Conversion of CII Opioid Medications to Buprenorphine in the chronic pain population

Insights and Clinical Pearls

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Disclosures

- Collegium Pharmaceuticals
  - Speaker
  - Advisor
- Averitas
  - Speaker
  - Advisor

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Objectives

- Review buprenorphine MOA (mechanism of action)
- Discuss current research on the topic of utilizing buprenorphine in the chronic pain population
- Review methodology and results from the Zimmerman research article
- Provide clinical pearls on conversion from full agonist CII opioid medications to buprenorphin buccal film
- Discuss key takeaways

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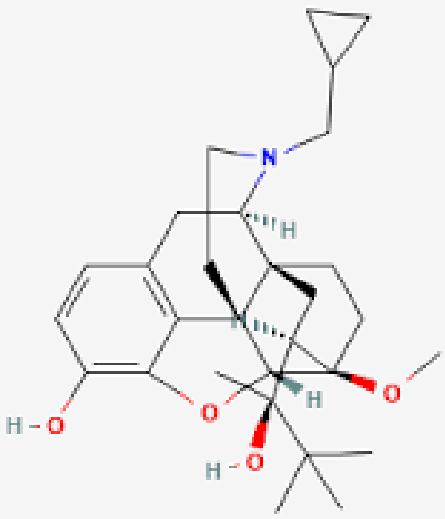
Buprenorphine

- Partial agonist at the mu-opioid receptor
- Antagonist at the kappa-opioid receptor
- Strong affinity for mu



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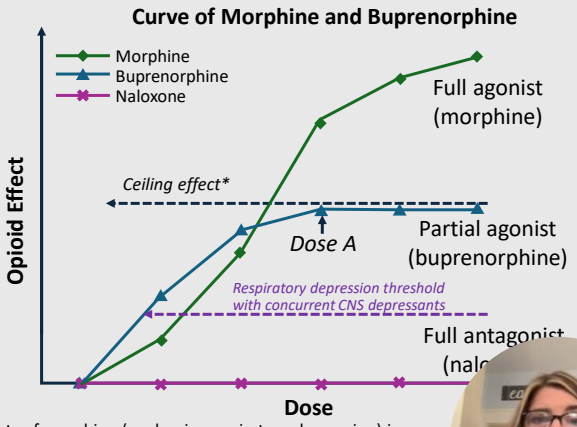
Benefits of Buprenorphine

- "Ceiling effect"
  - Limit to respiratory depression, euphoria, drug-liking effect seen
- Preferred in patients with history of substance use disorder
- Overall, lower risk of AEs (adverse events) and milder withdrawal symptoms vs full-agonist opioids
- Possible advantage for:
  - Patients with opioid-induced hyperalgesia
  - Patients with concurrent neuropathic pain



*Effects of morphine (analgesia, respiratory depression) increase
increasing doses. The nonanalgesic effects of buprenorphine incr
until "Dose A" is reached. No further effect is seen with increase i
dose beyond "Dose A."

Aiyer. Anesth Analg. 2018;127:529. Golembiewski. J Perianesth Nurs. 2010;25:413.

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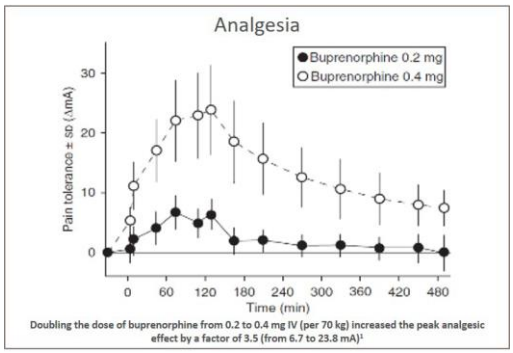
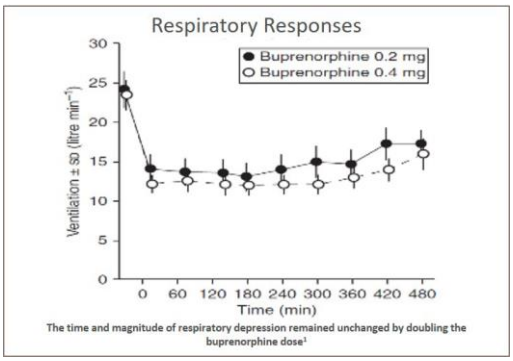


Doubling the dose of buprenorphine from 0.2 to 0.4 mg IV (per 70 kg) increased the peak analgesic effect by a factor of 3.5 (from 6.7 to 23.8 mA)[1]



The time and magnitude of respiratory depression remained unchanged by doubling the buprenorphine dose[1]

Dahan A, Yassen A, Romberg R, Sarton E, Teppema L, Olofsen E, Danhof M. Buprenorphine indu
ceiling in respiratory depression but not in analgesia. Br J Anaesth. 2006 May;96(5):627-32. do
10.1093/bja/ael051. Epub 2006 Mar 17. PMID: 16547090.

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Why switch?

- CDC guideline recommendations to lower MME

(milligram morphine equivalent)

- Improved safety profile
- Improved patient outcomes
- Long term efficacy
- Lower risk of adverse events
- Fewer adverse effects
- Drug clearance does not change with age, renal or hepatic impairment

Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. **DOI:** http://dx.doi.org/10.15585/mmwr.rr6501e1

Powell VD, Rosenberg JM, Yaganti A, et al. Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review. *JAMA Netw Open.* 2021;4(9). doi:10.1001/jamanetworkopen.2021.24152

Hale M, Urdaneta V, Kirby MT, Xiang Q, Rauck R. Long-term safety and analgesic efficacy of buprenorphine buccal film in patients with moderate-to-severe chronic pain requiring a… J Pain Res. 2017 Jan 25;10:233-240. doi: 10.2147/JPR.S120170. PMID: 28182123; PMCID: PMC5279817.

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Common Misconceptions

- Inadequate analgesia
- Only for opioid use disorder
- Fear of inducing withdrawal
- Perioperative concerns
- Patient acceptance
- Cannot use with a full mu agonist
- The need to precipitate withdrawal prior to induction

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PAIN Practice

Opioid Rotation from High-Dose Morphine to Transdermal Buprenorphine (Transtec®) in Chronic Pain Patients

Enno Freye MD, PhD, Astrid Anderson-Hillemacher MD, Ingrid Ritzdorf PhD, Joseph Victor Levy PhD

First published: 06 June 2007 | https://doi.org/10.1111/j.1533-2500.2007.00119.x | Citations: 47

Conclusion:

- Data supports transition from high dose morphine to TD bup is feasible

- 42 chronic pain patients MME 120-240 transitioned to TD (transdermal) buprenorphine
  - 120 MME (n=14)
  - 121-140 MME (n=13)
  - 241-800 MME (n=15)
  - Available doses TD buprenorphine:
    - 32, 52.5, 70 mcg/h
- EP ratio 1:75
  - 120 MME = 70 mcg/h TD buprenorphine
- Avg stable dose TD bup
  - 52.5mcg/h or 1260 mcg/d (1.2 mg/day)
  - Measured pain severity and sleep
  - Improvement across the cohort for 1 year
  - Pain relief increased from 5% to 76%
  - 5% reported insufficient relief
  - Relief with buprenorphine alone 77%
  - Need for breakthrough pain medication 17%
  - Sleep quality increased from 14% to 74%

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Comparative Study > Support Care Cancer. 2009 Jun;17(6):715-8.
doi: 10.1007/s00520-008-0546-6. Epub 2008 Dec 23.

Equipotent doses to switch from high doses of opioids to transdermal buprenorphine

Sebastiano Mercadante [1], Alessandra Casuccio, Walter Tirelli, Antonello Giarratano

Affiliations + expand

PMID: 19104845 DOI: 10.1007/s00520-008-0546-6

Conclusion:

- Results suggest that stable patients receiving relatively high doses of oral morphine and TD fentanyl could safely be switched to TD BUP while maintaining the same level of analgesia

- 11 cancer patients (one withdrew day 3)
  - 120-220 mg/d Morphine (n=4)
  - 50-100 mcg/d Fentanyl (n=6)
- Switched to transdermal buprenorphine
  - Fentanyl – BUP ratio 0.6:0.8
  - Morphine – BUP ratio 70:1
  - TD bup doses ranged from 70 mcg/h to 140 mcg/h (1.6mg/d to 3.36 mg/day)
- Data points:
  - Pain and symptom intensity
  - Opioid doses
  - Global satisfaction
  - Number of BTP (breakthrough pain) medica
- No significant changes in any of the data points were found

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Pain Med. 2016 May; 17(5): 899–907. PMCID: PMC4984426
Published online 2016 Feb 24. doi: 10.1093/pm/pnv110 PMID: 26917621

Evaluation of the Tolerability of Switching Patients on Chronic Full μ-Opioid Agonist Therapy to Buccal Buprenorphine

Lynn Webster, MD,[*] Daniel Gruener, MD,[†] Todd Kirby, PhD,[‡] Qinfang Xiang, PhD,[‡] Evan Tzanis,[§] and Andrew Finn, PharmD[¶]

Conclusion:

- Chronic pain patients treated with around-the-clock full mu opioid therapy can be switched to BBF (buprenorphine buccal film) at approximately 50% of the full mu-opioid agonist dose without an increased risk of opioid withdrawal or loss of pain control

- 35 chronic pain patients MME 80- 220
  - Morphine or oxycodone
- Group 1: MME 80-160. (n = 33)
  - Transitioned to 300 mcg bid
- Group 2: MME 161-220. (n = 6)
  - Transitioned to 450 mcg bid
- Monitored inpatient for two nights
- COWS score q30 minutes x 24h
- One patient in Group 1 experienced withdrawal, no withdrawal in group 2
- No significant differences in pain rating between treatments

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Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospective Analysis

- Data points
  - Daily morphine equivalent
  - Pain scores using NRS (numeric rating scale) before and after conversion
  - Proportion of patients who successfully converted to BBF
  - Proportion of patients who converted directly from Schedule II LAO (long acting opioid) to BBF with associated dose data
  - Reasons for BBF discontinuation
  - Adverse events

Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospective Analysis, *Pain Medicine*, Volume 22, Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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Methods

- patients treated between Jan 1, 2016 and June 30, 2019
- Treated with opioids for a **chronic pain condition**
- Converted to BBF from their schedule II long acting or short acting opioid
- BBF added to an established opioid regimen

Subgroups:

- MME prior to conversion
  - <90
  - 90-149
  - 150-199
- Those who remained on BTP medication following conversion
- Those who did not remain on BTP medication following conversion
- Pain score 1-5 and 6-10 pre-conversion
- Pain score 1-5 and 6-10 post-conversion

Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospective Analysis, *Pain Medic*
Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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Results

- Baseline characteristics (N=157)
  - 63% female
  - Mean age 54.5 years
  - Mean daily MME 190.8
- Prior to conversion 40.8% prescribed greater than or equal to 200 MME
  - These patients had the highest mean pain score (6.5) of all MME subgroups

Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospective Analysis, *Pain Me*
May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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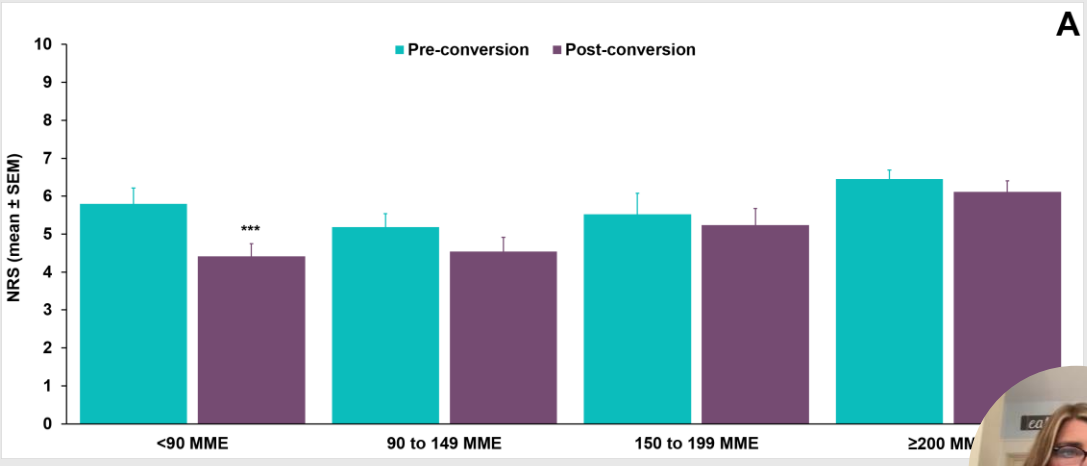
Results : NRS total



NRS pain scores before and after conversion to BBF for each baseline MME subgroup in the total patie

Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospective
Medicine, Volume 22, Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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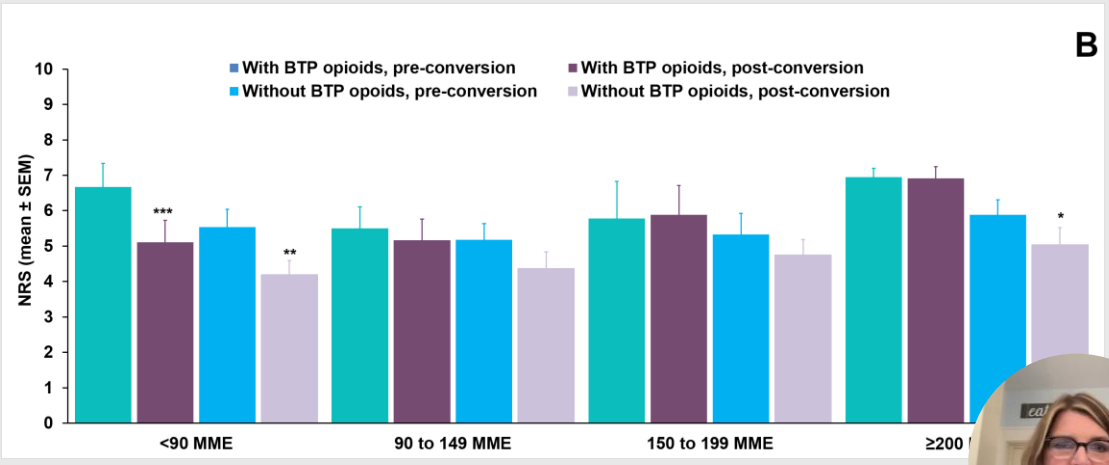
Results : NRS with w/o BTP meds



patients who received or did not receive opioids for BTP

Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospectiv
Medicine, Volume 22, Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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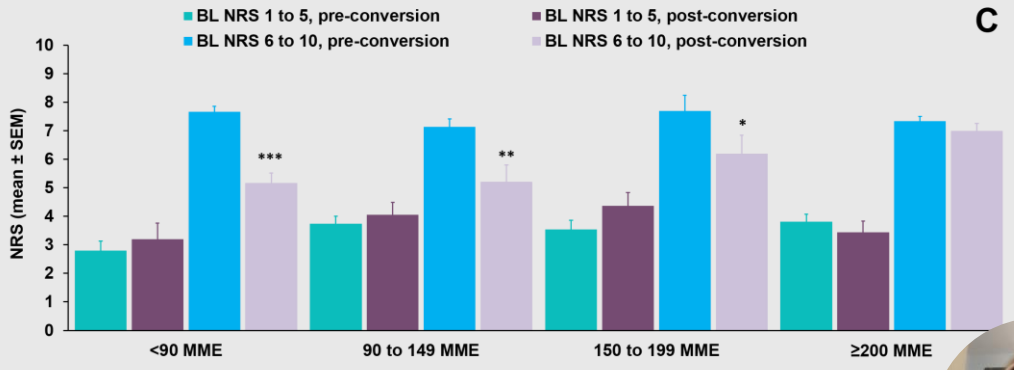
Results : NRS pre and post 1-5/6-10



range of NRS pain scores at baseline

*p<0.05; **p<0.01; ***p<0.001 by 2-sample paired t

Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospectiv
Medicine, Volume 22, Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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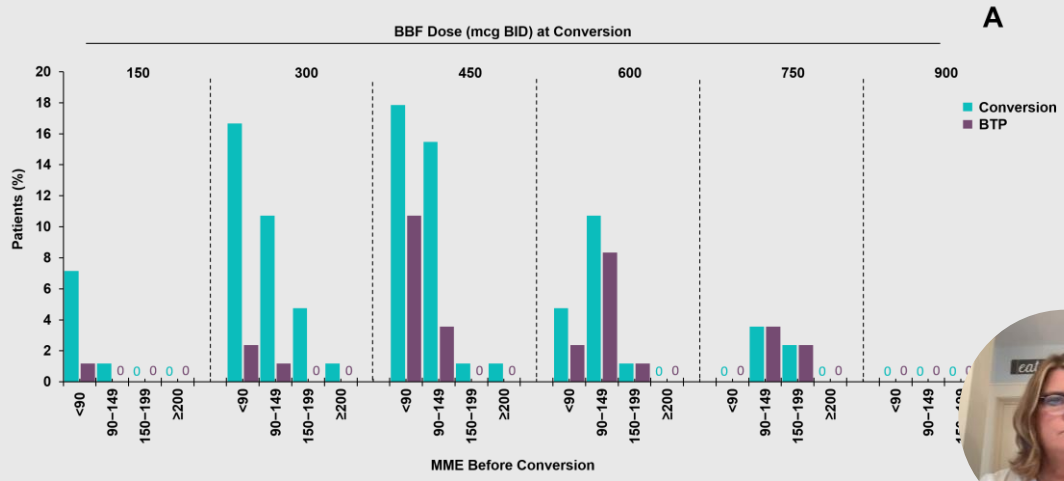
Results: Dose of BBF by pre conversion MME subgroup



Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospective
Medicine, Volume 22, Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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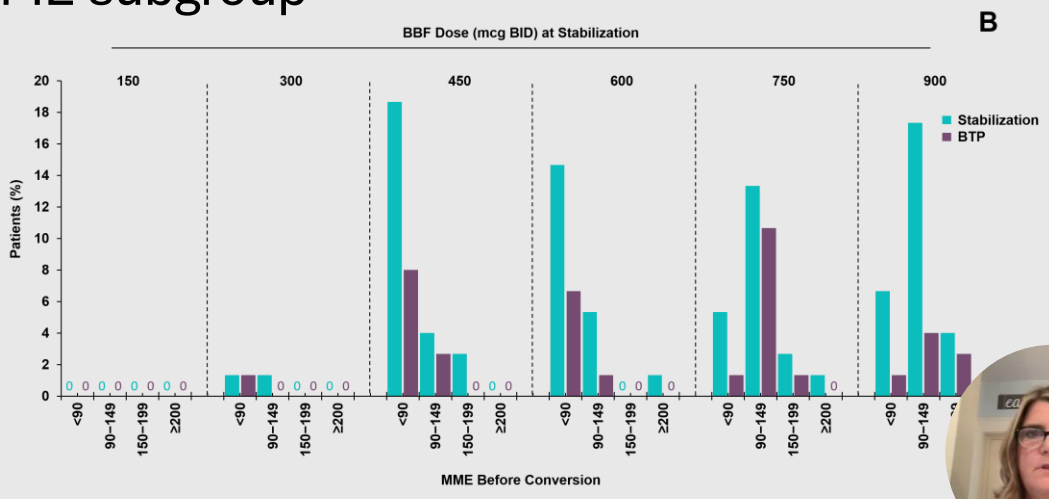
Conversion: Stabilization dose by pre conversion MME subgroup



Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrosp… *Medicine*, Volume 22, Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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Results: Difference in MME Before and After Conversion by Baseline MME Subgroup

Daily MME Range Pre- Conversion	Mean MME (mg) Pre- Conversion	Mean MME (mg) Post- Conversion	% Reduction in MME
<90 MME (n=39)	47.3	11.2	76.3%
90 to 149 MME (n=33)	114.3	17.7	84.6%
150 to 199 MME (n=21)	166.0	21.7	86.9%
>= 200 MME (n=64)	325.7	45.2	86.1%

Amanda Zimmerman, Rami Bikdash, Richard Rauck, Conversion of Schedule II Opioids to Buprenorphine Buccal Film: A Retrospective … *Medicine*, Volume 22, Issue 5, May 2021, Pages 1109–1115, https://doi.org/10.1093/pm/pnaa226

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Results: Proportion of patients successfully converted to BBF

- Of the 157 patients reviewed, 138 patients (87.9%) were successfully converted to BBF
  - 19 patients were not successfully converted
    - Adverse event (n=9)
    - Lack of efficacy (n=5)
    - Cost (n=2)
    - Patient choice (n=2)
    - Instructed to discontinue by another provider (n=1)
- Common Adverse reactions:
  - Difficulty concentrating
  - Dizziness
  - drowsiness
  - Headaches
  - Nausea
  - Palpitations
  - tremors

Amanda Zimmerman, Rami Bikdash, Ri… Schedule II Opioids to Buprenorphine Bu… e Analysis, *Pain Medicine*, Volume 22, Issue 5, …09–1115, https://doi.org/10.1093/pm/pnaa226

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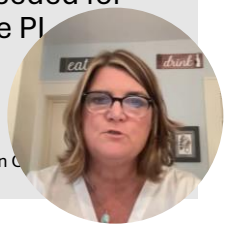
Consensus panel recommendations for transition from full mu agonist to Buprenorphine

- For patients taking <= 90 MME
  - Discontinue after last nighttime dose
  - Consider initiating an adrenergic alpha-2 agonist (e.g clonidine, lofexidine) or an immediate-release opioid (e.g. current opioid) to reduce the risk of withdrawal
  - Initiate Buprenorphine the following morning per the prescribing information, as either 10 mcg/h TD (transdermal) bup or 150 mcg BBF bid. Titrate as needed for pain per recommendations in the PI (package insert)



Webster L, Gudin J, Raffa RB, Kuchera J, Rauck R, Fudin J, Adler J, Mallick-Searle T. Understanding Buprenorphine for Use in C… Expert Opinion. Pain Med. 2020 Apr 1;21(4):714-723. doi: 10.1093/pm/pnz356. PMID: 31917418; PMCID: PMC7139205.

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- In patients transitioning from >90 MME
  - Discontinue after the last nighttime dose
  - Consider initiating and adrenergic alpha-2 agonist (e.g. clonidine, lofexidine) or an IR (immediate release) opioid (e.g. current opioid) to reduce the risk of withdrawal
  - Initiate buprenorphine the following morning as either TD bup 20 mcg/h or 300 mcg bid BBF and follow the recommendations in the PI for upward titration as needed
    - Note: 20 mcg /h is the highest dose of TD bup available in the US. If these doses are ineffective, consider higher doses of the BBF on the basis of risk/benefit analysis

* Short acting opioids have been suggested to prevent withdraw during the switch to buprenorphine

Webster L, Gudin J, Raffa RB, Kuchera J, Rauck R, Fudin J, Adler J, Mallick-Searle T. Understanding Buprenorphine for Use in Chronic Pain: Expert Opinion. Pain Med. 2020 Apr 1;21(4):714-723. doi: 10.1093/pm/pnz356. PMID: 31917418; PMCID: PMC7139205.

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JAMA Literature review

- Objective:
  - To synthesize the evidence on rotation to buprenorphine from full mu receptor agonists among individuals with chronic pain who were receiving LTOT (long term opioid therapy), including the outcomes of precipitated withdrawal, pain intensity, pain interference, treatment success, adverse events, or adverse effects, mental health condition, and health care use.
- 22 studies analyzed
  - 5 RCT (randomized controlled trials)
  - 7 case-control or cohort studies
  - 10 uncontrolled pre-post studies
- Most protocols adapted from OUD (opioid use disorder) models and used SL (sublingual) or buccal buprenorphine preparations

Powell VD, Rosenberg JM, Yaganti A, et al. Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review. *JAMA Netw Open*. 2021;4(9):e2124152. doi:10.1001/jamanetworkopen.2021.24152

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Table 1. Studies of Buprenorphine Rotation in Patients with Chronic Pain on Long-term Opioid Therapy

Source	Setting and select inclusion criteria	Design	Buprenorphine formulation	Sample size, including control participants (if any)	Outcomes						
					Pain intensity or severity	Pain interference	Precipitated opioid withdrawal	Treatment success	Adverse effects or adverse events	Mental health condition	ROB or quality assessment (instrument used)
Aurilio et al,[46] 2009	Outpatient; participants had chronic cancer pain with inadequate analgesia and intolerable opioid adverse effects; no SUD	Uncontrolled pre-post study	Transdermal patch	32	Yes	NA	NA	NA	Yes	NA	Inherently high ROB attributed to study design
Baron et al,[39] 2006	Inpatient setting for detoxification and/or buprenorphine initiation and then outpatient follow-up; participants had inadequate analgesia from current opioid regimen; no concern for overuse, abuse, or addiction	Cohort study	Sublingual without naloxone hydrochloride dihydrate	23	Yes	NA	NA	NA	NA	NA	6 of 9 (NOS)[a]
Berland et al,[47] 2013	Two-center inpatient or outpatient setting for buprenorphine initiation and then outpatient follow-up; participants had worsening pain and function despite increasing long-term opioid doses; 18 participants (24%) had "concern for addiction"	Uncontrolled pre-post study	Combination of formulations	76	Yes	Yes	Yes	Yes	Yes	NA	Inherently high ROB attributed to study design
Blondell et al,[35] 2010	Inpatient setting for buprenorphine initiation and stabilization and then outpatient follow-up; participants had chronic, nonmalignant pain and met *DSM-IV* criteria of opioid dependence to prescribed opioids	RCT	Sublingual tab or film with naloxone	12	Yes	Yes	NA	Yes	NA	NA	High (Cochrane Collaboration tool)[b]
Daitch et al,[49] 2012	Single-center pain clinic; all participants had inadequately controlled or worsening chronic pain and receiving LTOT	Uncontrolled pre-post study	Sublingual tab or film with naloxone	104	Yes	NA	NA	NA	Yes	NA	Inherently high ROB attributed to study design
Daitch et al,[50] 2014	Single-center pain clinic; all participants had high-dose opioids prescription (≥200 MME) for chronic pain	Uncontrolled pre-post study	Sublingual without naloxone	35	Yes	NA	Yes	NA	NA	NA	Inherently high ROB attributed to study design
Freye et al,[51] 2007	Mixed settings; all participants were prescribed >120 mg morphine sulfate/d with inadequate analgesia and/or severe adverse effects	Uncontrolled pre-post study	Transdermal patch	42	Yes	NA	NA	NA	Yes	Yes	Inherently high ROB attributed to study design
Malinoff et al,[52] 2005	Single-center pain clinic; all participants had worsening chronic pain despite escalating opioid doses; 8.4% of participants met *DSM-IV* criteria for opioid dependence diagnosis	Uncontrolled pre-post study	Sublingual tab or film with naloxone	95	Yes	NA	NA	Yes	Yes	NA	Inherently high ROB attributed to study design
Neumann et al,[37] 2020	Primary care–like outpatient; all participants had postsurgical chronic back pain and met *DSM-IV* criteria for opioid dependence to prescribed opioids	RCT	Sublingual tab or film with naloxone	19	Yes	Yes	NA	Yes	Yes	Yes	High (Cochrane Collaboration tool)[b]
Pade et al,[48] 2012	Specialty single-center clinic; participants were veterans who were referred to the clinic for combined chronic pain, high-risk opioid use (ie, high dose or combined with sedating medications), and/or co-occurring SUD	Uncontrolled pre-post study	Sublingual tab or film with naloxone	143	Yes	NA	NA	Yes	NA	NA	Inherently high ROB attributed to study design
Rosenblum et al,[34] 2012	Outpatient single-center pain clinic; participants with chronic pain were prescribed LTOT; all participants had aberrant opioid-related behavior but did not meet current *DSM-IV* criteria for any SUD diagnosis	Uncontrolled pre-post study	Sublingual tab or film with naloxone	12	Yes	Yes	Yes	Yes	Yes	NA	Inherently high ROB attributed to study design
Roux et al,[36] 2013	Inpatient research unit; all participants had chronic, nonmalignant pain and met *DSM-IV* criteria for opioid dependence diagnosis but were not seeking treatment	RCT	Sublingual tab or film with naloxone	51	Yes	NA	Yes	Yes	Yes	NA	High (Cochrane Collaboration tool)[b]

Powell VD, Rosenberg JM, Yaganti A, et al. Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review. *JAMA Netw Open*. 2021;4(9):e2124152. doi:10.1001/jamanetworkopen.2021.24152

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Table 1. Studies of Buprenorphine Rotation in Patients with Chronic Pain on Long-term Opioid Therapy (continued)

Source	Setting and select inclusion criteria	Design	Buprenorphine formulation	Sample size, including control participants (if any)	Outcomes						
					Pain intensity or severity	Pain interference	Precipitated opioid withdrawal	Treatment success	Adverse effects or adverse events	Mental health condition	ROB or quality assessment (instrument used)
Streltzer et al,[55] 2015	Outpatient single-center psychiatrist-run pain clinic; participants were using LTOT and referred by primary care for difficult-to-control chronic pain; all participants met *DSM-IV* criteria for opioid dependence diagnosis but frequently took opioids as prescribed	Uncontrolled pre-post study	Sublingual tab or film with naloxone	43	NA	NA	NA	Yes	NA	NA	Inherently high ROB attributed to study design
Sturgeon et al,[40] 2020	Outpatient single-center specialty opioid refill clinic for individuals with chronic pain who were prescribed a high dose of LTOT; all participants were initially offered tapering and were rotated to buprenorphine if they were not able to tolerate tapering to ≤90 MME or demonstrated aberrant opioid-related behavior	Cohort study	Sublingual without naloxone	240	Yes	NA	NA	Yes	NA	NA	6 of 9 (NOS)[a]
Tang et al,[53] 2020	Single-center inpatient setting in which individuals were initiated on buprenorphine while hospitalized and followed up as outpatients; all participants had either OUD or chronic pain–related opioid dependence	Uncontrolled pre-post study	Combination of formulations	23	NA	NA	Yes	Yes	NA	NA	Inherently high ROB attributed to study design
Webster et al,[27] 2016	Inpatient research unit; participants had chronic pain and physical opioid dependence (developed withdrawal symptoms with naloxone challenge) but no active SUD	RCT	Buccal	39	Yes	NA	Yes	Yes	Yes	NA	High (Cochrane Collaboration tool)[b]
POATS articles[c]											
Griffin et al,[44] 2016	Secondary analysis of POATS; limited to participants with chronic pain who participated in extended, 12-wk buprenorphine treatment	Case-control study	Sublingual tab or film with naloxone	148	Yes	NA	NA	NA	NA	NA	7 of 9 (NOS)[a]
Nielsen et al,[41] 2014	Secondary analysis of POATS; limited to participants who used methadone, extended-release oxycodone, immediate-release oxycodone, or hydrocodone before buprenorphine rotation and who had both predosing and postdosing withdrawal scores available	Case-control study	Sublingual tab or film with naloxone	569	NA	NA	Yes	NA	NA	NA	9 of 9 (NOS)[a]
Weiss et al,[45] 2014	Secondary analysis of POATS; limited to participants who were randomized in the extended, 12-wk buprenorphine treatment phase; 38.3% reported current chronic pain	Case-control study	Sublingual tab or film with naloxone	360	NA	NA	NA	Yes	NA	NA	8 of 9 (NOS)[a]
Weiss et al,[38] 2011	Primary analysis of the multisite RCT; outpatient setting; all participants with self-identified dependence on prescription opioids (n = 274 [42%]) had current chronic pain	RCT	Sublingual tab or film with naloxone	653	NA	NA	NA	Yes	Yes	NA	Some concerns (Cochrane Collaboration tool)[b]
Worley et al,[43] 2017	Secondary analysis of POATS; limited to participants with chronic pain who participated in the extended, 12-wk buprenorphine treatment phase and who completed at least 1 outcome assessment during the taper phase	Case-control study	Sublingual tab or film with naloxone	125	Yes	NA	NA	NA	NA	NA	9 of 9 (NOS)[a]
Worley et al,[42] 2015	Secondary analysis of POATS; limited to participants with chronic pain who participated in the extended, 12-wk buprenorphine treatment phase	Case-control study	Sublingual tab or film with naloxone	149	Yes	NA	NA	Yes	NA	NA	9

Abbreviations: *DSM-IV, Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition); LTOT, long-term opioid therapy; MME, oral morphine milligram equivalent; NA, not applicable; NOS, Newcastle-Ottawa Scale; OUD, opioid use disorder; POATS, Prescription Opioid Addiction Treatment Study; RCT, randomized clinical trial; ROB, risk of bias; SUD, substance use disorder.

[a] NOS case-control and cohort studies score range: 0-9, with higher scores indicating less ROB.

[b] Cochrane Collaboration tool assesses the ROB (range: low, unclear, or high) in 6 domains (sele performance, detection, attrition, reporting, and other). Overall ROB was scored from some c with more domains that are scored high risk indicating higher overall ROB.

[c] Primary analysis was based on Weiss et al[38]; other studies were secondary analyses that met th criteria.

Powell VD, Rosenberg JM, Yaganti A, et al. Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review. *JAMA Netw Open*. 2021;4(9):e2124152. doi:10.1001/jamanetworkopen.2021.24152

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> J Opioid Manag. 2023 Nov-Dec;19(6):543-554. doi: 10.5055/jom.0839.

Outpatient cross-titration to buprenorphine for chronic pain: A retrospective analysis

Satoru Ito [1], Mackenzie Welsh [1], Christina Bockman [1], Rebecca Dale [2], David Pilkington [3], Katherin Peperzak [2]

Affiliations + expand

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- **Objective:** To determine the efficacy and safety of the University of Washington's buprenorphine cross titration protocol for chronic pain in the outpatient setting
- **Methods:** Retrospective chart review on 150 patients
- **Results:** 15 of 31 patients successfully converted

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UWMC Protocol

Table 1. Buprenorphine product selection and target doses

MEDD	Product	Target dose
<60 mg	Buprenorphine/naloxone SL film/tablet*	2-4 mg/day
	Buprenorphine SL tablet	2-4 mg/day
	Buprenorphine TD patch†	Up to 20 mcg/hr
60-200 mg	Buprenorphine/naloxone SL film/tablet*	2-4 mg/day
	Buprenorphine SL tablet	2-4 mg/day
	Buprenorphine buccal film‡	Up to 900 mcg BID
200-400 mg	Buprenorphine/naloxone SL film/tablet*	4-6 mg/day
	Buprenorphine SL tablet	4-6 mg/day
>400 mg	Buprenorphine/naloxone SL film/tablet*	6-8 mg/day
	Buprenorphine SL tablet	6-8 mg/day

BID: twice daily; MEDD: morphine equivalent daily dose; SL: sublingual; TD: transdermal.
*Films may be more easily divided into 1/4 pieces compared to tablets and may be preferred for initial titration.
†Buprenorphine TD patch is not eligible for rapid titration due to weekly patch changes.
‡Buprenorphine buccal film is not to be used for MEDD >160 mg or rapid titration.

Table 2. Buprenorphine cross-titration schedule guide (continued)

(B) Cross-titration schedule

Timeline	Buprenorphine buccal film dose*	Full μ-opioid agonist
Week 1	Initial dose as above	Continue current regimen (option to trial reduction)
Week 2	Increase stepwise with next dosage form	Reduce regimen by 20-30 percent
Week 3	Increase stepwise with next dosage form	Reduce regimen by 20-30 percent
Week 4	Increase stepwise with next dosage form	Reduce regimen by 20-30 percent
Week 5	Increase stepwise with next dosage form	Discontinue

*Available buprenorphine buccal film strengths = 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg

Ito S, Welsh M, Bockman C, Dale R, Pilkington D, Peperzak K. Outpatient cross-titration to buprenorphine for chronic pain: A re… analysis. J Opioid Manag. 2023 Nov-Dec;19(6):543-554. doi: 10.5055/jom.0839. PMID: 38189196

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Discussion

- Many studies are **only transitioning for OUD**, not chronic pain.
- No information about patients who were **transitioned for OUD vs those who had chronic pain**
- Difficult to ascertain how many **chronic pain patients** are actually suffering from **OUD**
- There is no data to differentiate the effectiveness of **milligram vs microgram** dosing in the chronic pain population
- **No head to head data full mu agonist vs buprenorphine** preparations in the chronic pain population
- Some studies only used **milligram dosing** in the chronic pain population, and **not microgram dosing**
- **Variability in the TD dosing** with differences in availability in the US vs Eu
- **More studies** are needed to provide guidance to clinicians who want to u **buprenorphine to treat chronic pain**

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Clinical pearls

- Knowledge of mechanism of action
- Draw on your clinical experience
- Brainstorm with your colleagues
- Have patience
- Select the appropriate patients
- Don't be afraid to push the dose
- Use clonidine in high dose patients
- Continue BTP medication
- Educate, educate, educate (yourself and your patients)

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Key takeaways

- Reduce the long acting opioid to under 150 MED/day
- Leave/add the SAO (short acting opioid)
- Start at an adequate dose of buprenorphine
- Be available to your patient
- Empower your patient
- Create your own study to add to the data

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Thank you!

- Amanda Zimmerman, PA-C
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- Email me and I will help you ☺

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