Pain Management for Older Adults[1,2]

See RxFiles Pain Documents: RxFiles.ca/Pain

RxFiles.ca/Geri
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Introduction

- Pain is common in older adults – reported by over half of those surveyed.[3]
  - It is especially common in long-term care where up to 80% of residents reported pain.[31]
- The consequences of pain in older adults are significant and include depression, anxiety, immobilization, deconditioning, & increased healthcare costs.[32]
- Consider whether pain is acute (<3-month duration) vs chronic (≥3-month duration), along with the type(s) of pain involved.

Common Types & Examples[16] (can have >1 type of pain present at the same time)	
Nociceptive: somatic	Arthritis (e.g. knee, hand, hip), myofascial pain (e.g. neck), low back pain – MOST COMMON type of pain in older adults
Nociceptive: visceral	Gastritis, constipation, peptic ulcer disease
Neuropathic	Diabetic peripheral neuropathy, post-herpetic neuralgia, lumbar/cervical radiculopathy, post-stroke pain
Nociplastic	Irritable bowel syndrome, fibromyalgia

- The nervous system changes over time, making older adults less sensitive to some stimuli (e.g. heat, therefore increasing burn risk) and more sensitive to others (e.g. more likely to perceive pain, more likely to experience side effects from medications).
- Many of the principles of acute and chronic pain management are similar for older adults as in other populations. To explore related RxFiles resources, visit: RxFiles.ca/Pain.
  - However, when adults are living with frailty (See Geri-RxFiles: Frailty pg 8), pain management plans must consider not only patient comfort and physical function, but also strive to prevent injury, improve psychosocial function, prevent deconditioning, maintain homeostasis, and optimize quality of life.[11]

Pain Assessment for Older Adults

- Ask older adults about presence of pain / discomfort at each appointment.
  - Some older adults may not acknowledge their experience as "pain" & may identify more strongly when asked about pain using different terms (e.g. ask about discomfort, hurt, aching, soreness, &/or stiffness).
- Obtain a self-report of pain whenever possible, due to the subjective nature of pain (however, there may be cognitive, language, and literacy barriers to self-reporting).[10]
  - To assess ability to self-report, ask person to place a mark on a pain scale where severe pain is represented, & check for logical placement before proceeding with assessment.
  - Ask about the pain's location & quality, relieving / aggravating factors, perception of tolerability, functional limitations, impact on quality of life, & expectations for relief of pain – frail older adults may have difficulty identifying &/or communicating details regarding their pain experience.
- Consider the biopsychosocial components of the pain experience, including mental health, social supports (e.g. loneliness, grief), family attitudes, values, beliefs, & culture.
  - Ask about depression / anxiety, as low mood can intensify the pain experience.
- Assess nutrition, hydration, sleep, as well as bowel / bladder function & regularity, as these factors may contribute to pain & / or to behavioural changes which may otherwise be attributed to pain.

Pain Assessment for Older Adults continued

- Choose suitable *Pain Assessment Tools* (use same tool for initial & ongoing assessment):

1) If able to verbally report:
   Numeric Rating Scale (**NRS**, 0-10 scale) or
   Verbal Descriptor Scale (e.g. mild, moderate, severe) – to assess pain intensity;
   Douleur Neuropathique (**DN4**, includes clinical exam) – to assess neuropathic pain.

   Some other comprehensive multidimensional pain assessment tools include the:
   Pain Disability Index (**PDI**) &
   Brief Pain Inventory (short-form or long-form; **BPI**).
2) If able to self-report by pointing: Faces Pain Scale-Revised.
3) If unable to self-report due to cognitive impairment (e.g. dementia) use the:
   Pain Assessment in Advanced Dementia (**PAINAD**) Scale or
   Pain Assessment Checklist for Seniors with Limited Ability to Communicate (**PACSLAC-II**) tool.

   Also monitor pain-related behaviours (e.g. activity, agitation, sleep).
   Ensure assessments are comparable (e.g. consistently "before breakfast for five minutes").
4) To assess functional ability:
   Katz Index of Independent in Activities of Daily Living (**ADL**) scale;[23]
   Lawton-Brody Instrumental Activities of Daily Living (**IADL**) Scale;[24]
   Functional Independence Measurement (**FIM**) Instrument;[25] or
   Barthel Index.[26]

- Observe during movement & rest for signs of pain behaviours (e.g. wincing, grimacing, altered gait, emotional distress, sweating, groaning).
- Gather collateral information when available & relevant; collect observations from family / caregivers of the person's past "normal" & what they did to manage pain / discomfort.
- Establish the individual's potential acute & chronic causes of pain whenever possible (consider comorbidities, potential for procedural pain, incidents / trauma).[10]
- Review what matters most to patients & families (e.g. pain levels, alertness, constipation avoidance, mobility independence, opioid avoidance, longevity). Recognize & try to address discrepancies between patient & family priorities.
- **Resources**:
  - Pain Assessment in Cognitively Impaired Older Adults
  - Comprehensive Geriatric Assessment Toolkit Plus – Pain Assessment

Common Challenges in Pain Management for Older Adults

- Pain may be *over-* or *under*-reported (e.g. "eclipsed" by comorbidities; missed due to communication difficulties; disregarded by the person due to concerns about taking pain medication; over-emphasized in the context of concurrent loneliness or fear that something is being missed and the worry of causing damage with movement).
- Experiencing numerous chronic conditions can contribute to increases in the sources of pain & pain intensity (e.g. stroke, myocardial infarction, diabetes, peripheral vascular disease, osteoporosis, cancer).[11]
- Activity avoidance may result if an individual or caregiver believes that "hurt equals harm". This may lead to physical deconditioning, risk of falls, vascular pooling, increased pain with movement, constipation, poor sleep satisfaction, lower mood, & less socialization.
- Pain is highly prevalent in people with dementia (e.g. if bed-bound, at risk of pressure ulcers), & it can be challenging to assess due to limitations with ability to self-report. May present as agitation & alterations in behaviour (e.g. guarding, calling out, aggression).
- Older adults tend to experience greater sensitivity to adverse events (AE) related to medications, particularly centrally-acting pain medications. This limits the ability to use some medications safely, particularly when individuals live with frailty.
  - Approach medication trials conservatively ("start low, go slow") & with close monitoring.
  - Intentional and purposeful efforts should be made to: 1) discontinue medications that are ineffective, cause intolerable AE, and / or do not align with goals of care &, 2) avoid prescribing cascades (adding medications to treat AE related to another medication).

General Chronic Pain Management Principles for Older Adults

- Target a strategy to address the underlying cause / type of pain whenever possible.
- **Goal setting:** Focus on enhancing *function primarily*, alongside *potential for reduction in pain intensity*. Elimination of pain is often not realistic, & if pursued, may come at a cost of functional impairment, behavioural change, +/- AE (e.g. confusion / higher fall risk).
  - Help patients and families set realistic expectations, especially regarding function & daily activities (e.g. improved function / behaviour, 30% reduction in pain intensity).
  - Some suggest choosing "comfort-function-mood" goals: establish acceptable pain intensity, daily functional activity, and mood improvement / maintenance.[10]
- **Prioritize & optimize non-drug therapy. Utilize a multimodal approach** (e.g. using the "4 Ps of Pain Management": physical, psychological, preventative, & pharmacological).
  - Emphasize active strategies to address pain (e.g. physical therapy, activities to increase movement, engagement with social supports, relaxation techniques).
  - Passive strategies (e.g. medication, massage therapy) are seldom sufficient when used as monotherapy & **most effective when used as adjuncts to active strategies**.
  - Non-pharmacological interventions may improve pain severity without significant adverse effects and although can be used as stand-alone treatment, combining with pharmacological interventions can synergistically reduce pain severity.[33]
- If available, interdisciplinary chronic pain clinics may be helpful, especially if mental health or other polypharmacy impacts pain management.

Non-Pharmacological Strategies – 1st line for chronic pain

- Offer **education.** This might include:
  - validation of the pain experience,
  - encouragement that active strategies can improve function (e.g. posture, gait, confidence),
  - reassurance that "hurt does not equal harm",
  - reasonable expectations for passive pain management strategies, and
  - the benefits of a multimodal pain management approach.
- Ensure **basic comfort needs** are being met. This might include:
  - addressing hunger and/or thirst,
  - ensuring regular toileting, and
  - optimizing temperature (not too hot, not too cold).
- Utilize **physical interventions**. Involvement of a physical therapist can be helpful, particularly if there are difficulties with balance, strength, & conditioning. Interventions might include:
  - physiotherapy, graded exercise 10 to 20 to 30 min/day,
  - water-based therapies, hot baths,
  - Tai Chi, chair exercises / chair yoga, yoga,
  - heat / cold packs – monitor closely if sensitive & thin skin,
  - manual / massage therapies, acupuncture, and
  - electrical devices such as transcutaneous electrical nerve stimulation.
- Employ **psychological interventions**. Exploring changes in daily routine & having visitation times for family / friends can profoundly benefit pain. Interventions might include:
  - counselling, cognitive behavioural therapy,
  - mindfulness-based stress reduction, breath control exercises, relaxation,
  - coping techniques,
  - distraction, imagery,
  - problem-solving therapy,
  - music[12] / art / pet therapy,
  - humour,
  - hypnosis,
  - reminiscence therapy, and
  - spiritual care.
- Consider **preventative strategies** (e.g. assistive devices, mobility aids, braces, splints, activity pacing, regular repositioning, noise & light reduction).
  - Consulting an occupational therapist can be valuable to improve function at home.
  - Physical therapists can help recommend appropriate mobility aids, braces and splints.
  - Also consider smoking cessation, minimize alcohol consumption, strive for healthy eating, & seek to possibly improve sleep quality.
- Encourage engagement with **Chronic Pain Self-Management Programs**, which may be found locally or online (e.g. LivePlanBe).
  - **Other Resources**: https://www.healthinaging.org/a-z-topic/pain-management
    - https://www.arthritis.org/
    - https://geriatricpain.org/

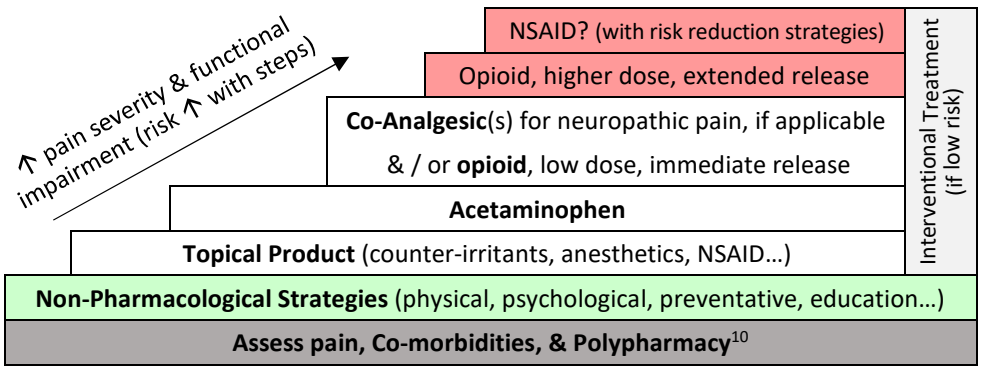
Pharmacological Strategies – General Approaches

- Consider an individual's level of frailty, functional status, comorbidities, polypharmacy, potential risks of treatment, preferences, past medication trials (those helpful & those not), renal and hepatic function, as well as allergies / intolerances.[10]
- Use low-dose, short-term (when possible / suitable), as an **adjunct to support non-pharmacological approaches**.
- Use the least invasive route of administration (e.g. oral, topical, or subcutaneous).
- Counsel individual / family regarding expectations (e.g. 30% reduction in pain, greater focus on improving function and ability to perform daily activities).
- Implement one medication change at a time to allow for assessment of effect.
- Plan for timely reassessment & documentation of goals, along with the beneficial and adverse effects of management strategies.

- Some recommend a stepped approach when adding medication to other multimodal pain management strategies (increase steps for higher pain severity AND functional goals not being achieved):[10, expert opinion]
  1) trial **topical agent**(s) (e.g. non-medicated, NSAID, capsaicin) +/- **acetaminophen**,
  2) consider low-dose immediate release (IR) **opioid** (breakthrough +/- scheduled),
  3) cautious change from immediate to extended-release (ER) opioid or use of oral NSAID.

  If component of neuropathic pain, consider use / addition of a co-analgesic:
  1) SNRIs (fewer anticholinergic properties compared to TCAs, however also associated with falls risk; **duloxetine** is better supported by evidence than venlafaxine).
  2) gabapentinoids (e.g. gabapentin, **pregabalin**; use caution given potential for edema & central nervous system (CNS) adverse effects; renal dose adjustment required).
  3) TCAs (limited role in older adults given anticholinergic properties, even at low doses for pain; **nortriptyline** may be less anticholinergic than amitriptyline).
     - Might combine if a single agent has some benefit, is tolerated, and there is desire for additional improvement in function; however, be alert for potential additive adverse effects when multiple drugs with CNS or cognitive side effects are used together.

Potential Stepped Approach:[10, expert opinion]



*Risks often exceed potential benefits, particularly for frail older adults for the following: oral NSAID, tricyclic antidepressants (TCAs), opioids (particularly at high doses), muscle relaxants, & cannabis.

Trial & Assessment of Regularly Scheduled Pain Medication for Chronic Pain

- May use regular administration of analgesics when pain is continual & ongoing.
- Establish the **goals** of therapy prior to initiation (e.g. what functional improvements might be desired by the patient and what is realistic for their circumstance?)
- Institute a **cautious dosing strategy**, starting with a low dose (often half the suggested initial dose) &/or longer dosing interval, then titrate up to *lowest-effective* dose, based on therapeutic response & tolerability.
- Allow **adequate time** for treatment effect where expected benefit is delayed.
- **Document** baseline status and any change in reported function, pain, or pain-related behaviour. Documentation is key to successful assessment.
- **Follow-up to assess** for tolerability in ~3 days & again for any benefit in pain / function as documented over ~1 to 4 weeks.
  - Monitor for ↑ use of pain meds (including looking at increases in use of "as needed" medication administration) without incremental benefits in pain and/or function.
- **Deprescribe** (stop or taper, as appropriate) if little to no documented benefit after an appropriate trial, if intolerable AE, & possibly also to assess if flare of pain has subsided.

Topical Agents

Topical products are the lowest-risk pharmacological option available. May be used for regional or localized pain, e.g. musculoskeletal (MSK) pain, OA, some neuropathic pain, low back pain. While use is generally not supported by evidence, some experts suggest regular application of even non-medicated lotions / moisturizers can be helpful – possibly due to touch therapy / massage, relaxation? Keep away from eyes.

- Generally well-tolerated due to minimal systemic absorption. May be an option if ESRD.

- Over-the-counter products: Counter-irritants (e.g. with menthol, camphor, &/or methyl salicylate, such as **RUB A535**, **SALONPAS**, or **capsaicin** 0.025% & 0.075% creams) / anesthetics (**lidocaine** 5% ointment, 4% & 5% creams) – evidence limited.[13]
- Compounded agents: different combinations of ingredients (e.g. ketamine, clonidine, gabapentin, baclofen) studied for neuropathic, nociceptive, and mixed pain types – none found to be better than placebo.[14] Cost can be prohibitive, generally not recommended.

NSAID - For OA or MSK pain in a localized area (e.g. 1 to 2 of the joints only) such as knee, hand, wrist, ankle (not effective for hip – joint is too deep for topical to be effective).

- Topical NSAIDs are likely underutilized: cost-effective, evidence to support use (e.g. for knee OA: as effective as oral NSAID & more effective than acetaminophen[19]) & safe / few AE.

- **Diclofenac diethylamine** **VOLTAREN EMUGEL** 1.16% gel applied TID to QID or **VOLTAREN EMUGEL EXTRA STRENGTH** 2.32% gel applied BID
- **Diclofenac sodium** **PENNSAID** 1.5% solution – 40 drops QID or 50 drops TID
  - Generally, schedule for ~7-**14** days to assess effectiveness for pain.
  - Diclofenac gel may also be compounded (usual concentration 4-16%), however systematic review evidence suggesting benefit (especially for acute pain) is largely based on the diclofenac Emulgel 1-2% concentration.[13]
  - Given the cost and potential for increased systemic absorption of higher strength compounded products, suggest optimizing commercially available preparations ahead of potential trials for compounded strengths.

Non-Opioid Pharmacological Oral Options

Acetaminophen TYLENOL

For nociceptive acute pain; mixed evidence for chronic low back pain and osteoarthritis (OA). While not generally helpful for neuropathic or nociplastic pain, potentially useful to trial if potential for a mixed type of chronic pain due to preferred safety profile relative to other analgesic options for older adults.

- **TYLENOL** 325 to 500mg every 6 hours (or up to 1000mg every 6 hours)
- **TYLENOL ARTHRITIS PAIN** or **TYLENOL MUSCLE & BODY** 650 to 1300mg long-acting (biphasic) formulation every 8 to 12 hours – Avoid crushing to maintain the dosing interval.

→ **Maximum daily dose** for short-term acute pain ≤ **3** to 4g/day. For chronic dosing suggest limiting to maximum ≤ 2 to 3g/day (lower end of dosing range for frail older adults, <50kg, or other risk factors for hepatotoxicity).[21] **Avoid** if severe hepatic dysfunction.

Adverse Events: Generally, well tolerated (does not generally cause stomach upset / sedation). Some observational studies suggest a possible ↑ in GI bleeding when taking >2-3g/day, as well as ↑SBP of ~5mmHg with 4g/day for 2 weeks.

Monitor: Liver function tests (LFTs) after 2-3wks of chronic use & periodically thereafter if patient at risk of hepatic impairment (e.g. pre-existing liver disease, alcohol consumption ≥3 drinks per day, malnutrition), consider monitoring BP if prior diagnosis of HTN.

Additional considerations:

- Effectiveness not well established for chronic / acute low back pain or OA & hepatoxicity possible with chronic use; however, generally carries lower risk than systemic alternatives.
- Some experts suggest trial of scheduled use at a therapeutic dose (limited to 2-3g/day) as a preferred option for patients with chronic pain & without severe hepatic impairment.
- Generally, schedule for ~7-14 days to assess effectiveness for chronic pain.
- Rectal administration (suppositories) an option.
- Watch for the potential for unintentional overuse of acetaminophen. Commonly found in combination over-the-counter (**OTC**) products! Sometimes also scheduled and put in bubble packs, plus then inadvertently taken in addition as an OTC product.
- Consider asking patients to bring in their acetaminophen bottles, to fully assess how much they are taking & to ensure they don't contain anticholinergic agents such as diphenhydramine and methocarbamol.
- Counsel that acetaminophen is different from the OTC anti-inflammatories, emphasizing that they are not interchangeable.
- **Potential risk factors for hepatotoxicity with acetaminophen**: dry body weight <50kg, older / frail patients, renal insufficiency, decompensated liver disease, chronic malnutrition / dehydration, cachexia, chronic alcohol consumption, long-term treatment with liver-enzyme-inducing medications.[21]
- **If dementia with worsening agitation / behaviours**: Might trial regularly scheduled administration of acetaminophen & assess for initial effect after 24 to 48 hours,[11] then reassess after 5-7 days to consider risks vs benefits of continuing treatment.
- **If heart failure (HF) or end stage renal disease (ESRD)**: Acetaminophen may be used. No dose adjustment required.
- **If cirrhosis**: Reduce maximum dose taken chronically to ≤ 2-2.6g/day for older adults (if used).

Non-Steroidal Anti-inflammatory Drugs (NSAID) & COX-2 Inhibitors, Oral SB

NSAIDs have a very limited role since older adults are at high risk of adverse events. Rarely safe for ongoing use for people living with frailty. Low doses effective for nociceptive pain; In most cases, limit use in older adults who are living with frailty to the lowest effective dose for a short-term (e.g. 1-2 days) for acute inflammatory nociceptive pain conditions for which the perceived benefits of treatment outweigh the risks. Generally, avoid use for chronic pain.[27] When used, prescribe with concurrent PPI. START

- **Naproxen ALEVE, ANAPROX, NAPROSYN, VIMOVO*** (includes esomeprazole) 250 to 375mg every 12 hours – safest CV profile? (suggested in meta-analysis, average age=61yrs, supported in subgroup analysis for adults >60yrs, however level of frailty not reported[28])
- **Ibuprofen ADVIL, MOTRIN** 200 to 400mg every 6 to 8 hours – Potential DI with ASA.
- **Celecoxib CELEBREX** 100 to 200mg every 24 hours – ↓ ulcer risk & antiplatelet effects.

Adverse Events: MANY

Renal concerns: All NSAID & COXIBs compromise renal function & ↑ risk of kidney injury (particularly in relative dehydration which is common). Avoid in patients with pre-existing renal dysfunction. Avoid in combination with diuretic/MRA + ACEi/ARB. Hold NSAID during acute illness to help prevent AKI (See RxFiles: Medications to Pause on Sick Days).

Bleeding & gastrointestinal (GI) concerns: All NSAID ↑ risk of GI ulcers & complications. COXIBs may offer GI advantage (when not combined with other antiplatelet agents).

Cardiovascular (CV) concerns: All NSAID & COXIBs can ↑ CV risk, even with short-term use; may ↑ BP (dose related) & risk of acute HF (promote fluid retention) / myocardial infarction.

S: Caution if eGFR <50 mL/min/1.73m^2, severe HTN (systolic BP >170 mmHg / diastolic BP >100 mmHg), known history of coronary, cerebral, or peripheral vascular disease (↑ risk of thrombosis), or HF requiring loop diuretics. Acetaminophen trial for OA & xanthine-oxidase inhibitor for gout each preferred over long-term NSAID use for these indications.

B: Avoid if CrCl <30mL/min & if symptomatic heart failure (caution if asymptomatic). May ↑BP (dose-related). Avoid combining with other concurrent NSAIDs.

Indomethacin INDOCID B: Avoid use - Has the most AE of all the NSAIDs in older adults (↑ risk of CNS effects, GI bleed, & AKI).

Ketorolac TORADOL B: Avoid use - ↑ risk of GI bleed & AKI.

SB: Risk of gastrointestinal bleed with NSAIDs - ↑ with age (e.g. >75yrs old). Avoid / use caution with NSAID if history of gastric or duodenal ulcer (unless pt can take a PPI or misoprostol – these ↓ but do not eliminate risk). Avoid: 1) chronic use, and 2) for short-term scheduled use in combo with corticosteroids, anticoagulants, or antiplatelet agents (unless alternatives not effective & the patient can take a concurrent GI protection agent).

DI: If on naproxen / ibuprofen + ASA EC 81mg/day (caution ↑ GI bleed risk), give ASA EC ≥2-4 hr pre- or ≥8hr post-NSAID. One observational study found an association between ↑ peptic ulcer risk for older adults when NSAID combined with acetylcholinesterase inhibitors.[20]

Monitor: Kidney function (at least annually, up to every 1-2 wks if renal risk / status change).

Additional considerations:

- May be an option if ESRD + on dialysis & anuric (further renal damage not possible, but GI/CV risks persist).

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) SB

For neuropathic pain and chronic low back pain; may also be helpful for OA of the knee, nociplastic pain (e.g. fibromyalgia), and if patient has concurrent depression / anxiety.

- **Duloxetine CYMBALTA**: 30mg daily; may ↑ to 60mg after ~**2** weeks if tolerating lower dose; maximum 120mg daily (though limited benefit at doses >60mg for chronic pain with ↑AE) – most evidence for ↑function & ↓chronic pain vs. other antidepressants.
  - Capsules can be opened & sprinkled on applesauce while maintaining its 24-hour action - do not chew pellets.
  - DI: Metabolized through CYP1A2 & 2D6*, also a CYP2D6 inhibitor – more drug interactions than other SNRIs
  - Generally, avoid if CrCl <30mL/min (B) & contraindicated in ESRD, however, anecdotal reports suggest that very low doses (~30mg/day) may be okay, with caution to monitor for nausea / diarrhea and avoid concurrent serotonergic agents.
- **Venlafaxine XR EFFEXOR XR**: 37.5mg daily; may ↑ to 37.5mg BID or 75mg daily after 4 to 7 days, 150 to 225mg daily for effective dose.

S: Use caution if severe HTN (SBP >180 / DBP >105 mmHg) as may ↑BP.

B: Caution if history of falls/fractures – may cause ataxia, ↓psychomotor function, syncope, or additional falls. May exacerbate / cause SIADH or hyponatremia – use with caution.

Adverse Events: Generally, well tolerated. May cause dry mouth, nausea, headache, agitation, insomnia, tremor, bleeding, and/or ↓sodium.

Monitor: Monitor electrolytes (sodium) one month after starting an SNRI for an older adult, and after a dose change, especially if the individual is taking a medication implicated in SIADH (e.g. diuretics, see Geri-RxFiles: Electrolyte Imbalances pg 159). Blood pressure.

Additional considerations:

- Less anticholinergic than tricyclic antidepressants (TCAs).
- Venlafaxine may ↑ blood pressure more than duloxetine, particularly at higher doses.

Gabapentinoids B

For neuropathic pain (including may be trialed for refractory trigeminal neuralgia) and nociplastic pain (e.g. fibromyalgia). Pregabalin in particular may be helpful if concurrent anxiety. Start low dose, titrate up cautiously based on tolerability & effect.

- **Gabapentin NEURONTIN**: 100 to 200mg at bedtime; may ↑ by 100 to 300mg weekly; usual dose for an older adult ranges from 300 to 600mg BID to TID.
- **Pregabalin LYRICA**: 25 to 50mg at bedtime; may ↑ by 25 to 50mg every 3-7 days; usual dose for an older adult ranges from 50 to 150mg BID.

B: Reduce dose with CrCl <60mL/min due to ↑ risk of CNS AE. Avoid combining with opioids or other CNS depressants (e.g. benzodiazepines).

Adverse Events: Dizziness, drowsiness, ataxia, diplopia, mental clouding / confusion, falls, fractures, & peripheral edema.

Monitor: Kidney function, excess sedation, peripheral edema, & fall risk.

Additional considerations:

- Maybe an option for neuropathic pain if renal impairment / ESRD (dose adjustment required, titrate cautiously)
- Avoid combining with other CNS depressants, including alcohol, sedatives, & opioids.
- Pregabalin may be preferred over gabapentin due to linear absorption as well as typically twice daily administration.
- Gabapentinoids are sometimes taken for non-medical reasons (i.e. differently than prescribed), as they can produce euphoria and anxiolytic effects. Use caution prescribing for people with a history of substance use disorder and be mindful that prescribing could make an individual a "target" for theft. Ensure secure storage and use.
- If functional benefit not established or AE outweigh benefit, taper to discontinuation.
- **Resource:** See the EMPOWER brochure for patient information about deprescribing for Gabapentinoids EMPOWER brochure.

Tricyclic Antidepressants (TCAs) SB - **Generally not recommended in older adults (3rd-line option) – MANY adverse effects!**

Use cautiously for older adults. Avoid use in individuals with cognitive impairment or a history of delirium. Use with caution in older adults with constipation, urinary retention, or falls. Might be used for chronic migraine prevention, and possibly for low back, neuropathic, & nociplastic pain (evidence is limited for these last three types of pain conditions; generally low-quality trials). In most cases, less anticholinergic agents (e.g. SNRIs) are preferred for neuropathic pain. If using, start low dose, then titrate based on tolerability & effect. If no benefits seen after a reasonable therapeutic trial (~4-8 weeks), deprescribe to ↓ the risk of adverse effects. Chronic use of anticholinergic drugs linked to ↑ risk for developing dementia.[34,35]

Some examples include:

- **Nortriptyline AVENTYL**: 10mg at bedtime; may ↑ to 20 or 25mg after ≥1 week – Generally preferred over amitriptyline: Less anticholinergic & less likely to cause hypotension and therefore may be better tolerated (though maintains the cardiac toxicity risks).
- **Amitriptyline ELAVIL**: 10mg at bedtime; may ↑ to 20 or 25mg after ≥1 week – Generally avoid; More anticholinergic than the secondary amines nortriptyline & desipramine.

S: Caution if dementia / delirium, narrow angle glaucoma, cardiac conduction abnormalities (may ↑QTc interval), lower urinary tract symptoms related to benign prostatic hyperplasia (BPH), chronic constipation, recent falls, or prior history of urinary retention (risk of worsening these conditions).

B: Avoid use; highly anticholinergic (See Geri-RxFiles: Anticholinergics chart, page 106), sedating, & causes orthostatic hypotension. Caution if history of falls/fractures – may cause ataxia, ↓psychomotor function, or syncope. May ↓urinary flow & cause urinary retention. May also exacerbate/cause SIADH or hyponatremia.

Adverse Events: MANY - Dry mouth, memory impairment / ↓ cognition / inattention / confusion (might mimic dementia), ↑ delirium risk, sedation, constipation, urinary hesitancy / retention, dizziness, orthostatic hypotension / ↑ fall risk, and impaired cardiac conduction (even at low doses used for pain). High risk of overdose lethality.

Monitor: Monitor for efficacy, toxicity, & anticholinergic intolerance. Monitor electrolytes (sodium) one month after starting a TCA for an older adult and after a dose change, especially if the individual is taking another medication implicated in SIADH (e.g. diuretics). Consider baseline ECG in those with cardiac history or other QT prolongation risk factors.

Additional considerations:

- Nortriptyline may be an option if renal impairment / ESRD (dose adjustment not required).

Cannabinoids

Possibly for moderate to severe treatment refractory chronic pain (low quality evidence that **SATIVEX** may help with neuropathic pain; CBD & whole plant formulations under-studied[29]), however adverse effects are common. Generally, reserve for situations in which other strategies (pharmacological and non-pharmacological) have not been sufficient to allow for achievement of functional goals / quality of life, and the potential benefits are deemed to outweigh the anticipated risks. [30]

- **Nabilone CESAMET**: 0.5mg HS, up to 2mg BID. – Available by prescription. Use for chronic pain is off-label.
- **Whole plant extract THC/CBD SATIVEX**: Buccal spray, 1 spray BID; may ↑ by 1 spray per day, up to ~4 to 5 sprays/day. – Available by prescription. Indicated for relief of spasticity related to multiple sclerosis who have not responded to other therapy & who experience benefit during an initial trial. Use for other types of chronic is off-label.
- **Whole plant cannabis products**: Many - Includes oils, capsules, dried plant, etc. – Numerous different THC/CBD ratios available from a variety of sources (e.g. retail cannabis stores, online from a licensed producer with authorization from a health care practitioner). Use for any indication, including chronic pain, is off-label. Expensive.

DI: Avoid combining with other CNS depressant & anticholinergic medications. CBD may inhibit metabolism of CYP 3A4, 2D6, and 3C19 substrates (e.g. duloxetine, amitriptyline, methadone, buprenorphine, oxycodone) to ↑ their effect. May also ↑ INR with concurrent warfarin.

Adverse Events: Dizziness, drowsiness, confusion, dry mouth, nausea, anxiety, & cognitive impairment are most common (generally, most AE associated with the THC component).

- Generally, avoid cannabinoid products for older adults who have mental health conditions, difficulty with balance or at falls risk, cardiovascular disease (may ↑ risk of heart disease or stroke, & blood pressure may ↑ or ↓), history of substance use disorder, and with driving.

Monitor: Excess sedation, ↓ cognitive acuity, fall risk, BP, & possibly LFTs (with ↑ CBD doses).

Additional considerations:

- Research about the risks & benefits of cannabis use in older adults is limited. Cannabis impacts parts of the brain known to change with age and may interact with medications and other chronic conditions which tend to be common in older adults.
- Insufficient evidence to recommend whole plant cannabis products.[17] Harms tend to outweigh benefits in most cases. If using, start with a high CBD/low THC non-inhaled product to minimize AE. Some suggest initial CBD dose of 5mg po daily or BID, may ↑ CBD by 5-10mg per day every 2-3 days to usual max 40mg/day. If adding THC at that point, initiate at 1mg/day, then may ↑ THC by 1mg weekly to max 40mg/day if tolerated.[15]
  - If a patient is planning to trial cannabis, advise having someone around when first trying it out & being in a safe comfortable location. Encourage documenting amount of intake and their experiences of use, with subsequent slow titration as tolerated.[16]
  - Counsel about delayed onset for oral doses to avoid risks of repeating dose too early.
- Ask patients about cannabis use, as they may be buying cannabis products without healthcare provider involvement & may not volunteer this information.
- **Resources**: A patient handout with general information about cannabis use for older adults is available from the Canadian Centre on Substance Use and Addiction, and a more detailed booklet for older adults is available from Active Aging Canada.

Other Pharmacological Options

- **Carbamazepine TEGRETOL** B: 100mg at bedtime, slowly titrate up by 100-200mg per day every 2 to 3 days, up to 400mg BID – first-line agent for short-term use in trigeminal neuralgia.

  B: May exacerbate / cause SIADH or hyponatremia.
  - **DI**: MANY - Metabolized by CYP3A4**, also a strong CYP3A4 inducer as well as induces a number of other CYP enzymes, though to a lesser degree
  - **Adverse Events**: Blood dyscrasias, may ↑ risk of heart failure & bradyarrhythmia, ↓sodium / SIADH, ataxia, falls, dizziness, drowsiness, nausea, constipation.
  - **Monitor:** CBC, excess sedation, & fall risk. Monitor electrolytes (sodium) one month after starting for an older adult, and after a dose change, especially if the individual is taking another medication implicated in SIADH (e.g. diuretics, see Geri-RxFiles: Electrolyte Imbalances, pg 159). May also monitor serum trough concentrations (e.g. annually or if signs of toxicity).

Additional considerations:

- Highly plasma protein bound & free portion is active. Monitor for increased AE / toxicity in hypoalbuminemia.
- "**Muscle Relaxants**" B – e.g. **cyclobenzaprine**, **methocarbamol**, **baclofen**
  ****Generally not recommended for older adults – MANY adverse effects!****
  - Occasionally used short-term (≤2 weeks for acute low back pain, no evidence for use in chronic pain), however, tends to have many CNS adverse effects, is anticholinergic, and may contribute to confusion & weakness – rarely safe for pain / muscle spasm in older adults.
  - May trial baclofen for pain associated with spasticity (e.g. multiple sclerosis), however, the low doses needed to avoid adverse effects may not be helpful.

  B: Muscle relaxants typically used to treat musculoskeletal complaints are poorly tolerated by older adults due to anticholinergic adverse effects, sedation, and ↑ risk of fractures; effectiveness at dosages tolerated by older adults is questionable.
  - Cyclobenzaprine is strongly anticholinergic: avoid if lower urinary tract symptoms or BPH (may ↓urinary flow & cause urinary retention), delirium (or at risk of delirium), dementia, or cognitive impairment. Caution if history of falls/fractures – may cause ataxia, ↓psychomotor function, or syncope.
  - Baclofen: Generally, avoid with CrCl <60mL/min due to ↑ risk of CNS AE & encephalopathy. If used, use the lowest effective dose & monitor for signs of CNS toxicity, including altered mental status, being cautious to avoid prescribing cascades.
  - **Adverse Events**: MANY - sedation, weakness, dizziness, confusion, delirium, nausea, orthostatic hypotension, constipation, urinary retention.
  - **Monitor:** Excess sedation, muscle weakness, orthostasis, & fall risk. Also, urinary function & cognitive effects.
- **Intra-articular corticosteroid or hyaluronic acid injections**: may be useful for pain associated with OA of the knee (though corticosteroids may only offer short-term benefit & evidence is conflicting for viscosupplementation).

Opioids SB – Indications, Cautions, Interactions, & Monitoring

For short-term use for moderate to severe acute nociceptive pain. May also be trialed for severe chronic nociceptive or neuropathic pain when non-pharmacological and nonopioid pharmacotherapy have not been sufficiently helpful for improving function, are contraindicated, or are not tolerated (though harms outweigh benefits in many cases).

S: Caution with combinations of medications that are likely to cause constipation (e.g. opioids with oral iron, anticholinergic agents TCAs, verapamil, aluminum antacids) for people with chronic constipation where non-constipating alternatives are available. Caution against using opioids long-term for OA (lack evidence for efficacy & ↑ risk of AE).

B: Avoid in older adults with delirium or at high risk of delirium. Avoid (except in the setting of severe acute pain) if history of falls or fractures (may cause ataxia, impaired psychomotor function, syncope, or additional falls) – if used, attempt to reduce the use of other CNS-active medications & implement strategies to reduce fall risk. Avoid duplication of opioid analgesics for daily regular use (i.e. optimize monotherapy rather than adding on another opioid agent).

- **Adverse Events (develop in the short-term)**: MANY - Nausea, sedation, confusion, falls, dry mouth, myoclonus, diaphoresis, respiratory depression, urinary retention, & pruritis (due to histamine release, not allergic). **Short- & long-term**: Constipation – may develop immediately after starting, however does not improve with time as tolerance to other AE develop.
- **Adverse Events (longer-term considerations)**: Include hormonal effects (↓testosterone & cortisol), falls & osteoporosis (fracture risk), central sleep apnea, disruption of normal sleep architecture, hyperalgesia, ?immune suppression, risk of developing opioid use disorder.
  - Symptoms of opioid withdrawal develop with discontinuation after opioids have been taken regularly for ~ more than 1 week.
- DI: Concurrent respiratory +/- CNS depressants (e.g. gabapentinoids, benzodiazepines, sedatives, alcohol, tricyclic antidepressants), MAOi (risk of serotonergic toxicity)
  - **Risk of serotonin syndrome:** Most opioids are considered low risk of serotonergic toxicity when combined with other low-moderate risk substances.
    - Fentanyl, tapentadol, & methadone are considered moderate-risk opioids → use with caution with other serotonergic substances (e.g. SSRIs, SNRIs, TCAs).
    - Tramadol is considered high risk → avoid combining with other serotonergic substances (e.g. SSRIs, SNRIs, TCAs) & CI with MAOi due to serotonin syndrome risk.[9]
- **Monitor**: Respiratory status, mental status, excess sedation, blood pressure, dizziness, GI function / constipation, signs of hypogonadism / sexual dysfunction, sleep apnea, quality of sleep, opioid-induced hyperalgesia, as well as for signs of taking medication differently than prescribed / self-titrated dose escalations / features of opioid use disorder (consider use of the Prescription Opioid Misuse Index or the Current Opioid Misuse Measure).

What are the potential ADVANTAGES with opioids?	
May be beneficial for moderate to severe acute pain	… when non-opioid analgesic combinations are insufficient and / or contraindicated.
May be beneficial for chronic pain	… small but statistically significant ↓pain & ↑function vs placebo, while comparison of opioids vs non-opioids suggests similar benefit for pain and functioning.[5] Might trial for people without current or past substance disorder & without other active psychiatric disorders, who have persistent problematic pain despite optimized non-opioid therapies.[1]
Low risk of certain types of end-organ damage relative to other analgesics (e.g. oral NSAID)	… less likely to cause GI ulcers, renal or hepatic toxicity, and possibly cardiovascular outcomes (e.g. exacerbation of heart failure).
Fast onset	… time to onset dependent on formulation and route of administration, but effect will typically be noted sooner than with antidepressant / anticonvulsant medications.
Variety of options for administration beyond oral tablets / capsules	… formulations include syrup / liquid / crushed tablets, transdermal, sublingual, rectal, and parenteral (IV/IM/subcut).

What are the potential DISADVANTAGES or PROBLEMS with opioids?	
CNS effects	… related to recent dosage changes, the total dose, & concomitant CNS depressant medications. May include over-sedation, delirium, & cognitive dysfunction (morphine: may impair CNS function for up to 7 days after an ↑ in dose[3]).
GI effects	… ↑ risk of constipation & bowel obstruction[4] in a population where this is already relatively common (See Geri-RxFiles: Constipation information on pg 69).
Falls & fracture risk	… ↑ rates; an observational cohort trial indicated there were significant ↑ rates of composite fracture for opioids versus NSAID (HR: 4.47, 95%CI 3.12 to 6.41); fall rate was also ↑ (HR: 1.64, 95% CI 1.09 to 2.47).[4]
Tolerance develops & may ↑ pain over time	… initially helpful doses may become less so over time due to tolerance. Opioids can also cause an ↑ sensitivity to pain known as hyperalgesia (see Dr Andrea Furlan's video explanation), typically when taken for longer periods and at higher doses. This ↑ in pain is particularly noted in fibromyalgia/other nociplastic pain-related conditions.
↑ Mortality & CV events?	… also noted in the Solomon observational cohort study (HR for mortality: 1.87, 95% CI 1.39-2.53; HR for CV risk: 1.77, 95% CI 1.39-2.24)[4]; however, due to the nature of the observational trial & modest ↑ HR, uncertain if this is true causation or due to confounding.
Polypharmacy	… often results in both pharmacodynamic & pharmacokinetic drug interactions.
Development of Opioid Use Disorder (OUD)	… prescribed opioids are associated with approximately a 5.5% risk of developing opioid use disorder.[1] Thought, prevalence rates of OUD specific to older populations are not well established.[22] Risk tends to be highest for people with a history of substance use disorder, at prescribed doses >120mg morphine equivalent dose (MED), and when taken for > 90 days.
Risk of Fatal Overdose[1]	**MED/day**: < 20mg | 20-49mg | 50-99mg | >100mg **Fatal overdose/year**: 0.1%/yr | 0.14%/yr | 0.18%/yr | 0.23%/yr
Targets for theft	… older adults who are prescribed opioids may become targets for theft, as opioids may be used for non-medical reasons by others. Ensure secure storage & use.

Opioids SB – Approach

Strive to avoid or minimize opioid use in older adults, whenever possible. If used, consider the following general principles for initiation:

- **Aim to deprescribe potentially interacting medications** (if possible) that have not had sufficient benefit to outweigh potential harms of combination with an opioid.
  - E.g. Before beginning an opioid trial for chronic pain, consider a gradual taper & eventual discontinuation of other CNS depressants, such as amitriptyline, gabapentin, benzodiazepines (these can ↑ falls, confusion & impairment, & are associated with ↑ risk when used in combination with opioids).
- **Begin with an immediate-release product** → to assess tolerability and effectiveness of the dosage (Exception: slow-release transdermal buprenorphine patch may be a reasonable option for opioid-naïve older adults with chronic pain if cost is not a barrier).
  - Common options include hydromorphone, morphine, or oxycodone.
- **Select the lowest effective dose** → Start with **25**-50% of the suggested initial dose that is recommended for younger adults (e.g. hydromorphone 0.5-1mg po BID).
  - Limit to <50mg morphine equivalent dose (MED)/day when used for acute pain.
  - During a trial for chronic pain, aim initially for <50mg MED/day, then titrate slowly based on tolerability & functional benefit.
- **Use the Opioid Manager tool** → to assist in opioid initiation & monitoring.
- **Implement universal precautions** → to help protect patients, staff, and society, consider including informed consent, one prescriber / one pharmacy, secure storage, proper disposal, limited quantity dispensed, and a take-home naloxone NARCAN kit.
- **Be proactive in preventing constipation! Add a laxative** START (e.g. senna SENOKOT, lactulose, bisacodyl, PEG 3350 LAX-A-DAY), ↑ hydration, dietary fibre (not a fibre laxative / supplement) for individuals ≥65 years old. (See Geri-RxFiles: Constipation information on pg 69).
- **Follow up with a 3-day tolerance check** → Check in to assess for any early signs of confusion, excess sedation, falls, GI concerns, etc which may warrant dose adjustment.
- **Use for the shortest period of time** → typically, 3-14 days for acute pain, depending on the severity & anticipated duration of the pain episode, or as a trial for chronic pain for ~1-3 months before being reassessed.
- **Titrate cautiously** → If longer-term therapy is considered after a beneficial trial, the max dose suggested is <90mg MED/d, since higher doses ↑ harm without incremental benefit.
- **Taper** (See Geri-RxFiles: Tapering pg 206) after being used regularly for 7 days or more.

Commonly Used Opioids SB

Immediate-release opioid products are recommended when initiating an opioid for acute pain or as a trial for chronic pain (alphabetical order):

- May be prescribed on a scheduled basis or PRN depending on the patient's needs (e.g. constant / continuous pain vs intermittent / incident pain)
- Initiate low dose, then titrate to find balance between tolerability & effectiveness
- Consider longer dosing intervals if frail, impaired renal function, or potentially interacting medications; may extend interval to every 6, 8, or 12 hours.

- **Hydromorphone DILAUDID** IR tab (g, also a 1mg/mL oral liquid): 0.25-1mg po up to q4h
  - Generally preferred over morphine for people with ↓ renal function (Stage 3 CKD or CrCl <20 to 30mL/min). May be an option if ESRD.
  - Usually recommended to give every 8 to 12 hours for initial therapy; may be adequate for some older adults.
- **Morphine MS-IR, STATEX, DOLORAL** IR tab (also 1&5mg/mL oral syrups): 2.5-5mg po up to q4h
  - Use ↓ dose in renal dysfunction or avoid using if severe impairment (CrCl <20 to 30mL/min; active M3G & M6G metabolites may accumulate & cause toxicity). Practically, it may be used cautiously & switched to an alternate agent if not tolerated.
  - Multiple dosage strengths and formulations are available → can help to initiate & titrate low dosages for older adults.
- **Oxycodone OXY-IR, SUPEUDOL** IR tab (g): 2.5-5mg po up to q6h
  - Immediate-release tablets are scored to allow for easy splitting to ½ tablet dose.
  - DI: More CYP enzyme interactions than morphine & hydromorphone. Metabolized by CYP 3A4 (major substrate) & 2D6 (minor substrate) – use caution with concurrent inhibitors & inducers*,** (see RxFiles: Drug Interactions chart).
  - Use caution in renal / hepatic dysfunction as plasma concentrations may ↑ up to 50%.
  - Its kappa agonism may ↑ risk of euphoria relative to other opioids.
  - Generic combination products with acetaminophen / ASA available (contain oxycodone 5mg / nonopioid 325mg), but ↑ unintentional nonopioid overdose risk & more costly.

Slow-release opioid products might be considered (at an equivalent daily dose) **when continuing an opioid on a regularly scheduled basis for chronic pain** after the lowest effective & tolerated dose has been established with a regularly scheduled immediate-release opioid product.

- These products are not indicated as PRN analgesics.
- Use caution with slow-release agents in cachectic patients (may ↓ absorption).

- **Hydromorphone HYDROMORPH CONTIN** (q12hr cap):
  - May sprinkle contents, however, do not chew beads.
- **Morphine KADIAN** (q24hr cap), **M-ESLON** (q12hr cap), **MS CONTIN** (g, q12hr tab):
  - May sprinkle contents of **KADIAN** & **M-ESLON**, do not chew beads.
  - **MS CONTIN** should not be crushed; may be given rectally.
  - **KADIAN** more costly than other slow-release morphine products, however has an advantage of being a once-daily option.
- **Oxycodone OXYNEO** (g, q12hr tab): More costly than most other slow-release options.
  - Do not crush or split.
  - Avoid this product when people have difficulty swallowing. Tablet becomes sticky when wet & there are reports of it getting stuck in the throat (causing gagging / choking).
  - **TARGIN** is a slow-release combination product of oxycodone/naloxone (q12hr tab) indicated for severe pain requiring daily, continuous, long-term opioid treatment.
    - The manufacturer indicates that the naloxone is to offer relief of opioid-induced constipation, though there is no data to suggest that this product is more effective than using oxycodone with an optimized laxative.
    - Do not crush or split.
    - **Maximum dose**: oxycodone/naloxone 40mg/20mg po q12hr (due to the naloxone component).

Other Opioids SB – Unique Properties & Comments (in alphabetical order)

- **Buprenorphine BUTRANS** (patch), **SUBOXONE** (sublingual tablet with naloxone, "bup/nal"):
  - o A partial mu-receptor agonist: offers analgesia with potential for↓ risk / severity of adverse effects (e.g. CNS depression, constipation).
  - o Not typically used for acute pain (but might add PRN if already taking scheduled bup/nal).
  - o Hepatic metabolism (CYP3A4); not affected by renal dysfunction. Can use in ESRD.
  - o DI: CYP3A4 inhibitors** ↑ AE & inducers ↓ effectiveness.
  - o **BUTRANS** transdermal patch can be initiated for opioid-naïve individuals at a dose of 5mcg/hr (can be a good option when used for chronic pain in older adults).
    - Long & delayed action; allow ≥3 days for steady state levels & effect.
    - **Maximum dose**: 20mcg/hr as per the product monograph.
    - Older adults may have altered pharmacokinetics due to poor fat stores, muscle wasting or altered clearance
    - Quite costly (up to ~$280/30days).
    - **Adverse Events**: Skin irritation common.
    - Some use a conversion of 10 mcg/hr buprenorphine patch ≈ 30mg MED/day.
  - o **SUBOXONE** sublingual is indicated for opioid use disorder (off-label for chronic pain).
    - May precipitate withdrawal in those already on opioids (consider low-dose initiation, also called "microdosing," if rotating to **SUBOXONE**).
    - **Maximum dose**: 24mg/day per the product monograph.
    - Duration of analgesia not well established, BID to TID dosing may be beneficial.
    - Naloxone is included in the formulation to deter injection and intranasal use of the buprenorphine, since naloxone by these routes will cause signs & symptoms of withdrawal in opioid dependent individuals. Naloxone is minimally absorbed when taken orally / sublingually.
- **Codeine** IR tabs (g), **TYLENOL #1,2,3,4** (IR products with added acetaminophen 300mg / caffeine 15mg - no caffeine in TYLENOL #4), **CODEINE CONTIN** (q12hr tab) : 15 to 30mg po every 4 to 6 hours (there is a dose limiting ceiling effect at >60mg/dose)
  - o There is debate about codeine's role in older adults. Evidence is lacking & adverse effects are common. May cause more constipation than other opioids. See RxFiles Q&A Summary: Management of Opioid-Induced Constipation.
  - o Prodrug: Requires conversion by CYP 2D6 into its active metabolite morphine for effect (some may lack this conversion enzyme which limits effect; others may metabolize it rapidly and experience ↑AE/overdose.
  - o **Maximum dose**: 600mg/day per manufacturer, but some suggest limited additional analgesia beyond 200mg/day.
  - o DI: CYP2D6 inhibitors*, such as paroxetine, can ↓ effectiveness .
  - o Combination with acetaminophen may ↑ analgesic efficacy; however, can limit ability to optimize the acetaminophen dose & ↑ risk of unintended acetaminophen overdose. If used, limit acetaminophen to ≤**3**-4g/day for acute use (ideally 2-3g/day for chronic use) to reduce hepatic risk.[2] Watch for **OTC** combination products that contain acetaminophen. The caffeine content of some products may also be problematic (stimulation, diuresis).
  - o Immediate release (IR) products contain codeine phosphate, slow release (SR) products contain codeine base – ↓ total daily dose by ~25% when converting from IR codeine to ER codeine.
- **Fentanyl DURAGESIC** (g, transdermal patch) : High potency; **not for opioid naïve** (patients are considered opioid tolerant after taking at least 60mg MED/day for ≥1 week) or those with poor response to codeine or tramadol. Also, not for acute or fluctuating pain.
  - o Caution: older adults may have altered pharmacokinetics due to poor fat stores, muscle wasting or altered clearance. If used, dose conservatively (↓ dose in ESRD).
  - o Onset of analgesia delayed by 12 to 24 hours. Allow ≥6 days prior to ↑ dose. Limited titration ability.
  - o High potency: the recommended maximum safe MED dose limit is reached quickly with available patch strengths & relative potency equivalency (e.g. a 25mcg/hr patch ≈ 90mg MED/day).
  - o Risk for administration error (e.g. accidentally applying multiple patches if old patch is not removed in memory impairment or with multiple caregivers / care staff).
  - o Applying heat (e.g. heating pad) ↑ absorption, effect, & ↑ overdose risk.
  - o May utilize a Patch Exchange Disposal Tool to facilitate safe product disposal.
  - o DI: CYP3A4 inhibitors** ↑ AE/risk of overdose; 3A4 inducers ↓effectiveness.
- **Methadone METADOL** (tabs & liquid) :
  - o Not for acute pain.
  - o Often reserved for patients with chronic pain & opioid tolerance. If initiating for someone who is opioid-naïve, start with very low dose to assess tolerability (e.g. initial dose of 0.5mg po TID).
  - o Has variable and unpredictable pharmacokinetics, should generally be prescribed by a clinician experienced with its use.
  - o Though it has a long half-life, the duration of analgesia is generally shorter, often necessitating a BID to TID dosing interval.
  - o May be helpful for neuropathic pain due to potential NMDA receptor antagonism (evidence not well established).
  - o Undergoes extensive hepatic metabolism (major substrate of CYP2B6 & 3A4, minor substrate of many others); Use caution / avoid with severe hepatic impairment. Can use at reduced dose in ESRD.
  - o DI: MANY! Use caution with any medication that inhibits/induces CYP enzymes (especially CYP3A4 inhibitors**), also other QTc prolonging substances (see RxFiles charts: Drug Interactions & QT Prolongation and Torsades de Pointes, or pg 43).
  - o **Adverse Events**: cardiac conduction abnormalities (↑QTc, especially with ↑doses).
- **Tapentadol NUCYNTA** (available as **IR** tabs as well as **ER** q12hr tab) :
  - o Dual mechanism agent: mu-receptor agonist PLUS ↑ norepinephrine effects (reuptake inhibitor).
  - o Should generally not be used as a PRN analgesic due to the norepinephrine effects.
  - o **Maximum dose:** 500mg **ER** to 600mg **IR** per day.
  - o Avoid use with severe hepatic impairment & with CrCl <30mL/min.
  - o **ER extended-release product**: do not crush or cut.
    - Generally, avoid this product for people with difficulty swallowing. Tablet becomes sticky when wet and may ↑risk of gagging / choking.
    - Avoid taking with alcohol → may ↑ dose release from this formulation.
  - o Quite costly (up to ~$360/30days).

Other Opioids SB – Unique Properties & Comments (continued)

- **Tramadol** IR tabs (g ULTRAM), **RALIVIA** (q24hr tab), **TRIDURAL** (q24hr tab), **ZYTRAM XL** (q24hr cap), **DURELA** (q24hr cap) :
  - Dual mechanism agent: mu-receptor agonist PLUS ↑ serotonin & norepinephrine effects (reuptake inhibitor).
  - Generally, do not use as a PRN analgesic due to the serotonin & norepinephrine effects.
  - Prodrug with unpredictable pharmacological effect: Requires conversion by CYP 2D6 into its active metabolite for effect (some may lack this conversion enzyme which limits effect; others may metabolize it rapidly and experience ↑AE / overdose).
  - Effect for pain is small to moderate; effect on function is small. While it avoids some of the potential GI & renal issues with NSAIDs, it has a limited opioid effect relative to more potent opioids yet numerous potential AE, particularly in older adults. There is debate about tramadol's role, given the uncertainty with which the prodrug converts to active metabolites & the potential for drug interactions.
  - **Adverse effects**: Numerous CNS (somnolence, vertigo, cognitive impairment), hypoglycemia, seizures (risk ↑ with higher doses & combinations with SSRI/TCAs), ↓ sodium, nausea, orthostatic hypotension, serotonin syndrome.
    - ↑ mortality over 1 year was suggested in a 2019 large cohort study (subject to confounders) for patients ≥50 yrs with OA taking tramadol vs NSAID (HR vs naproxen: 1.71, 95% CI 1.41-2.07).[6]
    - ↑ risk of visual & auditory hallucinations in pts >65yrs at "normal tramadol doses"[7]
    - ↑ risk of hip fracture over 1 year was suggested in a 2024 systematic review & meta-analysis of observational studies for patients ~63 yrs (mean age) with OA taking tramadol vs no treatment or codeine (HR 1.32, 95% CI 1.14-1.51).[8]
  - **Maximum dose**: 300mg (**DURELA**, **RALIVIA**, & **TRIDURAL**) to 400mg (IR products & **ZYTRAM XL**) per day.
  - If renal impairment (CrCl <30mL/min), avoid use of extended-release products, & reduce dose / extend interval of immediate release products.
  - B: May exacerbate / cause SIADH or hyponatremia – use with caution. Avoid ER products if CrCl <30mL/min & reduce the dose of IR products.
  - DI: Common. CYP2D6 inhibitors*, such as paroxetine, & 3A4 inhibitors**, such as phenobarbital, ↓ effectiveness. Do not combine with SSRIs & SNRIs. Caution with other serotonergic substances (e.g. TCAs, St John's Wort) & drugs that ↓ seizure threshold.
  - **Monitor:** Monitor electrolytes (sodium) within one month after starting tramadol for an older adult, and after a dose change, especially if the individual is taking another medication implicated in SIADH (e.g. diuretics).
  - Combination product with acetaminophen available (**TRAMACET**, g – contain tramadol 37.5mg / acetaminophen 325mg) also available, but ↑ unintentional acetaminophen overdose risk & may limit ability to safely optimize the acetaminophen dose.
  - Somewhat high cost (up to ~$220/30days).

Opioid Considerations for Specific Comorbidities / Concurrent Conditions

- **Heart failure:** Opioids may be an option → low risk of causing exacerbation (vs. NSAIDs).
- **Dementia:** Limited data about safety → use very low dose, monitor behaviours & tolerability closely, then titrate cautiously.
- **Falls risk:** Use opioids cautiously. Also educate patient and caregivers about preventative actions, including use of hip protectors, mobility aids (e.g. walker, cane), removal of tripping hazards (e.g. throw rugs), and taking their time to stabilize when moving from seated to a standing position. See Geri-RxFiles: Preventing Falls in Older Adults, page 89.
- **New onset delirium / agitation:** Rule out potential opioid-induced causes (including neurotoxicity, constipation, & urinary retention). Paradoxically, the presence of delirium should also trigger assessment for possible untreated or under-treated pain.[10]
- **Prescribing cascades:** Exercise caution regarding potential unintentional polypharmacy associated with adding medications to treat side effects:
  - for sedation (e.g. adding methylphenidate or modafinil to stimulate can cause psychiatric disturbances).
  - for nausea (e.g. adding haloperidol or metoclopramide to treat nausea can cause extrapyramidal effects, adding dimenhydrinate increases risk of delirium & anticholinergic effects).
- **Excess sedation:** Consider both medication & non-medication causes (e.g. insufficient hydration, metabolic causes, infection) & review the analgesics' selection / timing / ongoing necessity and/or other CNS depressant medication.
- **Nausea:** Note that this may resolve within 72 hours of the opioid initiation or dose ↑. If nausea persists & is deemed due to an opioid, stop / taper off the opioid if possible. Ensure opioid-induced constipation is well-managed, or this may exacerbate nausea!
- **Opioid intolerance / allergy:** Pseudoallergy (e.g. histamine release causing flushing, itching, hives, sweating, mild hypotension) common, particularly with codeine & morphine. Trial alternate opioid if non-opioid options not appropriate.
  - True allergy (e.g. severe hypotension, swelling of face / lips, difficulty breathing) rare. Stop opioid & change to non-opioid or possibly opioid from different chemical class.
  - Intolerance (e.g. delirium, vomiting), may rechallenge with much lower dose.

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- For patients with chronic pain who are currently taking ≥90mg MED/day, suggest tapering opioid to the lowest effective dose, potentially including discontinuation (weak recommendation).
  - When tapering, some patients may experience significant ↑ in pain or ↓ in function that persists for more than 1 month; taper may be paused or abandoned.
- For patients with chronic pain who are currently using opioids and have persistent problematic pain and / or problematic adverse effects, we suggest rotation to other opioids rather than keeping the opioid the same (weak recommendation).
- See Geri-RxFiles: Opioid Tapering Section, page 206.

*Common CYP-2D6 inhibitors include: amiodarone, bupropion, duloxetine, fluoxetine, paroxetine, ritonavir, ropinirole

** Common CYP-3A4 inhibitors include: clarithromycin, diltiazem, erythromycin, grapefruit juice, itraconazole, verapamil

Abbreviations: **ACEi**=angiotensin converting enzyme inhibitor(s) **AE**=adverse event(s) **AKI**=acute kidney injury **ARB**=angiotensin II receptor blocker **ASA**=acetylsalicylic acid **BID**=twice daily **BP**=blood pressure **BPH**=benign prostatic hyperplasia **CBD**=cannabidiol **CrCl**=creatinine clearance **CNS**=central nervous system **COX-2**=cyclooxygenase-2 **CYP**=Cytochrome P450 metabolic system **CV**=cardiovascular **d**=day **DI**=drug interaction **EC**=enteric coated **ECG**=electrocardiogram **eGFR**=estimated glomerular filtration rate **ER**=extended release **ESRD**=end stage renal disease **GI**=gastrointestinal **HF**=heart failure **hr**=hour **HS**=bedtime **HTN**=hypertension **INR**=internal normalized ratio **IR**=immediate release **LFT**=liver function tests **M3G**=morphine-3-glucuronide **M6G**=morphine-6-glucuronide **MAOi**=monoamine oxidase inhibitor(s) **MED**=morphine equivalent dose **MRA**=mineralocorticoid receptor antagonist **MSK**=musculoskeletal **NSAID**=Non-steroidal anti-inflammatory drug(s) **OA**=osteoarthritis **OTC**=over-the-counter **OUD**=opioid use disorder **po**=oral **PPI**=proton-pump inhibitor **PRN**=as needed **pt**=patient **QID**=four times daily **QTc**=corrected QT interval **SBP**=systolic blood pressure **SIADH**=syndrome of inappropriate antidiuretic hormone **SNRI**=serotonin reuptake inhibitor **SSRI**=selective serotonin reuptake inhibitor **TCA**=tricyclic antidepressant **THC**=delta-9-tetrahydrocannabinol **TID**=three times daily **wks**=weeks **yrs**=years

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COMMON ABBREVIATIONS USED IN THE GERI-RXFILES

STOPP	Screening Tool of Older Persons' potentially inappropriate Prescriptions
QE	Quality of Evidence
SR	Strength of Recommendation

B	Medication from the Beers List
S	Medication from the STOPP Criteria
♦	Infrequently used medication
♀	Female

♂	Male
BRAND	discontinued trade name
BRAND	trade name

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