

# Dissolution Techniques for Buprenorphine and Buprenorphine-Naloxone: Clinical Effectiveness and Guidelines

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### **Research Questions**

- 1. What is the comparative clinical effectiveness of sublingual buprenorphine tablets administered using dissolution practices versus standard administration of buprenorphine for the treatment of opioid use disorder or dependency?
- 2. What is the comparative clinical effectiveness of sublingual buprenorphine-naloxone tablets administered using dissolution practices versus standard administration of these drugs for the treatment of opioid use disorder or dependency?
- 3. What are the evidence-based guidelines regarding the dissolution of buprenorphine or buprenorphine-naloxone combination tablets for the treatment of opioid use disorder or dependency?

# **Key Findings**

No literature was identified regarding the comparative clinical effectiveness of sublingual buprenorphine or buprenorphine-naloxone tablets administered using dissolution practices versus standard administration for the treatment of opioid use disorder or dependency. Furthermore, no evidence-based guidelines were identified regarding the dissolution of buprenorphine or buprenorphine-naloxone combination tablets for the treatment of opioid use disorder or dependency.

### **Methods**

This report makes use of a literature search developed for a previous CADTH report. The original literature search was conducted in June 2016 on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were buprenorphine and forms of administration. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The initial search was also limited to English-language documents published between January 1, 2011 and June 16, 2016. For the current report, database searches were rerun on September 17, 2019 to capture any articles published since the initial search date. The search of major health technology agencies was also updated to include documents published since June 2016. Internet links are provided, where available.

### **Selection Criteria**

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

# **Table 1: Selection Criteria**

Population	Adults with opioid dependency, opioid use disorder, or substance use disorder
Interventions	Q1, Q3: Sublingual buprenorphine tablets administered using dissolution practices (e.g., crushing, mixing with saliva) Q2, Q3: Sublingual buprenorphine-naloxone combination tablets administered using dissolution practices
Comparators	Q1: Standard administration of sublingual buprenorphine tablets



	Q2: Standard administration of sublingual buprenorphine-naloxone tablets Q3: No comparator necessary
Outcomes	Q1-2: Clinical effectiveness (e.g., patient satisfaction, time to dissolution, opiate withdrawal symptoms [e.g., clinical opioid withdrawal score], safety [e.g., adverse reactions]) Q3: Evidence-based guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines

## Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

No literature was identified regarding the comparative clinical effectiveness of sublingual buprenorphine or buprenorphine-naloxone tablets administered using dissolution practices versus standard administration for the treatment of opioid use disorder or dependency. Furthermore, no evidence-based guidelines were identified regarding the dissolution of buprenorphine or buprenorphine-naloxone combination tablets for the treatment of opioid use disorder or dependency.

References of potential interest are provided in the appendix.

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

No literature identified.

Guidelines and Recommendations

No literature identified.



# **Appendix** — Further Information

# **Previous CADTH Reports**

 Marchand DK, Young C, Loshak H. Buprenorphine for opioid use disorder: a review of comparative clinical effectiveness, safety, cost-effectiveness, and guidelines (*CADTH* rapid response report: summary with critical appraisal). Ottawa (ON): CADTH: 2019 Apr;

https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1092%20Buprenorphine%20for%20OUD%20Final.pdf

Accessed 2019 Sep 23.

- Seal K, Argáez C. Buprenorphine formulations for the treatment of opioid use disorders: comparative clinical effectiveness, cost-effectiveness, and guidelines (CADTH rapid response report: reference list). Ottawa (ON): CADTH; 2018 Apr; <a href="https://www.cadth.ca/sites/default/files/pdf/htis/2018/RA0951%20Buprenorphine%20Formulations%20Update%20Final.pdf">https://www.cadth.ca/sites/default/files/pdf/htis/2018/RA0951%20Buprenorphine%20Formulations%20Update%20Final.pdf</a> Accessed 2019 Sep 23.
- CADTH. Crushed Buprenorphine or Buprenorphine-Naloxone for opioid dependency: a review of the clinical effectiveness and guidelines (*CADTH rapid response report:* summary with critical appraisal). Ottawa (ON): CADTH; 2016 Jul; <a href="https://www.cadth.ca/sites/default/files/pdf/htis/july-2016/RC0794-Crushed%20Suboxone%20Final.pdf">https://www.cadth.ca/sites/default/files/pdf/htis/july-2016/RC0794-Crushed%20Suboxone%20Final.pdf</a> Accessed 2019 Sep 23.

# Systematic Reviews and Meta-analyses

 Lagisetty P, Klasa K, Bush C, et al. Primary care models for treating opioid use disorders: what actually works? A systematic review. PLoSOne. 2017; 12(10):e0186315.
 PubMed: PM29040331

### Non-Randomized Studies

### Published Outside of the Literature Search Time Frame

 Muhleisen P, Nielsen S, Spence J, Lintzeris N. Crushing sublingual Buprenorphinenaloxone tablets: impact upon dissolution time for supervised dispensing. *Aust Pharm*. 2010 Feb;29(2):158-162. <a href="https://search.informit.com.au/documentSummary;dn=059179298330064;res=IELAPA">https://search.informit.com.au/documentSummary;dn=059179298330064;res=IELAPA</a> Accessed 2019 Sep 23.