses of 50 MME/day; those with a history of overdose, or concurrent benzodiazepine use): “We recommend that you keep naloxone on hand in case of an accidental overdose. Naloxone is a medication that can reverse the effects of an opioid. You can get naloxone at your local pharmacy without a prescription. The pharmacist will show you and your family how to safely use and store it.”[42] |
| **Addiction** | “Addiction is a disorder where a person cannot control their use of a drug and continues to use it compulsively even if it leads to negative consequences in their life. Not all those suffering with addiction use the drug to ‘get high’. When people take opioids for pain, there is a risk that some may develop an addiction to it: those at greatest risk have a history of addiction with alcohol or other drugs. However, we will make a plan to watch out for it to help keep you safe.” |
| **Treatment agreement** | • “To help us tell whether the opioid trial is working for you, we will make a treatment agreement together. A treatment agreement helps outline our goals and expectations for the trial, and how the trial will work.”
  - • See the relevant rows in this table for talking points to address common concerns. |
  - • Opioid information for patients: [http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b04.html](http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b04.html)
### Appendix C: Opioid prescribing and monitoring for chronic non-cancer pain (CNCP)

#### Part 2 of 7

## Evidence for opioids in CNCP conditions

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Examples of CNCP conditions where evidence supports opioid use*</th>
<th>Examples of CNCP conditions evidence is insufficient to support opioid use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol only</td>
<td>Fibromyalgia</td>
<td></td>
</tr>
<tr>
<td>Weak** or strong opioid</td>
<td>*Diabetic neuropathy, Peripheral neuropathy, Postherpetic neuralgia, Phantom limb pain, Spinal cord injury with pain below the level of injury, Lumbar radiculopathy, Osteoarthritis, Rheumatoid arthritis, Low-back pain, Neck Pain</td>
<td>*Headache, Irritable bowel syndrome, Pelvic pain, Temporomandibular joint dysfunction, Atypical facial pain, Non-cardiac chest pain, Lyme disease, Whiplash, Repetitive strain injury</td>
</tr>
</tbody>
</table>

* Studies lasted only 3 months.

** Weak opioids include codeine and tramadol. Strong opioids include morphine, oxycodone, hydromorphone, fentanyl, tapentadol, buprenorphine and methadone.

---

** Putting the evidence in perspective:**

While many opioid therapies have 2 or 3 dots under “Evidence level”, denoting a good quality of evidence, this simply means that the studies were well-designed, not that the effect was large. Most of the studies were no more than 3 months long, and the overall effect size of opioids is only moderate for pain (corresponding to a 1 or 2 point decrease on a 10-point pain scale) and low for improved function (corresponding to a 10% or smaller improvement in function). Non-opioid treatments are considered 1st-line in managing chronic non-cancer pain. Opioids should be used only if non-opioid treatments have failed or cannot be used.

---

### Weaker opioids

#### Drug/drug class

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Pain type</th>
<th>Evidence level</th>
<th>Role in therapy</th>
<th>Potential harms</th>
<th>Dosage**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Codeine</strong></td>
<td>Chronic low back pain, Osteoarthritis</td>
<td>***</td>
<td>Use only if patient does not respond to non-opioid therapies.</td>
<td>Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting.</td>
<td>Start: 15-30 mg q6h. Titration: q7d, increase by 15-30 mg/d. Max: 600 mg/d. Pearls: When used with acetaminophen, limit max acetaminophen dose to 3.2g/day. Maximum duration of therapy for breastfeeding women = 4 days (some women rapidly metabolize codeine to morphine; causing neonatal toxicity).</td>
</tr>
<tr>
<td><strong>Tramadol</strong></td>
<td>Chronic low back pain, Osteoarthritis</td>
<td>***</td>
<td>Use only if patient does not respond to non-opioid therapies.</td>
<td>Seizure risk (in patients at high risk of seizure or patients on medications that increase serotonin, such as selective serotonin reuptake inhibitors [SSRIs]). Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting.</td>
<td>Tramadol/acetaminophen (37.5/325 mg): Start: 1 tab q4-6h (max 4 tabs/d). Titration: q7d, increase by 1 tab q4-6h. Max: 8 tabs/d. Tramadol regular release: Starting dose (days 1-3): 25 mg QAM. Titration (as tolerated): Day 4-6: 25 mg BID. Day 7-9: 25 mg TID. Day 10-12: 25 mg QID. Day 13-15: 50 mg TID. Day 16 and thereafter: 50 mg QID. Tramadol controlled-release (CR): Start: 100-150 mg q24h (depends on brand). Titrate: q2-7d (depends on brand). Max: 300-400 mg/d (depends on brand).</td>
</tr>
</tbody>
</table>

---

March 2017
## Appendix C: Opioid prescribing and monitoring for chronic non-cancer pain (CNCP)

### Stronger opioids

<table>
<thead>
<tr>
<th>Drug/drug class</th>
<th>Pain type</th>
<th>Evidence level</th>
<th>Role in therapy</th>
<th>Potential harms</th>
<th>Dosage</th>
</tr>
</thead>
</table>
| **Morphine** | • Chronic low back pain  
• Osteoarthritis (Only continue if there is ongoing pain relief; regular review is required) | ** | • Use only if patient does not respond to non-opioid therapies. Among opioids, this is a 2nd-line opioid for mild to moderate pain and a 1st-line opioid for severe pain | • Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting  
• Abuse/addiction: Use with caution in patients with high risk of opioid abuse  
• Avoid in renal impairment (toxic metabolite can accumulate) | • Immediate release (IR):  
• Start: 5-10 mg q4-6h (max 40 mg/d)  
• Titrate: q7d, increase by 5-10 mg/d  
• Max: Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day**  
• Controlled release (CR):  
• Start: 10-20 mg od, bid, or tid (max 40 mg/d)  
• Titrate: q14d, increase by 5-10 mg/d  
• Max: Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day** |
| **Oxycodone** | • Chronic low back pain  
• Osteoarthritis (Only continue if there is ongoing pain relief; regular review is required) | ** | • Use only if patient does not respond to non-opioid therapies. Among opioids, this is a 2nd-line opioid for mild to moderate pain and a 1st-line opioid for severe pain | • Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting  
• Abuse/addiction: Use with caution in patients with high risk of opioid abuse | • Immediate release (IR):  
• Start: 5 mg q4-6h (max 30 mg/d)  
• Titrate: q7d, increase by 5 mg/d  
• Max: Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Conversion Table for corresponding oxycodone dose.  
• Controlled release (CR):  
• Start: 10 mg od, bid, or tid (max 30 mg/d)  
• Titrate: q14d, increase by 10 mg/d  
• Max: Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Conversion Table for corresponding oxycodone dose. |
| **Hydromorphone** | • Chronic low back pain  
• Osteoarthritis (Only continue if there is ongoing pain relief; regular review is required) | ** | • Use only if patient does not respond to non-opioid therapies. Among opioids, this is a 2nd-line opioid for mild to moderate pain and a 1st-line opioid for severe pain | • Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting  
• Abuse/addiction: Use with caution in patients with high risk of opioid abuse | • Immediate release (IR):  
• Start: 1-2 mg q4-6h (max 8 mg/d)  
• Titrate: q7d, increase by 1-2 mg/d  
• Max: Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Conversion Table for corresponding hydromorphone dose.  
• Controlled release (CR):  
• Start: 3 mg od or tid (max 9 mg/d)  
• Titrate: q14d, increase by 2-4 mg/d  
• Max: Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Conversion Table for corresponding hydromorphone dose. |
| **Fentanyl** | • Chronic low back pain  
• Osteoarthritis (Only continue if there is ongoing pain relief; regular review is required) | ** | • Use only if patient does not respond to non-opioid therapies. Among opioids, this is a 2nd-line opioid for mild to moderate pain and a 1st-line opioid for severe pain | • Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting  
• Abuse/addiction: Use with caution in patients with high risk of opioid abuse  
• Avoid placing sources of heat on top of patch (e.g., heating pads) | • Only use fentanyl in patients who have taken a morphine equivalent dose (MED) of at least 60-100 mg/day for at least 2 weeks  
• Use the Opioid Conversion Table to convert from other opioids  
• Do not switch patients directly from codeine to fentanyl (10% of Caucasian patients lack the enzyme that metabolizes codeine to morphine; these patients may not have developed a tolerance to opioids)  
• In Ontario, fentanyl patches must be prescribed and dispensed in accordance with the Patch For Patch program  
• The Opioid Patch Exchange Disposal Tool can help assist with patch exchange  
• Maximum fentanyl patch dose is 50 μg/hour evaluated at 24 hours  
• The Opioid Patch Exchange Disposal Tool can help assist with patch exchange  
• Maximum fentanyl patch dose is 50 μg/hour evaluated at 24 hours  
• The Opioid Patch Exchange Disposal Tool can help assist with patch exchange |
| **Methadone** | • Chronic low back pain  
• Osteoarthritis (Only continue if there is ongoing pain relief; regular review is required) | ** | • Use only if patient does not respond to non-opioid therapies  
• Methadone is primarily used for managing addiction but may sometimes be used to manage pain. It can only be prescribed by physicians with a special exemption from Health Canada. | • Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting  
• Abuse/addiction: Use with caution in patients with high risk of opioid abuse  
• Avoid in renal impairment (toxic metabolite can accumulate) | • Methadone is not intended for initial titration in an opioid trial.  
• Consult a specialist with expertise in methadone treatment.  
• Methadone is primarily used for managing addiction but may sometimes be used to manage pain. It can only be prescribed by physicians with a special exemption from Health Canada. |
## Appendix C: Opioid prescribing and monitoring for chronic non-cancer pain (CNCP)

### Stronger opioids

<table>
<thead>
<tr>
<th>Drug/drug class</th>
<th>Pain type</th>
<th>Evidence level</th>
<th>Role in therapy</th>
<th>Potential harms</th>
<th>Dosage</th>
</tr>
</thead>
</table>
| Tapentadol            | • Osteoarthritis (studied mainly in knee OA)  
                        • Low back pain | ***           | • Should be considered as an option for pain relief in patients with chronic low back pain and osteoarthritis | • Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting, hypotension  
                        • Abuse/addiction  
                        • May accumulate in severe hepatic impairment. | • Available as extended-release and controlled-release tablets.  
                        • Opioid-naive patients:  
                        • Starting dose: Start with the smallest patch: 5 mcg/hr; change patch every 7 days  
                        • Titration: Remove current patch and replacing with the next highest strength every 7 days as required. Patches available as 5, 10, 15, and 20 mcg/hr.  
                        • Tip: If pain occurs at the end of the dosing interval it is usually a sign that the dosage needs to be increased, not that the dosage interval needs to be decreased.  
                        • Maximum dose: 20 mcg/hr patch every 7 days.  
                        • Opioid-experienced patients:  
                        • Start on 5 mcg/hr or 10 mcg/hr patch, provide adequate rescue medication, and titrate by 5 to 10 mcg/hr every 7 days as required. (max 20 mcg/hr).  
                        • When to start:  
                        • Patients dependent on heroin or short-acting opioids: Start when objective signs of withdrawal occur (Clinical Opioid Withdrawal Scale [COWS] score of 13 or greater), but not less than 6 hours after the patient last used opioids.  
                        • Patients receiving methadone: First, reduce methadone to minimum dose tolerable by patient, then start buprenorphine/naloxone only when objective signs of withdrawal appear (COWS score of 13 or greater) and generally not less than 24 hours after the patient last used methadone.  
                        • Starting dose:  
                        • Day 1: 4 mg, then an additional 4 mg dose if needed. Usual dose target for Day 1 is 8-12 mg.  
                        • Titration: Increase by 2-8 mg to a level that holds the patient in treatment and prevents withdrawal effects  
                        • Usual maintenance dose:  
                        • 12 mg to 16 mg once daily, maximum 24 mg daily  
                        • Once stable, may give twice the patient’s daily dose every other day (e.g., give 16 mg every other day for a patient stabilized on 8 mg daily) or 3 times a week (with twice the daily dose on Monday and Wednesday and three times the daily dose on Friday), do not exceed 24 mg on any one day.  |
| Buprenorphine (transdermal) | • Chronic low back pain  
                        • Osteoarthritis | **           | • Useful if problems with oral administration.                                   | • Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting.  
                        • Abuse/addiction  
                        • Allow 3 weeks before re-using the same patch site, and avoid exposing the patch to direct sunlight (increases absorption).  
                        • Do not use in people weighing less than 40 kg.  
                        • May accumulate in severe hepatic impairment. | • May be used in opioid-naive and opioid-experienced patients (in patients taking up to 80 mg oral morphine equivalents [MME] per day).  
                        • Opioid-naive patients:  
                        • Starting dose: Start with the smallest patch: 5 mcg/hr; change patch every 7 days  
                        • Titration: Remove current patch and replacing with the next highest strength every 7 days as required. Patches available as 5, 10, 15, and 20 mcg/hr.  
                        • Tip: If pain occurs at the end of the dosing interval it is usually a sign that the dosage needs to be increased, not that the dosage interval needs to be decreased.  
                        • Maximum dose: 20 mcg/hr patch every 7 days.  
                        • Opioid-experienced patients:  
                        • Start on 5 mcg/hr or 10 mcg/hr patch, provide adequate rescue medication, and titrate by 5 to 10 mcg/hr every 7 days as required. (max 20 mcg/hr).  
                        • When to start:  
                        • Patients dependent on heroin or short-acting opioids: Start when objective signs of withdrawal occur (Clinical Opioid Withdrawal Scale [COWS] score of 13 or greater), but not less than 6 hours after the patient last used opioids.  
                        • Patients receiving methadone: First, reduce methadone to minimum dose tolerable by patient, then start buprenorphine/naloxone only when objective signs of withdrawal appear (COWS score of 13 or greater) and generally not less than 24 hours after the patient last used methadone.  
                        • Starting dose:  
                        • Day 1: 4 mg, then an additional 4 mg dose if needed. Usual dose target for Day 1 is 8-12 mg.  
                        • Titration: Increase by 2-8 mg to a level that holds the patient in treatment and prevents withdrawal effects  
                        • Usual maintenance dose:  
                        • 12 mg to 16 mg once daily, maximum 24 mg daily  
                        • Once stable, may give twice the patient’s daily dose every other day (e.g., give 16 mg every other day for a patient stabilized on 8 mg daily) or 3 times a week (with twice the daily dose on Monday and Wednesday and three times the daily dose on Friday), do not exceed 24 mg on any one day. |
| Buprenorphine/naloxone | NA                       | NA             | • Used for substitution treatment of adults with problematic opioid dependence. The naloxone component is to deter injection and intranasal use and abuse. | • Should only be prescribed by physician who:  
                        • Has experience in substitution treatment of opioid dependence  
                        • Has completed a recognized education program.  
                        • Must be dispensed daily under healthcare professional supervision until patient is stable enough to safely store take-home doses.  
                        • Co-ingestion with alcohol or other CNS depressants could lead to a fatal overdose.  
                        • Accidental consumption of even one dose by an opioid-naive person could lead to fatal overdose.  
                        • Side effects:  
                        • After first dose: withdrawal effects (e.g., shaking, sweating, headache, pain, muscle aches, nausea)  
                        • Other side effects: constipation, anxiety, tiredness, nausea/vomiting, dizziness, orthostatic hypotension. | • Do not use in opioid-naive patients.  
                        • When to start:  
                        • Patients dependent on heroin or short-acting opioids: Start when objective signs of withdrawal occur (Clinical Opioid Withdrawal Scale [COWS] score of 13 or greater), but not less than 6 hours after the patient last used opioids.  
                        • Patients receiving methadone: First, reduce methadone to minimum dose tolerable by patient, then start buprenorphine/naloxone only when objective signs of withdrawal appear (COWS score of 13 or greater) and generally not less than 24 hours after the patient last used methadone.  
                        • Starting dose:  
                        • Day 1: 4 mg, then an additional 4 mg dose if needed. Usual dose target for Day 1 is 8-12 mg.  
                        • Titration: Increase by 2-8 mg to a level that holds the patient in treatment and prevents withdrawal effects  
                        • Usual maintenance dose:  
                        • 12 mg to 16 mg once daily, maximum 24 mg daily  
                        • Once stable, may give twice the patient’s daily dose every other day (e.g., give 16 mg every other day for a patient stabilized on 8 mg daily) or 3 times a week (with twice the daily dose on Monday and Wednesday and three times the daily dose on Friday), do not exceed 24 mg on any one day. |
**General dosage/administration tips:**
- Start with immediate-release opioids instead of sustained-release or long-acting opioids. Do not use long-acting opioids unless the patient has severe, continuous pain and has been taking immediate-release opioids daily for at least 1 week.
- Titrate oral opioids until efficacy or intolerance.
- Use the lowest effective dose.
- Benzodiazepines can considerably lower the lethal opioid dose; consider tapering off of benzodiazepines or starting with a lower dose of opioid.
- Parenteral opioids are not recommended in CNCP (high risk of overdose, addiction, and infection).
- Use caution with controlled-release (CR) formulations: they can cause overdose if bitten/crushed (this converts them to immediate-release).
- Titrate oral opioids until efficacy or intolerance.

Opioids are subject to restrictions around prescribing and dispensing:
- Be aware of the risk of prescription fraud - see the College of Physicians and Surgeons of Ontario (CPSO) resource on Prescribing Drugs.
- Refills are not permitted on opioid prescriptions. For more information, see the regulations summary chart.
- Patients must present valid photo ID (e.g., driver’s license, photo health card, passport) when having an opioid prescription written by their prescriber and may also need to show ID when picking up opioid prescriptions at the pharmacy. To learn more, see this resource on Ontario’s Narcotics Strategy.
- Effective January 1, 2017, Ontario Drug Benefit (ODB) does not cover certain high-dose opioid formulations: see this Ontario Ministry of Health Bulletin for more details.

WATCHFUL DOSE: Recent guidelines recommend reassessing the benefit/risk of doses ≥50 MME/day and to “avoid or justify increasing dosage” at doses ≥ 90 MME/day.

LEGEND: CATEGORIES FOR LEVELS OF EVIDENCE (according to original guidelines’ taxonomy)

- Highest level of evidence (meta-analyses; systematic reviews of RCTs; RCTs with varying levels of bias)
- Mid-level evidence (systematic reviews of case studies; high quality case control or cohort studies; experimental studies w/o randomization; case reports or studies)
- Low-level evidence (expert opinion and/or clinical experiences of respected authorities/guideline development group)
### Appendix C: Opioid prescribing and monitoring for chronic non-cancer pain (CNCP)

#### Monitoring tips
- Monitor every 2-4 weeks for efficacy and tolerability
- Continue until optimal dose is reached (see definition)\(^{40}\)
- Do a 3-day “tolerance check” for those at high risk of sedation (elderly, on benzodiazepines, renal or hepatic impairment, COPD, sleep disorders, cognitive impairment)\(^{55}\)
- Call the patient 3 days after initiation or dose change to ask about signs of sedation\(^{40}\)

#### Optimal dose definition\(^{40}\)
- Improved function (based on goals agreed upon with patient)* OR
- At least a 30% pain reduction (2 points on a 0-10 scale) without loss of function**
- No additional analgesic benefit for 1 or 2 additional dose increases
- No serious side effects or complications
*Can assess pain and function with Brief Pain Inventory scale: [http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b09.html](http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b09.html)

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### Process for managing patients coming into your practice on opioids

#### i) Review appropriateness of therapy:
Patients entering your practice on opioids may not have received a proper opioid trial and may have inadvertently ended up on long-term opioid therapy for an acute condition that has since resolved.

<table>
<thead>
<tr>
<th>Review and document(^{40})</th>
<th>When to consider discontinuing opioids(^{56})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain condition diagnosis</strong></td>
<td>Pain condition has resolved:</td>
</tr>
<tr>
<td>Is patient on the opioid for a pain condition for which opioids have been shown to be effective? (See Table)</td>
<td>Patient receives definitive treatment for condition</td>
</tr>
<tr>
<td><strong>Risk screening</strong></td>
<td><strong>Risks outweigh benefits:</strong></td>
</tr>
<tr>
<td>Assess patient’s risk for abuse (may use Opioid Risk Tool)</td>
<td>Increased overdose risk</td>
</tr>
<tr>
<td>Opioids are not recommended for patients with an active substance use disorder. Facilitate treatment of the substance use disorder if not already addressed(^{56})</td>
<td>Clear evidence of diversion</td>
</tr>
<tr>
<td><strong>Goal setting</strong></td>
<td><strong>Clinical features of opioid use disorder (OUD) appear</strong></td>
</tr>
<tr>
<td>Ask patient about their goals for therapy (pain reduction, function improvement), and whether they feel the opioid is helping them achieve these goals: “Realistically, what would living well look like for you?”</td>
<td></td>
</tr>
<tr>
<td><strong>Informed consent</strong></td>
<td><strong>Side effects outweigh benefits:</strong></td>
</tr>
<tr>
<td>Review risks/benefits/goals of therapy (see Talking Points in the Opioid Trial section). Consider using an informed consent/treatment agreement (see sample treatment agreement).</td>
<td>Side effects impair functioning below baseline level</td>
</tr>
<tr>
<td><strong>Appropriateness of opioid and dose</strong></td>
<td><strong>Patient finds side effects intolerable</strong></td>
</tr>
<tr>
<td>Ask patient whether their pain and function have improved (can assess pain and function with Brief Pain Inventory scale)</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse events of current opioid treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Ask patient if they are having side effects and if so, the impact on their life.</td>
<td></td>
</tr>
</tbody>
</table>

#### ii) If opioid therapy is inappropriate, consider switching or discontinuing the opioid.

**Switch:** “Sometimes a medication is appropriate when it is started but becomes less appropriate as time goes on and things change. I usually review my patients’ pain medications regularly to make sure they are still on the best treatment for them. At this point, it seems that you might benefit from switching to a different opioid. How would you feel about that?”

**Discontinuation:** “Sometimes a medication is appropriate when it is started but becomes less appropriate as time goes on and things change. I usually review my patients’ pain medications regularly to make sure they are still on the best treatment for them. At this point, it seems that your opioid medication is no longer giving you enough benefits to warrant the risks of using it. How would you feel about trying to slowly decrease the dose?”

**If switching opioid, convert as described in the Opioid Conversion Chart (see p.12).**

**If discontinuing opioid, taper as described in Opioid Tapering Tips in the main tool.**
## Appendix C: Opioid prescribing and monitoring for chronic non-cancer pain (CNCP)

### Opioid Conversion Chart

**Step 1:** Calculate total daily dose of current opioid (from regular and PRNs).

**Step 2:** Convert the dose of the current opioid to oral morphine equivalent: Multiply the total daily dose by the number in **Column B**.

**Step 3:** Reduce the total daily dose to account for unpredictable cross-tolerance:
- If oral morphine equivalent from Step 2 > 75 mg: multiply by 0.50.
- If oral morphine equivalent from Step 2 ≤75 mg: multiply by 0.60-0.75.

**Step 4:** Convert to dose of new opioid: Multiply the amount from Step 3 by the number in **Column C**.

**Step 5:** An immediate release opioid may also be indicated for incident/breakthrough pain, especially during the titration period. To calculate a single PRN dose, use 10 to 15% of the total daily dose.

**Step 6:** Do a 3-day “tolerance check”: Contact patient after 3 days to check for pain control and signs of oversedation (slurred speech, emotional ability, ataxia, drowsiness). Adjust dose if needed based on side effects, pain relief, and use of rescue medication (add the 24 hour total of rescue medication to the total daily dose).

### Note:
Be cautious when switching from one opioid to another, particularly in the elderly, in patients taking several medications, and in patients with other co-morbidities. Dose conversion charts can be useful but there is significant inter-individual variability and limited evidence of their accuracy.

### Drug Conversion Table

<table>
<thead>
<tr>
<th>Drug*</th>
<th>Column A: Equivalence to oral morphine 30 mg</th>
<th>Column B: To convert to oral morphine equivalent, multiply by:</th>
<th>Column C: To convert from oral morphine, multiply by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30 mg</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Codeine</td>
<td>200 mg</td>
<td>0.15</td>
<td>6.67</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20 mg</td>
<td>1.5</td>
<td>0.667</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>6 mg</td>
<td>5</td>
<td>0.2</td>
</tr>
<tr>
<td>Meperidine</td>
<td>300 mg</td>
<td>0.1</td>
<td>10</td>
</tr>
</tbody>
</table>

### Methadone and Tramadol

Morphine dose equivalence not reliably established.

CDC guidelines have some information on methadone conversion factors: [https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf](https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf)

### Fentanyl**
- 0 – 134 mg morphine = 25 mcg/h
- 135 – 179 mg morphine = 37 mcg/h
- 180 – 224 mg morphine = 50 mcg/h
- 225 – 269 mg morphine = 62 mcg/h
- 270 – 314 mg morphine = 75 mcg/h
- 315 – 359 mg morphine = 87 mcg/h
- 360 – 404 mg morphine = 100 mcg/h

### Tapentadol***
Clinical studies demonstrated comparable pain relief between tapentadol (extended-release or controlled-release) and oxycodone CR at a dose ratio of 5:1. Clinical guidelines suggest that a switch to a new drug should be accompanied by a 50% reduction in the calculated dose.

### Buprenorphine (transdermal)
Start with 5 or 10 mcg/hr patch, provide adequate rescue medication and titrate as required (by 5 mcg/hr every 7 days to max 20 mcg/hr). Patch strengths available: 5, 10, 15 and 20 mcg/hr.* Studied in patients taking up to 80 mg oral morphine equivalents (MME per day; patients on longer-term or higher-dose opioids may experience withdrawal symptoms after starting transdermal buprenorphine.) Palliative care specialist guidance is recommended when switching from oral morphine to transdermal buprenorphine.

### Buprenorphine + naloxone
Used as substitution therapy in patients with problematic opioid dependence.

When to start:
- Patients dependent on heroin or short-acting opioids: Start when objective signs of withdrawal occur (Clinical Opioid Withdrawal Scale [COWS] score of 13 or greater), but not less than 6 hours after the patient last used opioids.
- Patients receiving methadone: First, reduce methadone to minimum dose tolerable by patient, then start buprenorphine/naloxone only when objective signs of withdrawal appear (COWS score of 13 or greater) and generally not less than 24 hours after the patient last used methadone.

Starting dose:
- Day 1: 4 mg, then an additional 4 mg dose if needed. Usual dose target for Day 1 is 8-12 mg.
- Titration: Increase by 2-8 mg to a level that holds the patient in treatment and prevents withdrawal effects.

Usual maintenance dose:
- 12 mg to 16 mg once daily, maximum 24 mg once daily.

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*These doses are approximations due to inter-individual variation.

**Re: Fentanyl:
- These estimates are conservative; therefore DO NOT use these values for reverse conversion (e.g., fentanyl to morphine).
- The 12 mcg fentanyl patch is generally used for dose adjustment rather than initiation of fentanyl treatment.
- Only use fentanyl in patients who have taken a morphine equivalent dose (MED) of at least 60-100 mg/day for at least 2 weeks.
- Do not switch patients directly from codeine to fentanyl (10% of white patients lack the enzyme that metabolizes codeine to morphine; these patients may not have developed a tolerance to opioids).

***Re: Tapentadol:
- Tapentadol has a dual mechanism of action: mu-opioid agonist plus norepinephrine reuptake inhibitor. Therefore caution is advised when switching to tapentadol from pure mu-opioids.