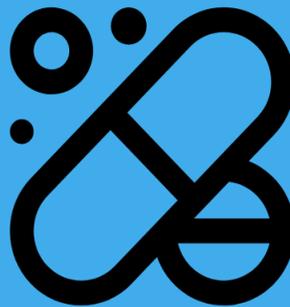


INFORMING YOUR CONSENT

Regarding Issues of the Safe
Supply Options for
Opioids in the



“Risk
Mitigation in the Context of
Dual Public Health
Emergencies” Guideline.

C.A.S.S.

CANADIAN ASSOCIATION FOR SAFE SUPPLY

SafeSupply.ca

**Regarding Issues of the Safe Supply Options for Opioids in the
“Risk Mitigation in the Context of Dual Public Health Emergencies” Guideline.
A briefing note by the Canadian Association for Safe Supply (CASS)**

While being critical of options chosen in BC’s recent guidelines, it is important to maintain perspective and realize the availability of these new safe supply options is significant and will be beneficial to many people who otherwise would need to rely on the illicit drug supply that is certainly a far worse option from a health perspective. This is a historic development in moving drug policy toward a public health based approach.

Issue:

The Risk Mitigation Guidelines recommend only oral tablets, generic hydromorphone 8mg or M-Eslon, for injection as Safe Supply options for opioid use, neither drug having been properly tested for safety when injected and both have known health risks associated with being injected. The guidelines do not offer injectable opioids, that have a basis of evidence showing an appropriate level of safety and efficacy when used as maintenance. There is no plan in the guideline to inform service providers and clients of the health risks of the tablet options offered, nor a strategy for educating on best practices to mitigate those risks.

Background:

In 2005, clinical trials started in Vancouver testing the safety and efficacy of injectable diacetylmorphine and/or hydromorphone for people who do not respond well to traditional forms of substitution treatment such as methadone¹². The evidence from these trials, in combination with clinical trials in Europe, confirms that providing injectable hydromorphone or diacetylmorphine reduces illicit drug use and the high-risk behaviors associated with it, and leads to overall greater stability and improved quality of life³⁴⁵ of participants. In May 2019, based on the evidence, Health Canada issued a Notice of Compliance to allow for injectable hydromorphone to be used as maintenance for addiction⁶. Health Canada also approved diacetylmorphine for the same use and has added the drug to its List of Drugs for an Urgent Public Health Need⁷ allowing for officials from health authorities import it and provide it to clients suited for injectable treatment. Since 2016 there have been no federal legal or regulatory barriers precluding injectable treatment to be provided as a program, but expansion of this option has moved very slowly⁸.

The recent emergence of the COVID epidemic combined with the ongoing overdose crisis created an expanded policy window for “safe supply” options to be considered. On March 19 2020 the federal government released a temporary Sect 56 exemption of the CDSA allowing more flexibility for the provinces to provide extended carries of OAT and greater access to Safe Supply. In response the BC Government released policy guidelines drafted by the BCCSU, *Risk Mitigation in the Context of Dual Public Health Emergencies*⁹, allowing for take-home options of opioids, benzodiazepines, (and stimulants) to be used outside of the context of treatment. Strangely, the guidelines recommend only Oral Dilaudid 8mg tablets and Oral M-Eslon for injection, even though neither option has been properly tested for safety and have known health risks when used this way. Injectable options of the same or similar drugs, that have been through evidence based regulatory processes and approved for opioid maintenance, are not included in the guideline.

Definitions:

Safe Supply: Safe supply refers to a legal and **regulated** supply of drugs with mind/body altering properties that traditionally have been accessible only through the illicit drug market.¹⁰

Regulated Drugs: New drugs are given a ‘market authorisation’ based on the evidence of quality, safety and efficacy presented by the manufacturer. The **regulator** will not only approve the drug but will also take great care to ensure that the accompanying information reflects the evidence that has been presented.¹¹

The Non-medicinal Contents of each drug:

[It is assumed that the Dilaudid 8mg tablets and M-Eslon will be immediate release because they have less excipients than extended release tablets that potentially can contaminate the blood stream if not properly filtered. Also, generic hydromorphone tablets are inferior to dilaudid brand tablets due to the waxy coating on the generic version].

1) Immediate Release Oral Hydromorphone 8mg tablets¹²:

- Lactose anhydrous – Basically this is milk sugar (from cows) and is meant to be a filler and a binder in pills. It is soluble.
- Magnesium stearate - is the magnesium salt of the fatty acid, stearic acid. Fatty acids are normal constituents of coconut oil, butter and other edible oils. The final product contains 4.0-5.0% magnesium, on a dried basis, and the fatty acid fraction is composed of ≥90% stearic and palmitic acids, at least 40% of which

are stearic acid. It is a very fine powder that is greasy to the touch and practically insoluble in water.¹³

- Drug and Cosmetic yellow No. 10 Lake- is manufactured by condensing quinaldine with phthalic anhydride to give the unsulfonated dye, which is then sulfonated with oleum. According to the FDA, lakes are formed by reacting straight dyes (such as D&C Yellow No. 10) with precipitants and salts. Aluminum is often a component

2) Immediate release Oral M-Eslon¹⁴:

- Hypromellose- is also known as soluble methylcellulose ethers. It is used as a thickening agent, binder, film former, and hydrophilic matrix material.
- maize starch- AKA corn starch.
- sucrose - sugar
- talc; - capable of clogging capillaries which can lead to all sorts of health problems starting with the lungs (lung granuloma)
- capsule shell contains gelatin and colouring agent (5 mg capsule – indigo carmine; 10 mg capsule – azorubine; 20 mg capsule – allura red AC (FD&C Red No. 40), brilliant blue FCF (FD&C Blue No. 1); 30 mg capsule – indigo carmine, quinoline yellow WS (D&C Yellow No. 10)).

Health Risks:

Oral hydromorphone and M-Eslon tablets are not meant to be injected and have not been tested for use in this way. A Health Canada assessment of the scientific literature of health issues related to injecting tablets include the following:

1. skin and soft tissue injuries (e.g., skin ulcers and cellulitis) ^[1]_[SEP]
2. lung, heart and other conditions related to blood vessels (e.g., blood clots, ^[1]_[SEP]endocarditis) ^[1]_[SEP]
3. local and generalized infections (e.g., abscesses around injection sites and ^[1]_[SEP]generalized blood infections) ¹⁵_[SEP]

The health problems can be created by either injecting in non-sterile conditions, or can be a result of introducing excipients (such as binding agents, fillers, sweeteners and dyes) into the bloodstream that can lead to clogging and other medical complications.

Mitigating Risks:

Proper filtration along with other safe injecting habits (clean hands, sterile water and equipment, cleaning injection site with alcohol swabs) should significantly lower but not eliminate adverse health events from injecting tablets. Ideally filtering tablets for

injections requires two filters, first going through a coarse filter to block larger excipients from clogging a second smaller 0.2µm filter that removes bacteria and other contaminants.¹⁶ If the two-filter process is too cumbersome then using either a sterile filter or a wheel filter can significantly reduce the odds of developing a health complication.^{17,18} If neither of these filters are available then using cotton and a cigarette filter does an effective job of removing contaminants.¹⁹

Considerations:

The Good: The availability of IR Oral Dilaudid 8mg tablets and IR M-Eslon as a take-home safe supply option is an amazing development in drug policy and will provide many people with a preferred choice of substances and effectively reduce their reliance on the illicit supply of drugs. Hopefully this will lead to more and better safe supply options.

Options for opioids are limited and not evidence based: Oral Dilaudid and M-Eslon are the only Safe Supply opioid options and neither have been properly tested for safety. There are known health risks that cannot be completely eliminated through filtering and can lead to both immediate health complications as well as complications that form over continued use over time. Although these options are better than the illicit supply in many respects, it is glaring that evidence-based options that have been tested for safety and efficacy have been overlooked.

Injectable hydromorphone or diacetylmorphine that have passed the rigorous testing required by the regulation process to assure safety could be provided in ampules or pre-loaded syringes and dispensed to take home. There are no legal or regulatory barriers precluding this from happening.

The Costs: The Health Canada Safe Supply guideline explains that healthcare providers may prefer tablet options because they are cheaper and more available than injectable versions²⁰. This justification is problematic because the tablets are not an economy version of an approved product, but rather they have not been tested by the minimum standards required of other drugs to be provided for this use at all. The off-label use is difficult to justify when tested drugs are available that can meet the need. The costs saved by taxpayers will be realized by clients who develop health problems from using drugs that are untested and potentially unsafe.

The service providers are working with what is at their disposal, the high cost and lack of availability of injectable hydromorphone is a problem to be solved at a higher level. In some provinces doses of liquid hydromorphone are not available at a strength higher than 10mg/ml on their provincial drug formularies, meaning the doses are not high enough to be practical to be used for maintenance. The price of liquid hydromorphone is also very high on the provincial formularies, especially in comparison to what is charged

to some hospitals. The pan-Canadian Pharmaceutical Association could be requested to renegotiate the price.

Informed Consent is Necessary- Transparency, Disclosure and Education: As mentioned earlier, these tablet options are a preferred substance by many people who inject drugs and for that reason they belong as safe supply options. But because they are being offered as part of a government intervention it is likely that clients and even some service providers will assume these options have gone through a regulatory process that confirms they are safe for injection use, which is not the case.

It is a duty of the proper authorities to ensure that all who consume these products are aware of the known unknowns due to the lack of testing and informed of the health risks associated with injecting tablets. This is especially important for all those people who have not had a history of injecting tablets and are not educated or aware of the risks or methods to mitigate the risks. There must be a province wide strategy in place to be sure that everyone is making an informed choice.

Science and Harm Reduction: In the struggle to take steps to end the war on drugs, advocates have always been able to rely on the scientific evidence in order to justify interventions that go against the grain of the status quo and counter criticisms that harm reduction measures are reckless and loose. In this instance we cannot say that the evidence is supporting this decision, as the evidence to inform the values of safety with these medications is not there. Meanwhile other options that have met the criteria of being evidence-based and formulated for humans to inject are being ignored. If a series of complicated health problems develop from this strategy it will be very difficult to defend the decision to take this approach, and it could risk the credibility of harm reduction measures in general. What's being presented in the guideline by decision makers as harm reduction and safe supply also includes a significant component of government cost reduction measures as well. We should not wait to inform people receiving prescriptions under the Dual Risk guidelines of potential health risks or how to mitigate them.

Recommendations:

1. That the government take steps needed to make available properly tested, evidence-based safe supply options proven to be safe and effective for injecting and to used as maintenance for opioid dependence. These should be added the primary options offered alongside the current options already included in the *Risk Mitigation in the Context of Dual Public Health Emergencies* Guidelines in order for clients to have an option that has met appropriate regulatory standards.

The most obvious option should be providing injectable hydromorphone in ampules or in preloaded syringes using either 10mg/ml or possibly 50mg/ml doses. Efforts should

be made to start the process of negotiating a lower price with Sandoz for injectable hydromorphone to match the rate that hospitals pay for the product.

Efforts to create a domestic supply of diacetylmorphine should continue. Until then, Health Canada has allowed for health officials to access and import diacetylmorphine through the use its *List of Drugs for an Urgent Public Health Need*. The emergence of COVID-19 also means that the recent Federal legislation in the *COVID-19 Emergency Response Act* could be used to “licence” drugs like diacetylmorphine, facilitating their domestic production.²¹

2. The government must ensure that the service providers and **ALL** clients receiving the tablet options are aware that tablets have not been properly tested for safety when injected and the practice is associated with numerous health risks, all of which should be made clear. Disclosure is an obligation for government as many clients of will have never injected tablets before and will start to now because it is the only legal option that suits their need. Knowing this is a government-approved program they will assume the product is safe.

3. There should be a proactive, peer-led and created educational component aimed to ensure all clients of the tablet options understand and are able to use best practices of injecting tablets.

4. Measure rates of illnesses associated with tablet injection, including infective endocarditis at provincial and federal levels.

¹ Oviedo-Joekes et al., “Diacetylmorphine versus Methadone for the Treatment of Opioid Addiction.”

² Oviedo-Joekes et al., “Hydromorphone Compared With Diacetylmorphine for Long Term Opioid Dependence.”

³ Ferri, Davoli, and Perucci, “Heroin Maintenance for Chronic Heroin-Dependent Individuals.”

⁴ Strang et al., “Heroin on Trial.”

⁵ Strang, Groshkova, and Metrebian, *New Heroin-Assisted Treatment*.

⁶ Government of Canada, “Notice of Compliance (NOC) Online Query.”

⁷ Health Canada, “Addressing the Opioid Crisis through Innovative Treatment Options and Investments in Frontline Projects and Research.”

⁸ Maghsoudi, Bowles, and Werb, “Expanding Access to Diacetylmorphine and Hydromorphone for People Who Use Opioids in Canada.”

⁹ “Risk-Mitigation-in-the-Context-of-Dual-Public-Health-Emergencies-v1.4.Pdf.”

¹⁰ “CAPUD Safe Supply English March 3 2019.Pdf.”

¹¹ Government of Canada, “Chapter 4—Regulating Pharmaceutical Drugs—Health Canada.”

¹² “Dilaudid-PM-EN.Pdf.”

¹³ Hobbs et al., “Magnesium Stearate, a Widely-Used Food Additive, Exhibits a Lack of in Vitro and in Vivo Genotoxic Potential.”

¹⁴ “M-ESLON-ENG-PM-2015-07-15-Clean.Pdf.”

¹⁵ Health Canada “Safe Supply Tool Kit 2019_EN.Pdf.”

¹⁶ McLean, Patel, and Bruno, "Injection of Pharmaceuticals Designed for Oral Use."

¹⁷ "UN68_Wheel_Filter_Guide_web.Pdf."

¹⁸ "Sterifilt, Presentation."

¹⁹ Ng et al., "Filtration of Crushed Tablet Suspensions Has Potential to Reduce Infection Incidence in People Who Inject Drugs."

²⁰ Health Canada guideline

"CAPUD Safe Supply English March 3 2019.Pdf." Accessed April 8, 2020.

<https://capud.ca/sites/default/files/2019-03/CAPUD%20safe%20supply%20English%20March%203%202019.pdf>.

"Dilaudid-PM-EN.Pdf." Accessed April 8, 2020. <http://purdue.ca/wp-content/uploads/2018/04/Dilaudid-PM-EN.pdf>.

Ferri, Marica, Marina Davoli, and Carlo A. Perucci. "Heroin Maintenance for Chronic Heroin-Dependent Individuals." Edited by Cochrane Drugs and Alcohol Group. *Cochrane Database of Systematic Reviews*, December 7, 2011. <https://doi.org/10.1002/14651858.CD003410.pub4>.

Government of Canada, Health Canada. "Notice of Compliance (NOC) Online Query," August 25, 2010. <https://health-products.canada.ca/noc-ac/info.do?lang=en&no=22105>.

Government of Canada, Office of the Auditor General of Canada. "Chapter 4—Regulating Pharmaceutical Drugs—Health Canada," November 22, 2011. https://www.oag-bvg.gc.ca/internet/English/parl_oag_201111_04_e_35936.html#hd5a.

Health Canada. "Addressing the Opioid Crisis through Innovative Treatment Options and Investments in Frontline Projects and Research." Backgrounders. gcnws, May 15, 2019. <https://www.canada.ca/en/health-canada/news/2019/05/backgrounder-addressing-the-opioid-crisis-through-innovative-treatment-options-and-investments-in-frontline-projects-and-research.html>.

Hobbs, Cheryl A., Kazuhiko Saigo, Mihoko Koyanagi, and Shim-mo Hayashi. "Magnesium Stearate, a Widely-Used Food Additive, Exhibits a Lack of in Vitro and in Vivo Genotoxic Potential." *Toxicology Reports* 4 (2017): 554–59. <https://doi.org/10.1016/j.toxrep.2017.10.003>.

-
- Maghsoudi, Nazlee, Jeanette Bowles, and Dan Werb. "Expanding Access to Diacetylmorphine and Hydromorphone for People Who Use Opioids in Canada." *Canadian Journal of Public Health*, March 27, 2020. <https://doi.org/10.17269/s41997-020-00315-4>.
- McLean, Stuart, Rahul Patel, and Raimondo Bruno. "Injection of Pharmaceuticals Designed for Oral Use: Harms Experienced and Effective Harm Reduction Through Filtration." In *Non-Medical and Illicit Use of Psychoactive Drugs*, edited by Suzanne Nielsen, Raimondo Bruno, and Susan Schenk, 34:77–98. Current Topics in Behavioral Neurosciences. Cham: Springer International Publishing, 2016. https://doi.org/10.1007/7854_2016_470.
- "M-ESLON-ENG-PM-2015-07-15-Clean.Pdf." Accessed April 8, 2020. <https://www.ethypharm.com/wp-content/uploads/2017/10/M-ESLON-ENG-PM-2015-07-15-clean.pdf>.
- Ng, Huei, Rahul P. Patel, Raimondo Bruno, Roger Latham, Troy Wanandy, and Stuart McLean. "Filtration of Crushed Tablet Suspensions Has Potential to Reduce Infection Incidence in People Who Inject Drugs: Filtration of Illicit Drug Injections." *Drug and Alcohol Review* 34, no. 1 (January 2015): 67–73. <https://doi.org/10.1111/dar.12196>.
- Oviedo-Joekes, Eugenia, Suzanne Brissette, David C. Marsh, Pierre Lauzon, Daphne Guh, Aslam Anis, and Martin T. Schechter. "Diacetylmorphine versus Methadone for the Treatment of Opioid Addiction." *New England Journal of Medicine* 361, no. 8 (August 20, 2009): 777–86. <https://doi.org/10.1056/NEJMoa0810635>.
- Oviedo-Joekes, Eugenia, Daphne Guh, Suzanne Brissette, Kirsten Marchand, Scott MacDonald, Kurt Lock, Scott Harrison, et al. "Hydromorphone Compared With Diacetylmorphine for Long-Term Opioid Dependence: A Randomized Clinical Trial." *JAMA Psychiatry* 73, no. 5 (May 1, 2016): 447–55. <https://doi.org/10.1001/jamapsychiatry.2016.0109>.
- "Risk-Mitigation-in-the-Context-of-Dual-Public-Health-Emergencies-v1.4.Pdf." Accessed April 8, 2020. <https://www.bccsu.ca/wp-content/uploads/2020/04/Risk-Mitigation-in-the-Context-of-Dual-Public-Health-Emergencies-v1.4.pdf>.
- "Safe Supply Tool Kit 2019_EN.Pdf," n.d.
- "Sterifilt, Presentation." Accessed April 8, 2020. <http://www.apothicom.org/sterifilt-general-presentation.htm>.
- Strang, John, Teodora Groshkova, and Nicola Metrebian. *New Heroin-Assisted Treatment: Recent Evidence and Current Practices of Supervised Injectable Heroin Treatment in Europe and Beyond*. EMCDDA Insights 11. Luxembourg: Office for Official Publ. of the Europ. Communities, 2012. <https://doi.org/10.2810/50141>.
- Strang, John, Teodora Groshkova, Ambros Uchtenhagen, Wim van den Brink, Christian Haasen, Martin T. Schechter, Nick Lintzeris, et al. "Heroin on Trial: Systematic Review and Meta-Analysis of Randomised Trials of Diamorphine-Prescribing as Treatment for Refractory Heroin Addiction." *British Journal of Psychiatry* 207, no. 1 (July 2015): 5–14. <https://doi.org/10.1192/bjp.bp.114.149195>.
- "UN68_Wheel_Filter_Guide_web.Pdf." Accessed April 8, 2020. http://harmreductionwa.org/wp-content/uploads/2017/06/UN68_Wheel_Filter_Guide_web.pdf.

²¹ Retrieved from: <https://theconversation.com/canadas-coronavirus-aid-package-guards-against-drug-shortages-with-compulsory-licensing-134974?fbclid=IwAR1DR2HnjKsXsX8VEDQYcCnr4GEZID0oZQkXbNnDu-AColmGHNDJCCUITmc>