Injection of Opioid Tablets: Risks and Harm Reduction
Information Summary

There are risks involved when substances are injected for medical or recreational purposes, however, many of these can be minimized by safer injection practices based on harm reduction principles [1, 2]. There is a body of research-based evidence about harm reduction related to injection drug use, much of it focused on reducing the risk of blood-borne infections such as HIV and Hepatitis C (HCV) [1, 2]. Harm reduction practices have also been developed over time by people who use drugs [3, 4].

In the context of the opioid overdose crisis in Canada, there is an urgent need to expand opioid substitution treatment to include other medications such as hydromorphone [5] and for safe supply initiatives [6], such as low-barrier regulated distribution programs [7]. Of one of the less explored features of some of these initiatives is the provision of hydromorphone tablets (that were manufactured for oral use) that may be injected by program participants [8].

The objective of this information summary is to survey the available information, and answer the following questions:

> *What are the harms associated with injecting hydromorphone or other opioid tablets that were manufactured for oral use, and what can be done to minimize these harms?*

Harms and best practices for injection-related complications

Much of the available information does not distinguish the harms associated with injecting hydromorphone or other opioid tablets manufactured for oral use from the harms associated with injection drug use in general [1, 2]. A good example of an overview of the harms from injection-related complications from all drugs is in the *Best Practice Recommendations for Canadian Harm Reduction Programs that Provide Service to People Who Use Drugs and are at Risk for HIV, HCV, and Other Harms: Part 2* [2], which groups risk factors for injection-related complications into broad categories:

- Drug form (e.g., pills may contain bulking agents that can lodge under the skin)
- Contamination of drugs (e.g., contaminated with disease-causing bacteria)
- Contamination of injection equipment and skin
- Injection sites (e.g., the neck, groin, or hands)
- Methods of injecting (e.g., “skin popping” and “muscle popping”)
- Missed injections (e.g., intravenous injection intended, but vein was missed and injection occurred in surrounding tissue)
- Length and frequency of injection and assistance with injecting
- Social, demographic, and health factors (e.g., sex work, unstable housing, and HCV)

The recommended best practices for harm reduction programs to prevent, assess and treat injected-related complications are [2]:

- Educate clients about factors that can lead to injection-related complications and how to prevent and treat injection-related complications

- Develop and implement assessment, treatment, and referral protocols for injection-related complications
- Train staff at needle and syringe programs and satellite sites to identify and provide education about injection-related complications to clients
- Assess the prevalence of injection-related complications
- Evaluate and publish any injection-related complications interventions undertaken

Harms and recommended practices for injecting oral opioids

There is a body of research evidence that has focused more closely on issues related to injection of oral opioids: this research is primarily concerned with quantifying and comparing the beneficial effects of using filters to remove harmful elements from injectable solutions made from drugs manufactured for oral use [9-16].

While the research reviewed did not include hydromorphone tablets, it did include a number of other opioids manufactured for oral use, including:

- MS Contin® [9, 14, 15], Kapanol® [15], and Skenan LP® [16] (morphine sulfate) sustained release tablets
- generic buprenorphine sublingual tablets [10, 13, 16]
- Subutex® (buprenorphine) tablets [11, 13, 15]
- Suboxone® (buprenorphine and naloxone) tablets and sublingual film [15]
- OxyContin® (oxycodone) sustained release tablets [12, 15]

This research highlights the specific health issues that can occur as a result of injecting oral opioids, which include [15]:

1) skin and soft tissue injuries (e.g., skin ulcers and cellulitis)
2) lung, heart and other conditions related to blood vessels (e.g., blood clots and endocarditis)
3) local and generalized infections (e.g., abscesses around injection sites and generalized blood infections)

These health issues can be caused by viral, bacterial or other matter introduced by injecting in non-sterile conditions. They can also be caused by the drug itself, but more commonly, by ingredients in the drug (such as bulking agents, coatings, waxes or gels) that are included to make the oral formulation work as intended, for example to maintain its stability, or to control the release of the drug once it is swallowed. In product information produced by drug manufacturers, these are listed as 'non-medicinal ingredients'; in research they are called 'excipients'.

Harms from non-sterile conditions

The non-sterile conditions in which injections occur can be responsible for introducing bacteria or other harmful matter into solutions that are injected. Viruses can be transmitted from one person to another when equipment used to prepare or inject drugs is shared (including syringes, filters, etc.) Bacteria or other matter can be present on equipment used to prepare drugs, which then gets into the solutions that are injected. Some bacteria that can be present

on the skin (or from the mouth, if saliva is used in the process to prepare drugs for injection) can be harmful when injected.

Harms from excipients

Ingredients that are included to make a drug manufactured for oral use work as intended are generally considered safe when swallowed, however, they may have adverse effects on the body whey they are dissolved into solutions and injected. They can clog needles or filters, become lodged within the skin or other blood vessels, and cause medical complications [2, 15]. A wide variety of excipients are used in the manufacture of oral drugs and each has their own properties, including different particle size, ability to dissolve in water, and response to heat [17]. An example of a specific excipient that has caused medical complications in people who inject drugs is talc, which can cause 'pulmonary talcosis' [10]. Talc is an excipient in MS Contin® and Kapanol® (morphine sulfate) and OxyContin OC® [15]. Dilaudid® (hydromorphone) immediate release tablets do not contain talc [18].

Recommended practices for injecting oral opioids

The available research on the beneficial effects of filtering opioids manufactured for oral use prior to injection provides a number of harm reduction practices that address the harms introduced by both non-sterile conditions as well as from excipients, these include [9, 15]:

- handwashing prior to injection
- using sterile water to prepare the solution to be injected
- alcohol swabbing at the injection site
- use of sterile injection equipment
- filtering the solution with a .2µm filter
- not heating the solution to be injected

Based on this research, it would seem likely that another recommendation could be that if oral hydromorphone tablets were to be provided to people who may inject them, it would be best to provide hydromorphone tablets with the least amount of excipients in them, or the least amount of excipients that are harmful if injected. For example, immediate release tablets are likely to have less (or less harmful) excipients compared to sustained released tablets.

Acceptability of harm reduction equipment to people who use drugs

Research has shown that the evidence (for example about the efficiency of wheel filters with small pore sizes) does not always translate into the acceptability of harm reduction equipment by people who inject drugs [16]. It is recommended that safer drug use education messages be prepared and delivered by people who use drugs [1].

Two 2015 reports from Institut national de santé publique du Québec (INSPQ) [19] and Centre intégré universitaire de santé et de services sociaux de l'Est-de-l'Île-de-Montréal (CIUSSS) [20] were part of an effort to increase the effectiveness of harm reduction equipment and to assess their acceptability to people who inject opioids in Québec. The INSPQ conducted a literature review and laboratory tests to make recommendations about choices related to harm reduction equipment that would be most appropriate for people who inject opioids. Their recommendations include maintaining current distribution of harm reduction equipment, and

adding some tools specifically for injection of oral opioid medications, such as a more appropriate filter, a larger container for preparing injection solutions, as well as syringes with larger volumes (3 ml). An evaluation of the acceptability of the recommended new tools (and the suggestions on how to prepare doses) to people who inject drugs in Montréal was carried out; most of the tools were acceptable, though some reported that they did not need syringes with larger volumes [20]. These reports contain a great deal of information that may be applicable to hydromorphone programs as they are the only laboratory and evaluation studies found to date that address injection of hydromorphone tablets that were manufactured for oral use. It should be noted that some of their recommendations (e.g., to heat solutions prior to injection) contradict other opioid filtration research [9]. The INSPQ and CIUSSS reports are publicly available, in French at www.inspq.qc.ca/publications/2045 and goo.gl/Hmc8H8. A thorough translation of these reports is required in order to more fully understand their contents and apply them to questions that may arise.

The current harm reduction equipment available in Ontario is provided by the Ontario Harm Reduction Distribution Program, which follows recommendations in the *Canadian Harm Reduction Programs that Provide Service to People Who Use Drugs and are at Risk for HIV, HCV, and Other Harms* [1, 2]. A list of the equipment they provide is available at www.ohrdp.ca.

Summary

There are risks involved when substances are injected for medical or recreational purposes, however, many of these can be minimized by safer injection practices based on harm reduction principles [1, 2]. Knowledge about harm reduction practices has been derived from research, as well as through the lived experience of people who inject drugs [3, 4].

There is limited literature on the harms associated specifically with injecting hydromorphone tablets that were manufactured for oral use (and what can be done to minimize these harms). Literature about harms and best practices for injection-related complications related to all drugs can be helpful in understanding the broad areas where harms are introduced by injecting drugs, and the need for education, protocol development, training and evaluation of interventions about addressing and reducing injection-related complications.

Research specifically about injecting oral opioids summarizes the specific harms that can be related to preparing and injecting solution of tablets manufactured for oral use in non-sterile conditions, and the non-medicinal drug ingredients (called 'excipients') that can have harmful effects if injected. This literature, which is derived mostly from research studies on the effect of filters on solutions of various morphine sulfate, buprenorphine, and oxycodone oral formulations that were prepared for injection, recommends several practices to reduce the harms from injection, including [9, 15]:

- handwashing prior to injection
- using sterile water to prepare the solution to be injected
- alcohol swabbing at the injection site
- use of sterile injection equipment
- filtering the solution with a .2µm filter
- not heating the solution to be injected

More recent research and evaluation from Montréal about improving the effectiveness (and ensuring the acceptability) of harm reduction equipment supplied to people who inject opioids provides more detailed information specifically about injecting hydromorphone tablets that were formulated for oral use [19, 20]. However, some of their recommendations (e.g., to heat solutions prior to injection) contradict other opioid filtration research [9]. Further analysis of these reports (including translation from French) is recommended.

Prepared by: Nicole Greenspan, Toronto Public Health
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