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Dear Colleagues,

For acute pain management, morphine has important effectiveness and safety advantages over codeine (which historically had been the most commonly used oral opiate at McMaster Children's Hospital). Codeine is a weak opiate analgesic with minimal intrinsic analgesic activity; it must first be metabolized to morphine which provides most of the analgesic effect. Because of the need for metabolism:

- Codeine has variable efficacy. Up to 10% of the population does not effectively metabolize codeine to morphine, resulting in poor pain control.<sup>1</sup>
- Codeine has caused toxicity (including deaths) due to high levels of morphine in ultra-rapid metabolizers (up to 40% in some populations).<sup>2,3</sup>
- Codeine has a higher potential for drug interactions than other opiates that may result in either reduced effectiveness or increased levels of morphine.

To avoid the unpredictably variable analgesia and potential for toxicity, a simpler approach is to use morphine. Hydromorphone or oxycodone are alternatives for patients who cannot tolerate morphine because of adverse effects.

For children, The Institute for Safe Medication Practice Canada and Canadian Association of Pediatric Health Centres recommend the evaluation of the use of oral codeine and consider the use of oral morphine as the oral opioid of choice. Other hospitals (including The Hospital for Sick Children and Children's Hospital of Eastern Ontario) have replaced codeine with morphine and/or restricted the use of codeine

Please see the attached document which contains the above information as well as a dosing chart for staff and learners. We will be working with nursing educators as well as patient information specialists to ensure all staff and families are educated about this change.

Please let us know if you have any questions or concerns.

Regards,

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<sup>1</sup> Sistonen J, Sajantila A, Lao O, Corander J, Barbujani G, Fuselli S. CYP2D6 worldwide genetic variation shows high frequency of altered activity variants and no continental structure. *Pharmacogenet Genomics* 2007;17(2):93-101

<sup>2</sup> Ciszkowski C, Madadi P, Phillips MS, Lauwers AE, Koren G. Codeine, ultrarapid-metabolism genotype, and postoperative death. *N Engl J Med*. 2009 Aug 20;361(8):827-8.

<sup>3</sup> [http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/\\_2008/tylenol\\_cod\\_eine\\_hpc-cps-eng.php](http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2008/tylenol_cod_eine_hpc-cps-eng.php)