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Oral opioid agonists for the treatment of opioid use disorder

English summary

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SUMMARY

Oral opioid agonists for the treatment of opioid use disorder

Introduction

Opioid use disorder (OUD) is associated with high mortality and morbidity rates and is considered a highly complex medical condition by the Canadian healthcare system. The disorder is usually managed with opioid agonist therapy (OAT), which quickly relieves withdrawal symptoms and then reduces long-term physical and psychological dependence, thus preventing relapse, transmission of infectious diseases, overdose mortality and criminal recidivism. Buprenorphine-naloxone and methadone are the two oral OATs approved by Health Canada for the treatment of OUD. Despite the recognized benefits of OAT and the various measures taken to facilitate its use, including doing away with the requirement for prescribers to obtain an exemption from the federal government to prescribe methadone, regardless of its indication, and the addition, in 2018, of buprenorphine-naloxone to the regular list in Québec's public prescription drug insurance plan, few people in Québec with OUD appear to be receiving OAT at present.

This lack of access to OAT is due mainly to a significant shortage of medical personnel in the area of addiction in Québec, particularly in the field of OUD, while no training on prescribing OAT is included in the academic curriculum for physicians. Improving management and the offer of services is, in fact, a public health need figuring among the Québec government’s priorities (2018-2028 Interministerial Addiction Action Plan [PAID]). Furthermore, the more recent introduction into the market of buprenorphine-naloxone, which has different characteristics from those of methadone and carries a risk of withdrawal caused upon treatment induction, requires clarification and tools for prescribers, who are not always comfortable with this more complex clinical situation. With this perspective in mind, MSSS asked INESSS to develop clinical recommendations to promote the optimal use of opioid agonists in the treatment of OUD.

Methods

The development of this OUG on oral opioid agonists and the *Aide-mémoire : discussion avec l’usager* (user discussion checklist) is based on the best available scientific data arising from a systematic review of primary studies, consultation on the user’s perspective, recommendations on best clinical practices and pharmacoeconomic analyses. These sources were supplemented with legislative and organizational contextual elements specific to Québec and with experiential knowledge provided by several Québec experts and clinicians who collaborated on the project. This systematic review was conducted in collaboration with a scientific information specialist using the following databases, with the aim of identifying clinical practice guidelines [CPGs], guidance documents and consensus conference reports: PubMed [National Library of Medicine], Embase [Ovid], Evidence-Based Medicine Reviews [EBM Reviews; Ovid] and

the Cochrane Database of Systematic Reviews. The literature search covered the period from each database's inception to January 2020. Only publications in French and English were retrieved. In addition, a manual literature search was conducted by consulting the websites of health technology assessment agencies and organizations, government bodies and professional associations or orders related to the project's topic, as well as leading websites in the field of drug addiction. The bibliographies of the retained publications were scanned for other relevant documents. In addition, the Google search engine was used to find publications from North American regulatory agencies, including those of the Food and Drug Administration [FDA] and Health Canada. Lastly, official OAT product monographs were consulted.

To ascertain user preferences regarding methadone and buprenorphine-naloxone, individuals undergoing treatment with opioid agonists were consulted via individual interviews. The information obtained helped INESSS enrich and adapt the *Aide-mémoire : discussion avec l'usager* checklist, particularly with regard to material on perceived advantages and disadvantages.

Results

Anyone who uses opioids, whether illicit or prescription, is at risk for developing OUD. Therefore, early identification of factors and behaviours suggestive of opioid misuse is paramount for facilitating management and thus preventing the problem from becoming too pronounced before it is treated. After the diagnosis is made and in order to allow for comprehensive, global management, the individual should be thoroughly evaluated before prescribing treatment for OUD. This assessment should include identifying their at-risk behaviours (e.g., sharing drug paraphernalia) and drug use-related complications, such as STBBIs and tuberculosis, as well as all comorbidities, including physical and mental health problems and psychoactive drug use habits. Refusal by the individual to have their comorbidities assessed or managed should not, however, prevent proposing and initiating OAT, unless there is a contraindication, since the benefits of this treatment are substantial, particularly for reducing the risk of overdose.

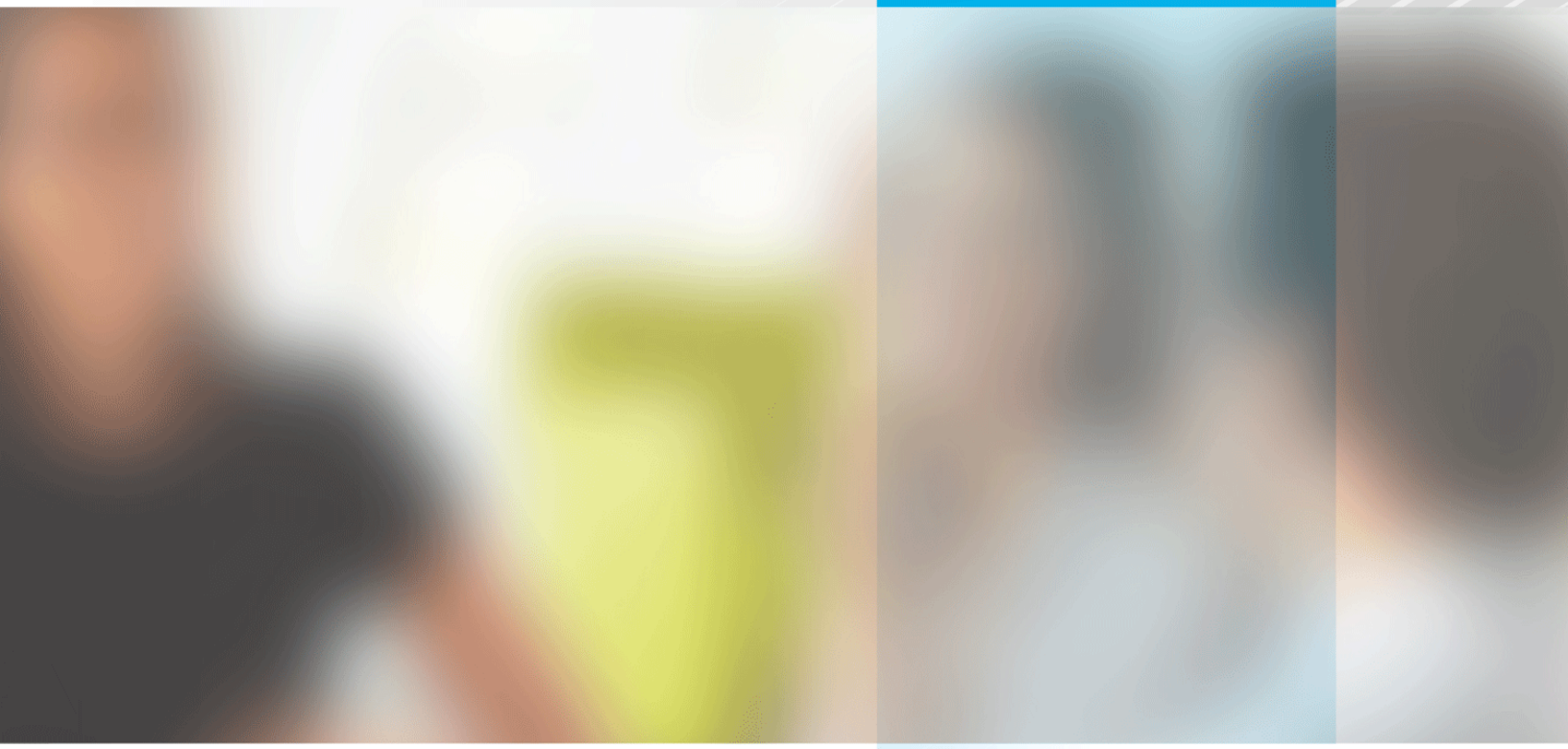
Although similar in efficacy, buprenorphine-naloxone has significant advantages over methadone, making it a generally safer treatment option. First, the presence in this formulation of naloxone, an opioid antagonist that is not absorbed during sublingual administration, decreases the potential for buprenorphine abuse by limiting its inappropriate use via the intravenous route. Secondly, the buprenorphine component, a partial opioid agonist, provides greater safety by reducing the risk of overdose and the severity of withdrawal symptoms when the therapy is discontinued. These characteristics make for safer use and open up the possibility of unsupervised doses. Several of the consulted users confirmed that buprenorphine-naloxone is the treatment of choice for individuals who wish to completely stop using illicit drugs. It is also perceived as having far fewer adverse effects, and it makes changes of locale easier since it is available in tablet form.

Despite some of buprenorphine-naloxone's advantages, methadone remains an available and effective option for treating individuals with OUD. Some of the consulted users did, in fact, express a strong preference for methadone. It is therefore up to healthcare professionals to propose a flexible treatment adapted to each patient's situation, values and preferences, and based on professional and clinical judgment. To this end, the decision to treat and the choice of treatment should be made in partnership with the patient and, if possible, their family, friends or significant others, in order to involve the patient in the treatment plan. The different options should be presented to the patient in such a manner that they fully understand the advantages and disadvantages.

In addition to OAT induction, a major challenge for qualified professionals during the follow-up period is to anticipate and address any problem that might arise and negatively affect the continuity of the care and the taking of OAT, which could have major consequences for the patient, including withdrawal and relapse.

Conclusions

The recommendations developed by INESSS take into account the most recent evidence likely to support Québec practice with OAT. Incorporated into the optimal use guide and the checklist aimed at facilitating discussion between the professional and the patient, the recommendations focus overall on clarifying the main elements to be considered during the clinical assessment, on the choice of pharmacological treatment, on the principles of OAT induction and stabilization and on the elements to be considered when monitoring OAT.



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