To: VCH OAT Providers Network, VCH Overdose Community of Practice, VCH Community Action Teams

Re: Illicitly Manufactured Benzodiazepines in the Local Drug Supply

Over the past few weeks VCH has become increasingly concerned about the emergence of illicitly manufactured benzodiazepines and benzodiazepine analogs in the local drug supply due to their potential impact on risk, presentation and management of overdose and treatment of opioid use disorder.

VCH has received numerous reports of mixed opioid-benzodiazepine overdoses from the community involving people who consumed what they thought were opioids in Vancouver and recently in Powell River. Drug testing has identified samples of street drugs sold as opioids containing fentanyl and illicitly manufactured benzodiazepines such as flualprazolam and flubromazolam as well as benzodiazepine analogs such as etizolam. VCH has also received reports that etizolam is being sold in Vancouver and that people who use benzodiazepines may have consumed it intentionally.

This is a concerning trend because benzodiazepines when taken with opioids increase the risk of overdose and the risk of death. Opioids and benzodiazepines cause sedation and respiratory depression via separate pathways in the brain. In combination, these drugs act synergistically to worsen sedation and decrease the drive to breathe.

Although naloxone should still be administered to reverse opioid toxicity and restore breathing in mixed opioid benzodiazepine overdoses, symptoms of benzodiazepine toxicity such as drowsiness and sedation may persist for hours since they may not respond to naloxone. We encourage community sites to call 911 so that paramedics can assist in the management of these complex overdoses. Benzodiazepines may also cause disinhibition and put people at risk of sexual violence. Following benzodiazepine overdose people may experience blackouts and memory loss.

Although we believe that only a minority of opioids sold in the region are contaminated with benzodiazepines and that most people would be exposed intermittently, this raises some clinical concerns for patients on opioid agonist treatment (OAT) with methadone, buprenorphine/naloxone (Suboxone), sustained release oral morphine (Kadian), as well as injectable treatments (diacetylmorphine, hydromorphone).

Firstly, those exposed to benzodiazepines unintentionally may experience sedation that could be interpreted as a side effect of OAT (e.g. dose too high). A dose reduction in this clinical scenario might lead to increased use of illicit opioids. Secondly, patients that have been regularly exposed might become dependent on benzodiazepines and suffer unexpected withdrawal symptoms when their drug

supply changes. Symptoms of benzodiazepine withdrawal, such as anxiety and sleeplessness, may be difficult to distinguish from symptoms of opioid withdrawal. Increasing OAT dose in this scenario could increase risk as the patient would be on a higher opioid dose and would still have untreated benzodiazepine withdrawal.

If clinicians, or patients, are concerned about exposure to benzodiazepines, they should make use of urine drug testing. However, point of care urine drug tests may not detect all benzodiazepines, including illicitly manufactured benzodiazepines such as those that have been identified in the local drug supply. Sending a urine sample to a lab for confirmatory testing may be of greater benefit.

If clinicians need assistance managing clinical scenarios, we encourage them to call the Race Line for Consultative Expertise in Addiction Medicine (www.raceconnect.ca or 1-877-696-2131).

Patients should also be advised to make use of supervised consumption, overdose prevention and drug checking services if they are available in their community.

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