CPSS College of Physicians and Surgeons of Saskatchewan

PRESCRIPTION REVIEW PROGRAM
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OATP Opioid Agonist Therapy Program

DRUG PROGRAMS
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Opioid Agonist Therapy Program

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RE: Codeine use in pediatrics

Dear Dental Colleague,

The *Prescription Review Program* (PRP) is Saskatchewan's educationally focused prescription monitoring program administered by the College of Physicians and Surgeons of Saskatchewan.

Recently, we conducted an analysis to assess codeine prescribing in Saskatchewan patients under the age of 18 years in response to the updated Health Canada advisory warning that individuals under 18 years of age should not use non-prescription pain relief products containing codeine (previously not recommended for children under the age of 12 years)[1]. Health Canada provided an additional warning about the use of prescription cough and cold products containing opioids and the risk of opioid use disorder in children and adolescents (<18 years of age) as well as the risk of opioid toxicity[10]. Current literature suggests that early exposure to opioids in childhood and adolescence may put patients at risk for opioid-related adverse events throughout life[2,6].

Historically, codeine was the preferred opioid analgesic in pediatrics, given the perception of safety and a wide therapeutic index[2]. While there may be a lower incidence of CNS and respiratory depression after a single dose, the lower risk may not exist after subsequent doses[9]. As such, the thinking surrounding codeine safety changed around 2011 when the WHO noted that "efficacy and safety were questionable in an unpredictable portion of the pediatric population"[2]. Today, unless codeine has already been prescribed for a chronic condition, initiating treatment with codeine is not recommended.

Codeine, a prodrug with weak binding to the mu opioid receptor, has highly unpredictable metabolic properties, making it a risky therapeutic option for the pediatric population. The bioactivation to morphine provides the analgesic properties of codeine. Codeine is converted to morphine with the hepatic cytochrome P450 2D6 enzyme and analgesia is dependent on the individual's CYP2D6 gene. As a result, those with inactive CYP2D6 are "poor metabolizers" and will experience reduced pain relief as a result of the medication, given the reduced conversion to morphine. On the other hand, "ultra-rapid metabolizers" are at risk of overdose and adverse/toxic effects (which have resulted in pediatric deaths)[13], even at lower doses, because of the rapid and complete metabolism to morphine[3,4].

It has been estimated that anywhere from 77-92% of patients are considered "normal metabolizers", suggesting expected enzyme activity and morphine formation; thus "normal metabolizers" are candidates for dosing based on labeled recommendations[3]. Unfortunately, without genetic testing, gene variation is unknown in our general population.

Tramadol, like codeine, is not recommended in the pediatric population given its unpredictable metabolism and risk of serious breathing problems associated with its use.[18]

An initial pain assessment is an important step for optimal pain management.[17] An appropriate assessment using a developmentally appropriate tool should include pain location, quality, duration and intensity.[17] Age appropriate assessments tools are available through The Canadian Pediatric Society's updated pain guidance.

It is always important to treat pain as a multimodal approach, combining physical, psychological, and pharmacologic interventions to establish the best pain-management treatment plan for each individual.[19] Multimodal analgesia for acute pain is most effective for pediatric pain management, preventing transition from acute to chronic pain[13]. For chronic pediatric pain, a multidisciplinary approach is recommended (e.g., physical therapy; occupational therapy; psychological intervention; "normalizing" life with school, sleep, and social activities; etc.) [13] with non-opioid medications and counselling, infrequently requiring opioid use[20].

Canadian Pediatric Society (CPS) Pain Management Guidelines and Protocols[17]

Analgesics for pain should be used in a stepwise manner, combined with physical and psychological strategies.

- **Step 1** (mild to moderate pain): ibuprofen; acetaminophen can be used first line for mild pain if ibuprofen is contraindicated;
- **Step 2** (moderate to severe pain): morphine± is the medicine of choice (acetaminophen +/- ibuprofen used as co-analgesia)
    - *Patients presenting with acute moderate to severe pain unlikely to be resolved by physical and psychological strategies and first line analgesics should be offered pharmacological interventions on an escalating basis. Opioids should be used judiciously, with appropriate dosing assessment to avoid adverse events and careful monitoring*
- Dose at regular intervals, while monitoring side-effects
- Consider the appropriate route of administration (e.g., IM can be painful with erratic absorption; rectal can have unreliable bioavailability)
- Adapt treatment to the individual child

Therapeutic Options[5]

Abdominal (acute)	• Use of opioids* does not delay surgical decision (relaxed patient may provide better exam and better diagnosis)
Minor Burns	• Cold compress • Ibuprofen or acetaminophen
Earache	• Warm cloth • Ibuprofen or acetaminophen (initiate quickly) • Auralgan (antipyrine & benzocaine) – avoid with perforated ear drum
Emergency Trauma	• Musculoskeletal: ibuprofen (superior to acetaminophen or codeine) • Opioids* (e.g., morphine±) if moderate to severe pain** • Cold compresses (e.g. for sprains), splinting, elevation, bandaging +\- dressing (immobilizing can decrease pain)
Heel Poke	• Breastfeeding, sucrose, sucking
Immunization	• Pressure at site • Sucrose (infants up to 12 months of age) • Topical anesthetics
Open wound (foreign body ruled out)	• Topical anesthetic (e.g., LET, lidocaine 4%/epinephrine 0.1%/tetracaine 0.5%) – avoid mucous membranes; avoid epinephrine on digits, nose tip, ear, penis • Tissue adhesive
Post-Op (analgesia)	• NSAID + acetaminophen • May add opioid* PRN for 3-5 days for severe pain (caution adeno-tonsillectomy) • -cold/warm compress • Epidural • Start analgesia before child wakes up (e.g. suppository)

**Appropriate monitoring for respiratory depression, sedation and reduced consciousness is essential[8]*
±For acute/persisting pain treatment, if an opioid is indicated, morphine is usually preferred over codeine or tramadol because of the CYP 2D6 polymorphisms and case-reports associated with overdose from codeine[11,14,18]
***In an RCT of children presenting to the ED with an uncomplicated extremity fracture, children received oral morphine (0.5mg/kg) or ibuprofen for 24 hours after discharge. No significant difference in analgesic efficacy was noted between oral morphine and ibuprofen; morphine was associated with significantly higher adverse effects[7]. Ibuprofen is also comparable to oral morphine for sprains, following minor orthopedic procedures and tonsillectomy, with less risk for adverse effects.[17]*

Topical Anesthetics (for Intact Skin)[5]

Drug	Application	Caution
Emla (lidocaine + prilocaine)	60+ min prior with occlusion	• Vasoconstriction • Rare risk of methemoglobinemia
Ametop (tetracaine gel)	3-45 min with occlusion	• Vasoconstriction • Must refrigerate
Maxilene (Liposomal Lidocaine)	15-45 + min prior	• Minimally vasoactive

Topical analgesics may also be considered for chronic pain[8].

General Non-Pharmacological Suggestions (as age appropriate)[5,8,20]

- Affirmative language
- Parental counselling – parental anxiety in the context of children undergoing acute procedural pain is one of the most powerful predictors of pain outcomes[15]
- Consider psychology/psychiatry consult if necessary
- Physical comfort strategies (e.g., kangaroo care, comfort positioning, facilitated tucking or touch)
- Distraction (books, bubbles, TV, breathing, breastfeeding, music, virtual reality, conversation)
- Techniques to reduce stimulation (e.g., minimizing harsh lighting and/or noise)[20]
- Hot/cold compresses (not for neonates)
- Warm blanket
- Massage
- Activity out of bed
- Elevation
- Splinting, bandaging, dressing
- Injury site pressure

Oral Analgesic Therapies and Dosing[21]

Drug	Dosing	Max Daily Dose
• Acetaminophen[#]	• 10-15 mg/kg/dose every 4-6 hours	• 75 mg/kg/day (maximum of 1000mg/dose) • Newborn (4-40 wks.): 60 mg/kg/day
• Ibuprofen[#]	• 5-10 mg/kg/dose every 6-8 hours	• 40 mg/kg/day (maximum of 500mg/dose)
• Naproxen	• > 2 years old: 5-7mg/kg every 8-12 hours	• 20 mg/kg/day (maximum of 500mg/dose)
• Antidepressants (e.g., TCAs), anticonvulsants (e.g., gabapentin), SNRI's (e.g. duloxetine)		

[#]*Consider initiating opioid-sparing analgesics (with side-effect monitoring) using upper doses to get the pain under control.*

Ibuprofen has been shown to be more effective than acetaminophen for children's pain, particularly for acute pain, musculoskeletal trauma, headache, and post-dental extraction with a comparable safety profile.[17] Caution is advised with alternating between acetaminophen and an NSAID because of the increased risk of adverse effects and potential for errors. Monotherapy is preferred, however, if insufficient, switching is an alternative or combining acetaminophen + NSAID may be used short-term (noting the different dosing frequency is important). For example, the combination of acetaminophen and ibuprofen to manage dental extraction or tonsillectomy pain is superior compared with acetaminophen alone.[17] If a combination is used, advise caregiver to verify each dose and write down time of each administration to keep track.[21] Post-operative pain should be dosed as scheduled ("around the clock") and pre-ambulation or pre-procedure (excluding vaccination) analgesics are usually dosed PRN[8].

Acetaminophen and NSAIDs may have a "ceiling effect" meaning that escalations above the recommended daily maximum dose are unlikely beneficial and may put the patient at a higher risk of adverse effects[8].

As a reminder, if adequate non-opioid measures are ineffective and an opioid is indicated based on clinical judgment, it is strongly recommended that for acute pain and as initial therapy for chronic pain, the opioid prescription duration should not exceed 5-10 doses or 2- 3 days[20] (with back-up analgesia for beyond three days and plans for follow-up, as necessary) at the lowest effective dose alongside appropriate patient/parent/caregiver counselling for use, risk, management of adverse effects (including overdose), storage and potential for misuse[2]. One study showed that 14% of parents gave zero doses of prescription opioids to their children and 79% had leftovers after day 3 post-procedure; as such, discussion around proper disposal is also essential[6]. It is recommended that acetaminophen and opioids are prescribed individually (i.e. not combination products such as acetaminophen with codeine) so that acetaminophen can be administered regularly, and the opioid can be used for breakthrough pain[12].

If opioids are used, they should be given alongside non-opioid analgesics to ensure that only the lowest dose of opioids is used[19]. We recognize that tramadol or codeine are often prescribed to give the lowest opioid dose possible. There is a 1mg/ml morphine oral liquid commercially available for lower dosing of morphine (e.g. 4.5mg of morphine is the approximate amount of codeine in a Tylenol #3 tablet).

The Canadian Pediatric Society issued a position statement in March 2021 entitled *The use of oral opioids to control children's pain in the post-codeine era*[16] which provides five recommendations for practice to safely manage pediatric pain:

- Effective and safe pain control should be a focus of treatment plans for children with acute or chronic conditions, based on best practice guidelines and current evidence.
- Pain control should involve both pharmacologic and nonpharmacologic approaches and be appropriate for the case, setting, and nature of the pain.
- Medication choice and administrations should be both commensurate with the nature and severity of the pain and demonstrated to be effective and safe for use in children. Analgesics should be used in a stepwise manner, beginning with acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) before progressing to opioids.
- While there are a number of oral opioid formulations available for analgesia for children, oral morphine is still the drug with the strongest evidence base for efficacy and safety. Other oral opioids appear promising, but more evidence is needed to establish their efficacy, safety, and role in therapy before using them routinely.
- Research into pain management for children in both acute and chronic settings is urgently needed.

Pediatric pain matters and needs to be treated safely and effectively. This correspondence is provided in hopes of assisting with the management of pediatric pain, incorporating some of the current evidence and resources on the topic.

Sincerely,

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Excellent Resources:

- Solutions for Kids in Pain (SKIP): *https://www.kidsinpain.ca/*
- Commitment to Comfort: https://childkindinternational.org/wp-content/uploads/Commitment-to-Comfort-Parent-Guide.pdf
- Best Practices in pain assessment and management for children (CPS): *https://cps.ca/en/documents/position/pain-assessment-and-management#ref21*
- Solutions for kids in pain: Opioids and Pain in Youth: A toolkit for health professionals toolkit

References:

1. Government of Canada. Non-prescription pain relief products containing codeine are not recommended for use in people under 18 years of age. Recalls and safety alerts, 2020. Available from: https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2020/73635a-eng.php
2. Matthews DC, et al. Patterns of opioid prescribing by dentists in a pediatric population: a retrospective observational study. CMAJO, 2019;7(3): E497-E503.
3. Dean L. Codeine Therapy and CYP2D6 Genotype. 2012 Sep 20 [Updated 2017 Mar 16]. In: Pratt VM, McLeod HL, Rubinstein WS, et al., editors. Medical Genetics Summaries [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2012-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK100662/
4. Regier L. Opioid Analgesics: Comparison Chart. RxFiles 12th ed. Saskatoon, SK: RxFiles; 2019.
5. Regier L, Jensen B, Kessler B. Pediatric Pain: Treatment Considerations, Q&As. RxFiles 14th ed. Saskatoon, SK: RxFiles; 2023.
6. Voepel-Lewis T, Wagner D, Tait AR. Leftover prescription opioids after minor procedures: an unwitting source for accidental overdose in children. JAMA Pediatr, 2015;169: 497-8.
7. Poonai N, et al. Oral administration of morphine versus ibuprofen to manage post fracture pain in children: a randomized trial. CMAJ, 2014;186(18): 1358-1363.
8. SHA Department of Pharmaceutical Services (RUH, SCH, SPH). Policies and Procedures: Pain Management – Pediatric Care. Available from: https://www.saskatoonhealthregion.ca/about/NursingManual/1045.pdf
9. Sick Kids. Use of Codeine in Children. Available from: http://www.sickkids.ca/PDFs/Pharmacy/28845-HSC%20codeine%20memo_external%20Apr%2023%202010.pdf
10. Government of Canada. Prescription cough and cold products containing opioids and the risk of opioid use disorder in children and adolescents (<18 years of age). Recalls and safety alerts, 2020. Available from: https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2020/73741a-eng.php.
11. Blott S, Regier L. Acute Pain Tx: Special Populations. RxFiles 12th ed. Saskatoon, SK: RxFiles; 2019.
12. O'Donnell FT Rosen KR. Pediatric Pain Management: A Review. Mo Med, 2014;111(3): 231-237.
13. Friedrichsdorf SJ, Goubert L. Pediatric pain treatment and prevention for hospitalized children. PAIN Rep, 2020;5(1): e804.
14. World Health Organization. WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses. Geneva: WHO Press, 2012.
15. Alberta Pain Strategy 2019-2024. Available from: https://c36f002a-8c54-42d7-906f-b68d77154ebf.filesusr.com/ugd/21223c_e7d98c0da5fa44048f56a9b264fb681c.pdf
16. Rieder M, Jong G. Canadian Paediatric Society, Drug Therapy and Hazardous Substances Committee. The use of oral opioids to control children's pain in the post-codeine era. Paediatr Child Health. 2021; 26 (2): 120-123. Available from: https://cps.ca/documents/position/the-use-of-oral-opioids-to-control-childrens-pain-in-the-post-codeine-era
17. Trottier E, Samina A, Dore-Bergeron MJ, Chauvin-Kimoff; Canadian Paediatric Society Acute Care Committee, Hospital Paediatrics Section, Paediatric Emergency Medicine Section. Best practices in pain assessment and management in children, 2022; 27 (7); 429-437. Available from: https://cps.ca/en/documents/position/pain-assessment-and-management#ref21
18. Government of Canada. Summary Safety Review- Tramadol-containing Products- Assessing the Potential Risk of Serious Breathing Problems (Respiratory Depression) in Children and Adolescents, 2017. Available from: https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/safety-reviews/summary-safety-review-tramadol-potential-risk-serious-breathing-problems-children-adolescents.html
19. Solutions for Kids in Pain. Opioids and Pain in Youth: A toolkit for health professionals, 2023. Available from: https://www.kidsinpain.ca/youth-in-pain
20. Health Standards Organization (HSO). Pediatric Pain Management (Organizational Competency CAN/HSO 13200 :2023). Health Standards Organization (HSO), 2023. Available from: https://store.healthstandards.org/products/pediatric-pain-management-can-hso-13200-2023-e
21. Wiebe A, Regier L, Jensen B, Kessler B. Pediatric Pain: Drug Comparison Charts. RxFiles [Internet]. 2025 January. Available from: https://www-rxfiles-ca.ezproxy.shirp.ca/RxFiles/uploads/documents/members/CHT-Pain-Peds.pdf