The Pharmacy Access to Resources and Medication for Opioid Use Disorder (PhARM-OUD) Guideline

A Joint Consensus Practice Guideline from the National Association of Boards of Pharmacy and the National Community Pharmacists Association

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The PhARM-OUD Steering Committee is honored that the following organizations have indicated their support for this guideline:

American Pharmacists Association
American Association of Psychiatric Pharmacists
Vital Strategies
American Society of Addiction Medicine
American Society of Health Systems Pharmacists

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Introduction

Barriers to buprenorphine access

Buprenorphine is a partial opioid agonist indicated for the treatment of opioid use disorder (OUD) in individuals over the age of 16. Buprenorphine is the only agonist medication for opioid use disorder that can be dispensed directly to patients in community pharmacies in all 50 states pursuant to a prescription issued by any prescriber with a valid Drug Enforcement Administration (DEA) registration. Patients receiving treatment with buprenorphine are upwards of 60 percent less likely to die of an opioid overdose than those not in treatment.[1,2] Pharmacists play an important role in facilitating access to medication for opioid use disorder (MOUD) and can effectively reduce the risk of opioid overdose mortality in their communities by dispensing buprenorphine.

Still, around half of all pharmacies in the United States do not stock buprenorphine or are otherwise unwilling or unable to dispense buprenorphine products for the treatment of OUD.[3,4] Buprenorphine availability is limited for a variety of reasons, however, administrative barriers to supply remain persistent.[5] In the first years of the 21st Century, increases in prescription opioid-related morbidity and mortality created an imminent need to curtail inappropriate opioid prescribing and the available evidence suggests that these efforts were successful.[6] In 1999, there were 1.26 prescription opioid overdose deaths per 100,000 Americans. By 2017, prescription opioid related mortality increased to 5.05 deaths per 100,000 Americans. By 2022, this declined to 4.31 deaths per 100,000 Americans. Between 2017 and 2022, total opioid overdose deaths increased from 47,600 in 2017 to 81,806 in 2022. The bulk of the increase in total overdose deaths can be attributed to the introduction of fentanyl and its analogues to the U.S. drug supply. In 2010, 1 death per 100,000 residents was attributed to synthetic opioids, including fentanyl. By 2021, that number had risen to 21.8 deaths per 100,000 residents.[6,7]

Rising synthetic opioid related mortality has created a pressing need to make treatment accessible. Unfortunately, efforts taken to limit inappropriate opioid prescribing have inadvertently and adversely impacted access to buprenorphine. As a partial opioid agonist and DEA Schedule III controlled substance, buprenorphine is subject to federal and state limitations on opioid supply. In 2019, the SUPPORT Act reinforced and modified provisions of the Controlled Substances Act requiring all DEA registrants that distribute controlled substances to report suspicious orders to DEA. While DEA registered pharmaceutical distributors have always been required to report suspicious controlled substance orders, the SUPPORT Act required DEA to establish a centralized database for collecting suspicious order reports. The resultant Suspicious Order Reporting System (SORS) allows pharmaceutical distributors to report orders determined to be unusually large, deviating from a normal ordering pattern, or deviating from a normal ordering frequency.[8] Importantly, individual pharmaceutical distributors are tasked with defining the parameters that constitute a suspicious order from each pharmacy in their distribution network and reporting these orders directly to DEA through SORS. Of note, very little public guidance is provided on what defines a suspicious order.

The 2021 National Opioid Settlement Agreement added additional monitoring requirements for controlled substance orders that were reflected in a joint agreement between impacted pharmaceutical distributors and the states. Exhibit G of the final injunctive relief agreement, referred to in this document as the injunctive relief, establishes a standard for suspicious order reporting to prevent diversion and inappropriate prescribing of controlled substances. The document details procedures designed to identify pharmacies with abnormal ordering of highly diverted controlled substances, defined at the drug level, and high-risk formulations defined at the formulation level. In the context of the injunctive relief agreement, highly diverted controlled substances include oxycodone, hydrocodone, hydromorphone, tramadol, oxymorphone, morphine, methadone, carisoprodol, alprazolam, and fentanyl. High-risk formulations include, but are not limited to, 10 mg

hydrocodone, 8 mg hydromorphone, 2 mg alprazolam, and single-ingredient buprenorphine. The terms of the injunctive relief agreement state that high-risk formulations of highly diverted controlled substances may be added, removed, or revised based on the injunctive relief distributors' assessment and regulatory guidance.[9]

The injunctive relief agreement describes quantitative metrics to identify "red flags" that may indicate that a pharmacy is engaging in controlled substance diversion or is otherwise enabling misuse or diversion by dispensing controlled substance prescriptions with no evident medical indication. The "red flags" in the injunctive relief document are all defined at the pharmacy level and do not necessarily apply to individual prescriptions. These include the ratio of prescriptions issued to self-paying patients to all prescriptions dispensed and the ratio of out of area customers receiving controlled substances to those receiving non-controlled substance prescriptions. Distributors have agreed to develop unique thresholds for each pharmacy in their distribution network. If an order crosses a pharmacy's threshold, the distributor is compelled to discontinue shipment and report the order to DEA through SORS.

Note that red flags are defined as ratios: numbers with a numerator and a denominator. Crossing a red flag threshold is only likely if pharmacies engage in sustained patterns of dispensing highly diverted controlled substances or if their dispensing pattern changes significantly without cause relative to their total prescription volume. It is almost impossible for any dispensing pharmacist to predict whether their pharmacy will cross a threshold as the terms of injunctive relief do not allow distributors to discuss thresholds with pharmacies and few pharmacists have access to the historical dispensing and wholesale purchase data that would be required to estimate their thresholds.

It is important to note that neither the terms of injunctive relief terms nor the SUPPORT Act in any way bar pharmacies from ordering or dispensing high risk formulations of highly diverted controlled substances. The terms also make no explicit mention of buprenorphine/naloxone combination products. The current regulatory environment, fears of DEA enforcement, and the potential inconvenience associated with cancelled controlled substance orders are often cited barriers to buprenorphine dispensing in community pharmacies. This guidance seeks to advance community pharmacists' understanding of the balance between regulatory compliance and clinical need in an effort to encourage them to prioritize providing access to MOUD. It is important for pharmacists to provide care for persons with OUD in the same way that they would prioritize dispensing medication for the management of other chronic disease states. Even where increased scrutiny may be indicated, pharmacists should still put forth a good faith effort to provide care.

Policy intended to ease access to buprenorphine

More recent policy changes have focused on improving access to MOUD. In March 2020, DEA and the Department of Health and Human Services (HHS) exercised authority granted to them by the Ryan Haight Act to exempt DEA registered prescribers from the requirement to examine a patient in person before prescribing controlled substances. This temporary exemption allows prescribers to initiate buprenorphine and continue patients on treatment through a virtual health, or telehealth, encounter.[10,11] In December 2022, the Mainstreaming Addiction Treatment (MAT) Act and Medication Access and Training Expansion (MATE) Act were signed into law. The MAT Act allows any DEA registered practitioner with prescribing authority, including advanced practice registered nurses, pharmacists and physicians assistants, among others, to prescribe buprenorphine for the treatment of OUD. The MATE Act requires that all DEA registered prescribers complete a one time, eight-hour training on opioid use disorder treatment prior to renewing their DEA license. The MAT Act eliminates provisions of the Drug Abuse Treatment Act of 2000 that required prescribers to obtain an X-waiver from the DEA to prescribe buprenorphine.[12,13] Recognizing that the MAT Act would increase buprenorphine prescribing and increase demand for treatment, DEA released a letter to registrants in

March of 2024 asking distributors to reexamine quantitative thresholds for buprenorphine orders to ensure that pharmacies could purchase a sufficient quantity of buprenorphine to meet the needs of patients with OUD.[14,15]

Rationale for the creation of this guidance

As policy changes, pharmacies and pharmacists should expect to dispense more buprenorphine. The in-person visit exemptions, the elimination of the X-Waiver, and recent guidance on buprenorphine wholesale should all encourage pharmacists to make buprenorphine more accessible. Current practice guidelines for the clinical management of OUD do not provide guidance on important regulatory aspects of care that impact pharmacy practice. This guidance for pharmacists directly addresses these areas and more to help pharmacists make dispensing decisions that optimize the quality of care for individuals prescribed buprenorphine.

Controlled substance dispensing is difficult and requires that pharmacists make deliberate efforts to verify the legitimacy of prescriptions prior to dispensing. Fulfillment of the pharmacist's corresponding responsibility is critical to ensuring that controlled substances, including buprenorphine, are not used inappropriately or diverted.[16] Conversely, assuming that buprenorphine is being prescribed inappropriately and wrongly denying care for persons with OUD can have disastrous consequences for patients. Delaying the initiation of care or refusing care to an established patient dramatically increases a patient's risk of death due to opioid overdose.[17] This document seeks to help pharmacists balance the risks and benefits to themselves, their employer, and, most importantly, their patients that accompany each buprenorphine dispensing decision. The overarching recommendation of this document is that pharmacists should make a good faith effort to provide high quality care to persons with OUD by always maintaining an adequate supply of buprenorphine and filling legitimate prescriptions in a timely manner. If a pharmacist can verify that a buprenorphine prescription is legitimate and fulfill their corresponding responsibility, they should dispense. Doing so ensures that patients with OUD, a chronic medical condition, can receive the treatment that they need.

This document is not a clinical practice guideline. High quality, evidence based clinical practice guidelines are publicly available from the Substance Abuse and Mental Health Services Administration (SAMHSA, *TIP 63: Medications for OUD*) and the American Society of Addiction Medicine (*The ASAM National Practice Guideline for the Treatment of OUD).* While this document does provide clinical context for community pharmacists, pharmacists are encouraged to refer to guidance from ASAM and SAMHSA for more detailed clinical information. The intent of this guidance is to inform pharmacists' decision making at the point of care in community pharmacies, not to supplant evidence based clinical guidance from other sources.

Intended audience

This guidance is intended to be used by practicing pharmacists involved in the dispensing of medication for OUD in the community pharmacy setting. The contents may also be useful for educators and pharmacy preceptors involved in training pharmacy students or residents in colleges of pharmacy or affiliated experiential programs. Finally, the recommendations of this document should be used by pharmacies (i.e., independently owned pharmacies or pharmacy corporations with multiple locations under common ownership) to guide the development of patient-centered policy for persons with OUD in community pharmacies.

Interpreting the recommendations

At many points in this document, pharmacists are recommended to dispense medication for OUD if they are able to verify that a prescription is legitimate and fulfill their corresponding responsibility. Here, that corresponding responsibility is defined as the pharmacist's obligation to

resolve any concerns that the pharmacist knows about the validity of the prescription, exercising his or her independent professional judgment. To be effective, a prescription for a controlled medication must be issued for a legitimate medical purpose consistent with the usual course of a practitioner's professional practice; knowingly filling a purported prescription not so issued is subject to penalties.[18] If the pharmacist cannot verify, and document, that these criteria have been met, they have not fulfilled their corresponding responsibility. Pharmacists are, first and foremost, autonomous practitioners and should be encouraged to use their professional judgement in a way that most effectively addresses the health needs of their patients. In the rare case that a pharmacist feels that dispensing buprenorphine would not benefit their patient, would not be appropriate, or would otherwise cause harm, pharmacists should carefully document their decision and explain their rationale to the patient and prescriber as appropriate. In general, however, if, in their professional judgement, the prescription is legitimate and the patient is expected to benefit from treatment, pharmacists should dispense buprenorphine in a manner that is consistent with the recommendations of this guidance as long as, in their professional judgement, the prescription was issued for a legitimate medical purpose.

In many cases, to fulfill their corresponding responsibility, pharmacists will need to carefully interpret prescription or payment characteristics that have classically been associated with misuse or diversion of controlled substances, often called "red flags".[19] This term is inconsistently used to refer to a multitude of prescription characteristics and the intended interpretation varies with the context of use. Many pharmacists interpret "red flags" as indicators for prescription denial rather than a cue for further inquiry.[19,20] This document addresses several indicators directly including cash payment, travel distance to prescriber and pharmacy and early refills, and urges pharmacists to take a nuanced approach to fulfilling their corresponding responsibility in the presence of potential indicators of misuse and diversion. For this reason, the term "red flag" is not used in this document, the term "potential indicator of nontherapeutic dispensing" is used where stylistically necessary.

Finally, this guidance is a set of consensus best practice recommendations from a multidisciplinary panel of experts in addiction medicine, pharmacy practice, psychiatric pharmacy, and pharmacy regulatory affairs. Note that this guidance represents best practices for dispensing pharmacists in all community pharmacies. It is important to note that state and federal law, as well as state pharmacy rules, take precedence over these recommendations. Pharmacists, particularly in states where they may obtain their own DEA registration, can offer more proactive medication management services than are reflected by this guidance. Furthermore, this document is focused on the treatment of opioid use disorder with buprenorphine as buprenorphine is the only agonist medication for opioid use disorder that can be dispensed at community pharmacies in all fifty-states. Pharmacists have an emerging role in dispensing extended-release naltrexone and pending legislation may expand access to methadone in community pharmacies. Efforts to extend access to other modalities of OUD treatment should be applauded and are consistent with the overall recommendations of this guidance. The overall priority of this guidance, however, remains improving access to buprenorphine in community pharmacies. Pharmacists can also help prevent harm for all people who use drugs by promoting access to harm reduction supplies including naloxone, safe injection, and drug checking supplies as well as by referring patients with possible substance use disorder to screening and treatment providers in their communities. We describe harm reduction strategies for individuals receiving treatment with buprenorphine in this document but pharmacists are encouraged to review the materials linked below when developing new harm reduction programs in their own pharmacies:

Empathetic patient-pharmacist relationships

Much of the decision making in community pharmacies relies on the quality of the patient-pharmacist relationship. Effective pharmaceutical care depends on developing mutual trust between pharmacist and patient. As all community pharmacists know, building a trusting relationship takes time and requires building a level of rapport with patients that includes being able to consistently meet their care needs. When a pharmacy is not consistently able to fill prescriptions or when pharmacy staff do not treat patients with respect and dignity, patient relationships degrade. Pharmacists should commit to giving patients with opioid use disorder the same level of service and trust given to all of their patients. Patients initiating treatment or those searching for a new pharmacy after a gap in therapy may be experiencing symptoms of withdrawal including pain, nausea, and agitation. They may have also had their prescription denied at multiple other pharmacies. Most pharmacists enter the profession with the goal of helping people. Empathy is fundamental to our profession and patients with opioid use disorder deserve empathy. Developing a trusting relationship starts with that first encounter. Being able to meet a patient where they are at and provide care will build the rapport needed to retain the patient, ensure that their treatment needs are continuously met for the duration of their care, and set the stage for the development of lasting, mutually beneficially pharmacist-patient relationships.Fair and adequate reimbursement for clinical and dispensing services

Like most medical practices, behavioral health clinics, and inpatient treatment facilities, pharmacies are businesses that must operate at a sufficient margin to cover the costs of dispensing and providing cognitive clinical services to their patients. One of the most salient barriers to buprenorphine supply, and to all pharmacy practice, is reimbursement for goods and services delivered at the pharmacy. Pharmacists are highly capable and accessible practitioners. Patients receive services from pharmacies twice as often as they do from other sources of care.[21] The authors of this guidance recognize that reimbursement remains a central barrier to pharmacists' ability to provide care for the patients that rely on them. Pharmacists can work at the top of their license by providing supportive care services as state law allows, including vaccination, point-of-care testing, medication therapy management, and HIV prophylaxis to patients prescribed buprenorphine. Doing so not only allows pharmacists to maximize the financial viability of providing care to persons with OUD but sends a strong signal to policymakers and payers that pharmacists are a critical part of the care team and vital to the successful provision of treatment. While this is not an advocacy document, efforts to ensure that pharmacists are adequately compensated for dispensing and cognitive services would improve access to care for individuals with OUD and other chronic disease states.

Development of this guidance

This document was developed through a multi-stage process that involved practicing pharmacists, physicians, and experts from a variety of professional settings. In the first phase, investigators held focus groups with community pharmacists in Texas, California, and West Virginia to identify barriers to buprenorphine dispensing in community pharmacies. In the second phase, a panel of 22 experts was recruited to develop and refine recommendations to directly address barriers elicited through the preliminary focus groups.

The expert panel consisted of present and former members of State Boards of Pharmacy, individuals with expertise in drug enforcement and pharmaceutical wholesale as well as addiction medicine physicians, psychiatric pharmacists with expertise in substance use disorder treatment, and community pharmacists. These individuals participated in a four-round Delphi panel using a modified version of the RAND Appropriateness Method.[22] Prior to the first round of the Delphi panel,

participants were provided an evidence packet consisting of relevant clinical trials, observational studies, policy documents, and white papers to support the formation of their recommendations.

In the first round of the Delphi panel, panelists were first asked to evaluate a series of 16 vignettes describing barriers to buprenorphine access. Panelists then responded to a series of open-ended questions providing recommendations to address that barrier. Members of the steering committee then reviewed the panel's suggestions and aggregated similar recommendations. In the second round, panelists reviewed each statement developed in the first round and rated the appropriateness of that statement on a nine-point scale anchored from 1: "Not at All Appropriate" to 9: "Extremely Appropriate." In this context, an appropriate recommendation was defined as a recommendation that, if followed, would confer greater benefit than harm to patients and the surrounding community. Recommendations that at least 75 percent of responding participants rated as seven or higher on the nine-point scale were deemed to have reached consensus. In round three, statements that did not reach consensus were modified based on panelist feedback and subjected to another round of appropriateness rating. Finally, on March 8, 2024, panelists were provided the opportunity to participate in a live meeting to discuss, modify, and re-rate the remaining recommendations that had not yet reached consensus.

The final recommendations were organized into nine main recommendations and 35 supporting recommendations. Members of the steering committee then drafted detailed rationale, grounded in the available evidence, policy, and statute, to support the formation and implementation of each recommendation and supporting recommendation. Panelists and all members of the steering committee were provided with the opportunity to review and suggest edits to the rationale sections. The consensus statements were not modified at this phase as they had already been accepted by the panel. A public comment period was held between April 15, 2024 and May 31, 2024. Public comments were compiled, and the National Association of Boards of Pharmacy (NABP) hosted a review meeting with a secondary expert panel on June 11, 2024. The recommendations, supporting recommendations, and rationale were modified in response to feedback gathered during the public comment period. Of note, this document is the first in a planned series of statements emanating from the work of this expert panel. Future releases will include guidance to boards of pharmacy and a statement on pharmacist/prescriber communication and collaboration. All releases, including the current, will be reviewed and accepted by the NABP and the National Community Pharmacists Association (NCPA) prior to final publication. The protocol for the development of this guidance was registered with Open Science Framework in April of 2023.[23]

Executive summary

A summary of the panel's recommendations and supporting recommendations is below. Rationale supporting each recommendation is available within the document.

Recommendation 1 | Maintenance pharmacotherapy with buprenorphine

Pharmacists should maintain a sufficient supply of buprenorphine in their pharmacies and be willing to dispense buprenorphine to patients with OUD. Declining to dispense buprenorphine can lead to interruptions in OUD treatment, force patients into withdrawal, and increase risk of recurrent opioid use, and death.

Supporting recommendations

- Pharmacists should not decline to dispense buprenorphine solely due to the duration of maintenance treatment. OUD is a chronic medical condition and there is no recommended length of treatment. The duration of treatment depends on the treatment prescriber's clinical judgement and the patient's individual circumstances.
- Pharmacists should generally dispense buprenorphine in response to prescriptions issued by licensed prescribers with an active DEA registration assuming the following conditions are met:
    - The patient has no known contraindications to buprenorphine.
    - The pharmacist can verify that the prescriber is in good standing with their state licensing board and maintains an active DEA registration.
    - There is no compelling evidence of misuse or diversion.
- Declining to dispense buprenorphine is a measure of last resort and should only be considered after discussion with the patient and their prescriber when the pharmacist strongly suspects prescription forgery, prescription alteration by the patient, dangerous misuse, or diversion.
- Concerns about buprenorphine's regulatory status should not deter pharmacists from stocking and dispensing it.
- Pharmacists should dispense legitimate buprenorphine prescriptions issued by all DEA registered prescribers with prescriptive authority.

Recommendation 2 | Potential indicators of misuse or diversion and prescription drug monitoring programs

Pharmacists should use their state's prescription drug monitoring program (PDMP), where operational and available, to make informed buprenorphine dispensing decisions. The information in the PDMP profile should be used as a supplement, rather than as a substitute for clinical judgement when reviewing a buprenorphine prescription.

Supporting recommendations

- The presence of potential indicators of nontherapeutic dispensing on the prescription or in the PDMP profile does not always indicate that a pharmacist should decline to dispense buprenorphine. In the following scenarios, pharmacists should discuss their concerns with the prescriber and patient and document the discussion before determining whether they should dispense:
    a. If a patient is not filling their most recent prescription
    b. A patient has received or is receiving buprenorphine from multiple prescribers
    c. A patient's PDMP profile or the pharmacy's prescription database indicate multiple concurrent buprenorphine prescriptions

d. The patient presents with signs of CNS depression, hypotension, or other adverse effects that may be attributable to buprenorphine pharmacotherapy

- Pharmacists should dispense buprenorphine to patients initiating therapy with buprenorphine regardless of whether they have an established prescription drug monitoring program profile.
- Distance from either the patient's or prescriber's address to the pharmacy, particularly for patients receiving buprenorphine via telehealth, is not a reliable indicator of buprenorphine misuse or diversion.
- Pharmacies should immediately retire policies that prohibit employee pharmacists from filling buprenorphine prescriptions solely due to the pharmacy's distance from prescriber or patient home address.
- As buprenorphine access is diminished in areas of socioeconomic vulnerability, distance-based algorithms may disproportionately impact persons of color and low-income individuals who cannot access buprenorphine in their communities and perpetuate stigma toward persons in treatment.
- Pharmacists should dispense buprenorphine to cash-paying patients. Cash payment alone is unlikely to indicate buprenorphine misuse or diversion. Patients may pay cash due to a lack of insurance, the use of manufacturer rebates, or to maintain privacy in self-insured employer group plans.
- If a pharmacist declines to dispense buprenorphine to a new or existing patient, they should first discuss this with the prescriber and clearly document their rationale for refusing to fill.

Recommendation 3 | Early refills

Occasional requests to refill buprenorphine early are unlikely to indicate misuse of buprenorphine but may instead indicate that a patient has been asked to change their dose, lost or damaged a dosage unit, or is attempting to refill their medication in advance of a change in residence or insurance benefits. Before making a dispensing decision, pharmacists should discuss the context of the request with the patient, contact the prescriber, and document their rationale for dispensing or declining the prescription.

Supporting recommendations

- A pattern of early refill requests for a single patient or among patients under the care of the same prescriber is more indicative of potential misuse or diversion than a single request for an early refill. Pharmacists should still discuss their decision to decline the prescription with the prescriber and document the nature and content of this discussion prior to deciding to dispense or decline the prescription.
- Pharmacy chains and owners should provide guidance on early refills to staff pharmacists. Guidance should be tailored to patients receiving buprenorphine for the treatment of OUD rather than a general controlled substance refill policy. The early refill policy should be communicated to patients when they initiate buprenorphine pharmacotherapy. Pharmacists should be allowed to use their professional judgement to dispense buprenorphine earlier than allowed by employer policy.

Recommendation 4 | Telehealth

Pharmacists should dispense buprenorphine prescriptions issued by virtual health, or telehealth, prescribers if the prescription is legitimate, and the pharmacist can fulfill their corresponding responsibility.

Supporting recommendations

- Pharmacists are encouraged to evaluate telehealth prescriptions in the same manner and to the same standard that they would prescriptions originating from in-person encounters.

- Pharmacists have the right to inquire about the nature of the patient-prescriber relationship formed regardless of the place of service. If pharmacists are concerned about the quality of the patient-prescriber relationship, they should contact the prescriber rather than deny the prescription.
- Pharmacists should continue to dispense buprenorphine to telehealth patients even if they change prescribers.

Recommendation 5 | Buprenorphine monoproduct

Current clinical evidence supports the efficacy of buprenorphine monoproduct for the treatment of OUD.

Supporting recommendations

- Buprenorphine monoproduct may be preferred for pregnant patients, those with dental lesions, and those who cannot afford combination products. Use should not be limited to these populations.
- Pharmacists may discuss the indication for monoproduct with the prescriber but should not prefer buprenorphine/naloxone combination products to buprenorphine monoproduct.

Recommendations 6 | Optimizing the safety and effectiveness of buprenorphine pharmacotherapy

Pharmacists and pharmacy technicians should do the following to optimize the quality of care for persons prescribed buprenorphine:

- Pharmacists should counsel patients on buprenorphine's potential adverse effects and encourage patients to report adverse events if they emerge.
- Pharmacists should offer to dispense naloxone to patients prescribed buprenorphine for the management of OUD.
- As with any medication, pharmacists should educate patients about the dangers of certain drug combinations (particularly full opioid agonists, benzodiazepines, and sedative hypnotics) and the risks associated with alcohol use while taking buprenorphine.
- Pharmacists should provide counseling on the safe storage and disposal of buprenorphine products.
- Pharmacy technicians can provide valuable support to the process of care. Where not otherwise prohibited by state law, technicians can improve the efficiency of care by extracting information from prescription monitoring programs, contacting prescribers, reminding patients to refill their prescriptions, and assisting with reimbursement issues.

Recommendations 7 | Care coordination and prescriber communication

Pharmacists can meet the comprehensive care needs of their patients and prevent interruptions in pharmacotherapy for OUD by doing the following:

- Extending the same level of medication therapy management, immunization, and point-of-care testing services to patients with OUD as they do to other patients.
- Implementing collaborative practice agreements that could potentially enable pharmacists to monitor buprenorphine pharmacotherapy, provide supportive care, and potentially create opportunities to bill for cognitive services provided.
- Promoting adherence to treatment for OUD by being willing and able to refer patients in treatment to local primary care, mental health, and peer support providers upon patient request.

- If a pharmacist needs to clarify a buprenorphine prescription for whatever reason, they should make every effort to promptly contact the prescriber through direct communication via phone, email, or pager rather than fax while following state and federal privacy rules.
- If pharmacists cannot promptly reach a prescriber to renew or clarify a buprenorphine prescription, they should consider dispensing a partial quantity of the prescription to prevent interruptions in care.

Recommendation 8 | Stigma toward persons with OUD

Pharmacists, pharmacy technicians, and all pharmacy staff should approach persons living with OUD with empathy, compassion, and support, recognizing and addressing how their biases may impact their ability to provide care and make appropriate, patient-centered decisions.

Supporting recommendations

- Pharmacists should not require patients to transfer prescriptions for non-controlled substances to their pharmacy before dispensing buprenorphine.
- Pharmacists should not rely on a patient interview to attempt to identify patients who may misuse or divert buprenorphine.
- Pharmacists should model empathetic behavior and speech for other pharmacy staff when interacting with patients with opioid use disorder.

Recommendation 9 | Employer oversight

Pharmacy policies for buprenorphine dispensing should prioritize flexibility, allowing individual pharmacists to exercise their professional judgment when deciding whether to dispense a prescription for buprenorphine.

Supporting recommendations

- Pharmacy policies defined by numerical thresholds, such as distance to prescriber, distance to home, or days' supply, should not be used to guide clinical decision making. Numerical thresholds should not be used to deny buprenorphine prescriptions.
- Pharmacy corporations should prioritize appointing registered pharmacists to management positions responsible for establishing corporate controlled substance dispensing and purchasing policies

Recommendation 1 | Maintenance pharmacotherapy with buprenorphine

Pharmacists should maintain a sufficient supply of buprenorphine in their pharmacies and be willing to dispense buprenorphine to patients with OUD. Declining to dispense buprenorphine can lead to interruptions in OUD treatment, force patients into withdrawal, and increase risk of recurrent opioid use and death.

Supporting recommendations

- Pharmacists should not decline to dispense buprenorphine solely due to the duration of maintenance treatment. OUD is a chronic medical condition and there is no recommended length of treatment. The duration of treatment depends on the treatment prescriber's clinical judgement and the patient's individual circumstances.
- Pharmacists should generally dispense buprenorphine in response to prescriptions issued by licensed prescribers with an active DEA registration assuming the following conditions are met:
    - The patient has no known contraindications to buprenorphine.
    - The pharmacist can verify that the prescriber is in good standing with their state licensing board and maintains an active DEA registration.
    - There is no compelling evidence of misuse or diversion.
- Declining to dispense buprenorphine is a measure of last resort and should only be considered after discussion with the patient and their prescriber when the pharmacist strongly suspects prescription forgery, prescription alteration by the patient, dangerous misuse, or diversion.
- Concerns about buprenorphine's regulatory status should not deter pharmacists from stocking and dispensing it.
- Pharmacists should dispense legitimate buprenorphine prescriptions issued by all DEA registered prescribers with prescriptive authority.

Rationale

Long-term maintenance pharmacotherapy

Buprenorphine is widely accepted as safe and effective for the treatment of OUD and is the only agonist medication for OUD that can be dispensed directly to patients in community pharmacies in all 50 states. Prevailing practice guidelines from the ASAM and the Substance Abuse and SAMHSA recognize buprenorphine as a first-line treatment for OUD. Buprenorphine is indicated for the primary treatment of opioid use disorder in all adolescents and adults over the age of 16 and the available evidence supports the safety and efficacy of use across the lifespan.[1,24,25] Importantly, there is no maximum known safe duration of buprenorphine pharmacotherapy and no known minimum effective duration of treatment.[26,27] Patients progress through OUD treatment at varying rates and the duration of pharmacotherapy for any given patient cannot be known at the time of treatment initiation. Many patients will continue to benefit from treatment with MOUD for the rest of their lives. What is known is that risk of morbidity and mortality increase significantly for treatment episodes shorter than 180 days[28] and that treatment durations of 365 days or longer are associated with significant reductions in mortality. In a cohort of patients with OUD, those who remained in treatment for 91-180 days had a significantly higher risk of all-cause mortality (aHR: 2.94, 95 percent CI: 1.11-7.79) than those who remained in treatment for 365 days or longer.[29] Other observational research indicates that durations of 15 months or longer are associated with relative reductions in risk of overdose (173 percent), opioid related hospitalization (128 percent), and all cause inpatient admission (52 percent) compared to those in treatment for 6-9 months.[30] The available evidence supports long-term, continuous treatment with buprenorphine. Pharmacists can facilitate long-term treatment by being prepared and willing to dispense buprenorphine to patients with OUD.

Maintaining access to buprenorphine

Access to MOUD in community pharmacies is a major barrier to treatment persistence. A 2022 telephone audit of pharmacies in 5,734 pharmacies in 11 states found that only 48 percent of community pharmacies reported that they were willing and prepared to dispense a one-week supply of buprenorphine.[3] In a more recent telephone audit of 5,283 pharmacies, 57.9 percent of pharmacies reported buprenorphine availability.[31] Failure to maintain supply of buprenorphine is a significant barrier to continuity of pharmacotherapy for OUD. If established patients are forced to identify a new pharmacy due to lapses in inventory, their odds of a gap in medication possession of seven days or longer increase by 1.67 times.[32] Short disruptions in treatment like those that occur when a patient cannot fill their prescription on time dramatically increase risk of mortality. In the first two weeks after patients discontinue treatment for OUD, their immediate risk of mortality is eight times higher than it is while receiving treatment.[17]

In light of this evidence, it is critical that pharmacists maintain buprenorphine in their inventory and that they dispense buprenorphine upon receipt of a valid prescription from a DEA registered prescriber as long as the patient has no known medical contraindications to buprenorphine, the pharmacist can verify that the prescriber is in good standing with their state licensing board and the DEA, and that the prescription was issued for a legitimate medical purpose. OUD is a chronic disease, and abruptly disrupting pharmacotherapy for a patient with a chronic condition is insensible. Failing to dispense buprenorphine in a timely manner to patients with OUD could result in adverse clinical sequelae including overdose or death.[33]

Stable access is critical at all points in care. Patients ready to initiate treatment with buprenorphine, particularly those recently discharged from the inpatient or emergency setting following an opioid overdose, are often in active withdrawal and need treatment immediately.[34] Only 28.5 percent of patients who receive buprenorphine in the emergency department setting are able to successfully fill a subsequent buprenorphine prescription post-discharge.[33] A first prescription for any medication should be viewed as a critical transition of care. When a patient with no known history of pharmacotherapy for OUD presents to a community pharmacy with a new buprenorphine prescription, this is an opportunity for a pharmacist to provide, rather than deny, care. In most circumstances, pharmacists should favor dispensing buprenorphine to patients new to their pharmacy. If the pharmacist cannot dispense due to limited medication availability, they should make a good faith effort to help the patient identify a pharmacy that can dispense by searching the inventories of pharmacies under common ownership, where possible, or by making a warm handoff via telephone introduction to a pharmacy with buprenorphine in stock.

Buprenorphine formulations and inventory management

To prevent potentially lethal treatment interruptions, pharmacists should stock multiple buprenorphine formulations indicated for the treatment of OUD. In most pharmacies, this will involve stocking several doses of transmucosal buprenorphine/naloxone films and tablets as well as several formulations of buprenorphine without naloxone, also known as buprenorphine monoproduct. Sublingual buprenorphine/naloxone films indicated for the treatment of OUD are available in 2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, and 12 mg/3 mg formulations. Sublingual buprenorphine/naloxone tablets are available as 2 mg/0.5 mg and 8 mg/2mg formulations. Buprenorphine monoproduct, or buprenorphine formulated without naloxone, is available in 2 mg and 8 mg sublingual tablets. Importantly, buccal film (Belbuca) and transdermal (Butrans) formulations indicated for the treatment of chronic pain are also available.

Formulations indicated for the treatment of opioid use disorder may be prescribed off-label for the treatment of chronic pain. Buprenorphine is an excellent analgesic and the same partial agonist properties that reduce overdose risk for persons with opioid use disorder apply to the treatment of

chronic pain.[35] In March of 2024, the Department of Veterans Affairs (VA) published a national guidance document on the use of buprenorphine for the management of chronic pain. Within, the VA recommends buprenorphine for patients who have had limited progress toward functional goals or inadequate analgesic benefit from full opioid agonists and for those with high potential for adverse effects on full opioid agonist therapy. The VA guidance recommends that Food and Drug Administration (FDA) approved formulations for pain should be used for those taking opioid agonists at a daily dose of less than 50 mg morphine equivalents and suggests that all buprenorphine formulations, including those indicated for the treatment of OUD, should be considered in individuals prescribed more than 50 mg morphine equivalents.[36] The FDA recognizes that drug may be prescribed for unapproved uses when the prescriber deems their use medically appropriate.[37] All buprenorphine formulations may be medically appropriate for the management of pain.

Prescribers will also frequently prescribe fractional doses that require patients to divide films using a ruler and razor, a practice that has been shown to result in fractions with consistent dose distribution.[38] Inventory decision making will depend on local patient needs and prescriber preferences but pharmacists should carry more than one formulation to ensure that they can meet their patients' needs. Daily doses may range from anywhere between 1 mg to 32 mg or higher for patients with a history of synthetic opioid use.[39] While pharmacists are encouraged to keep multiple buprenorphine products in their inventory, they will likely encounter scenarios where they do not have the prescribed product in stock. To prevent delays, pharmacists should consider making therapeutic substitutions where possible. Sublingual buprenorphine/naloxone products may be used interchangeably, although bioavailability may differ between film and tablet preparations.[24] Pharmacists should generally contact prescribers before changing dosage forms but should not let limited availability lead to interruptions in care. Patients should be monitored after a therapeutic substitution for symptoms of over or under medication. Sedation, emergent cravings, or other new adverse events should be reported to the prescriber. To prevent future lapses in availability, pharmacists should strongly consider setting inventory par levels to ensure that buprenorphine stock is replenished as medication is dispensed.

Standards for enforcement of the Controlled Substances Act

Given the risks of morbidity and mortality associated with buprenorphine discontinuation, there are very few circumstances in which the potential benefits to the patient of refusing to dispense outweigh the risks of early discontinuation. Buprenorphine is classified as a DEA Schedule III controlled substance. While it is recognized that the regulatory status of buprenorphine may make it difficult to purchase and dispense buprenorphine, filling legitimate prescriptions is unlikely to result in adverse legal action against the pharmacy or regulatory inquiry from the DEA or other parties. The federal Controlled Substances Act authorizes pharmacists to dispense controlled substance prescriptions issued for a legitimate medical purpose. The treatment of opioid use disorder is a legitimate, and necessary, medical purpose. Furthermore, enforcement usually requires a sustained pattern of aberrant prescribing or dispensing behavior for DEA or other enforcement agencies to be able to demonstrate that pharmacists have violated the Controlled Substances Act.[20]

In July of 2022, in the *Ruan vs United States* decision, the Supreme Court found that controlled substance prescribing is authorized unless the prescribers have "knowingly or intentionally" acted in an unauthorized manner.[40] In brief, although DEA may continue to use investigative findings (e.g., a review of the pharmacy or prescriber's financial practices, disregard of indicators of nontherapeutic dispensing, or failure to assess medical necessity) to prove a prescriber or pharmacist's subjective intent, Ruan places the burden of proof on DEA to demonstrate that the prescriber or pharmacist knowingly or intentionally issued or dispensed a controlled substance

prescription written for an illegitimate medical purpose before the Controlled Substances Act can be enforced.[41] Assuming that the pharmacist fulfills their corresponding responsibility by verifying that a buprenorphine prescription was issued for a legitimate medical purpose, dispensing buprenorphine in the routine course of care for persons with OUD is highly unlikely to result in investigation, adverse action against the pharmacist's license, or liability to the pharmacy or pharmacist. An excellent lay summary of the implications of *Ruan vs United States* for practicing pharmacists may be found here:

- https://www.uspharmacist.com/article/dea-must-prove-knowing-and-intentional-violations-of-the-controlled-substances-act

The Mainstreaming Addiction Treatment Act

Prescribers no longer need an X-DEA registration to prescribe buprenorphine. The Mainstreaming Addiction Treatment (MAT) Act and the Medication Access and Training Expansion (MATE) Act were signed into law in December of 2022. The MAT Act allows all prescribers with an active DEA registration and Schedule III prescriptive authority to prescribe buprenorphine for the treatment of OUD. The MATE Act requires that all DEA registrants complete a one-time, eight-hour training on OUD treatment prior to renewing their DEA license. The provisions of the MAT and MATE Acts therefore eliminate the need for prescribers to complete requisite training and obtain a Drug Abuse Treatment Act of 2000 waiver, commonly known as an X-waiver, to dispense buprenorphine.[12] Pharmacists, therefore, should no longer expect an X-DEA number on buprenorphine prescriptions as the MAT Act eliminates the X-waiver. The passage of this legislation creates a clear need for community pharmacists to provide reliable access to medication for OUD.

Distributor thresholds and wholesale buprenorphine purchase

On March 8, 2024, the DEA issued a letter to registered pharmaceutical distributors encouraging them to review quantitative thresholds for buprenorphine to ensure that pharmacies can order a sufficient quantity to provide care for persons with opioid use disorder.[14] In this letter, DEA stated that the passage of the MAT Act was expected to result in a higher volume of buprenorphine prescriptions thus increasing demand for buprenorphine. This document provides a signal of DEA's support for accessible OUD treatment, a need that distributors are aware of.

Although purchase thresholds may periodically impact a pharmacy's ability to order buprenorphine, they should not be used as a reason to deny prescriptions. Crossing a buprenorphine threshold may not impact a pharmacy's ability to order other controlled substances. Distributors have the discretion to cancel individual order lines but may allow other controlled substances included in the same order to ship if a threshold is exceeded for one drug or drug family. If pharmacists feel that they cannot order enough buprenorphine to fill legitimate prescriptions, they should request a threshold change directly from their distributor. Since implementing the terms of injunctive relief, the nation's three largest distributors have all implemented a threshold review process to allow pharmacies that are unable to meet the legitimate medical needs of their patients to request a review and subsequent modification of their pharmacy's specific thresholds.[42–44] Threshold change request procedures vary with each distributor and pharmacists are encouraged to contact their distributor directly if a threshold change is needed to meet the medical needs of their patients. Under the injunctive relief, distributors are required to do extensive due diligence prior to changing a threshold including a review of patient and dispensing data and, in some cases, an on-site visit. The injunctive relief agreement prohibits distributors from telling pharmacies what their thresholds are. In no way should pharmacists assume that they will cross their threshold by dispensing a normal volume of buprenorphine. Crossing a distributor threshold may result in cancellation of a controlled substance order but it is unlikely to immediately result in immediate DEA investigation. Previous decisions against pharmacies, including the Gulf Med Pharmacy Decision and Order, involve a sustained, egregious pattern of nontherapeutic dispensing.[19] For these reasons, pharmacists should neither attempt to guess their distributor

thresholds nor should they assume that crossing a threshold will result in adverse legal consequences. They should, instead, focus on dispensing legitimate prescriptions for buprenorphine and should work closely with their distributors to modify thresholds that prevent them from providing care for patients with opioid use disorder.

Recommendation 2 | Interpreting prescription drug monitoring program data

Recommendation: Pharmacists should use their state's PDMP, where operational and available, to make informed buprenorphine dispensing decisions. The information in the PDMP profile should be used as a supplement, rather than as a substitute for clinical judgement when reviewing a buprenorphine prescription.

Supporting recommendations

- The presence of potential indicators of nontherapeutic dispensing on the prescription or in the PDMP profile does not always indicate that a pharmacist should decline to dispense buprenorphine. In the following scenarios, pharmacists should discuss their concerns with the prescriber and patient and document the discussion before determining whether they should dispense:
    a. A patient is not filling their most recent prescription.
    b. A patient has received or is receiving buprenorphine from multiple prescribers that are not members of the same practice or same practice group.
    c. A patient's PDMP profile or the pharmacy's prescription database indicate multiple concurrent buprenorphine prescriptions.
    d. The patient presents with signs of CNS depression, hypotension, or other adverse effects that may be attributable to buprenorphine pharmacotherapy.
- Pharmacists should dispense buprenorphine to patients initiating therapy with buprenorphine regardless of whether they have an established prescription drug monitoring program profile.
- Distance from either the patient's or prescriber's address to the pharmacy, particularly for patients receiving buprenorphine via telehealth, is not a reliable indicator of buprenorphine misuse or diversion.
- Pharmacies should immediately retire policies that prohibit employee pharmacists from filling buprenorphine prescriptions solely due to the pharmacy's distance from prescriber or patient home address.
- Distance-based algorithms may disproportionately impact persons of color and low-income individuals who cannot access buprenorphine in their communities and perpetuate stigma toward persons in treatment.
- Pharmacists should dispense buprenorphine to self-paid patients. Self-payment alone is unlikely to indicate buprenorphine misuse or diversion. Patients may pay cash due to a lack of insurance or to maintain privacy in self-insured employer group plans.
- If a pharmacist declines to dispense buprenorphine to a new or existing patient, they should first discuss this with the prescriber and clearly document their rationale for refusing to fill.

Rationale

Prescription drug monitoring programs

PDMPs are clinical decision support tools that allow clinicians to monitor all controlled substance prescriptions dispensed to a patient from all community pharmacies within a state. Several state PDMPs allow prescribers to see dispensing activity in other states that share the same operating interface. In the context of OUD treatment, it is important to note that federal law permits Opioid Treatment Programs (e.g., methadone clinics) to report dispensing from OTP-owned pharmacies to the state PDMP only with patient consent.[45] This almost always means that prescriptions dispensed in the OTP setting will not be visible in the PDMP. Furthermore, while all states require dispensers to report data to the PDMP, most states do not require emergency departments and inpatient facilities to report data to the PDMP.[46] Despite these limitations, PDMPs have been shown to effectively reduce

drug diversion[47] and lead to reductions in potentially inappropriate opioid prescribing.[48] In theory, PDMPs allow pharmacists and prescribers to identify patterns of controlled substance use indicative of misuse or diversion.[16] Potential indicators of nontherapeutic dispensing, commonly called "red flags," may include a pattern of early refills, the use of dangerous combinations of medication (e.g., hydrocodone, alprazolam, and carisoprodol), or the receipt of large quantities of high-risk controlled substances over a sustained period of time with no clear medical indication. The presence of red flags does not always indicate misuse or diversion. Patients who have seen multiple prescribers, for instance, may truly be in the care of multiple specialists. As discussed in the introduction to this document, inconsistencies in buprenorphine availability may cause patients to use multiple different pharmacies. SAMHSA offers an excellent overview of PDMPs for prescribers at the link below:

- https://store.samhsa.gov/sites/default/files/sma16-4997.pdf

Still, failing to address potential indicators of nontherapeutic dispensing may increase a pharmacy's risk of inspection by the DEA and state regulatory authorities potentially exposing the pharmacy to liability. Such indicators, however, are neither defined by statute nor guidance by the DEA but through a series of enforcement action levied against pharmacies over the past three decades.[20] The uncertainty surrounding enforcement and the lack of direct guidance from DEA may potentially lead to overly conservative clinical decision making at the point of care and cause pharmacists to decline to dispense legitimate prescriptions.[49,50]

In no circumstance should the presence of any single potential indicator of nontherapeutic dispensing immediately disqualify a patient from filling a prescription for medication for OUD. Rather, their presence should lead to a patient-centered discussion on the appropriateness of the course of therapy with both the patient and the prescriber. Both parties should be provided the opportunity to discuss the prescription with the pharmacist before a dispensing decision is made. If the pharmacist is able to determine that the patient is using the medication for a legitimate medical purpose and document their discussion with the prescriber and the patient in the patient's pharmacy profile, they have fulfilled their corresponding responsibility and should dispense.[16,41] If the prescriber and patient are unable to provide a satisfactory explanation for the pattern of controlled substance use that led to the discussion, the pharmacist should consider declining the prescription but should still carefully document their discussion with the prescriber and patient in the patient's profile. In all circumstances, the pharmacist should weigh the risks of declining to dispense (e.g., withdrawal, return to illicit opioid use, and overdose) against the benefits of declining. Every time a pharmacist declines to dispense buprenorphine, they are potentially placing the patient at risk of harmful, and potentially fatal, gaps in care.[17] The decision to decline should not be made lightly.

Buprenorphine diversion risk

Buprenorphine is occasionally misused or diverted, however, buprenorphine is rarely diverted for recreational use. First, buprenorphine diversion is rare. In 2022, buprenorphine represented only 5.07 percent of all narcotic analgesics seized by agencies that report to the National Forensic Laboratory Information System.[51] Over 90 percent of individuals who use diverted buprenorphine do so to prevent cravings and 29 percent use it to save money on treatment costs.[52] In one survey of individuals currently receiving treatment for opioid use disorder, only 3 percent reported that buprenorphine resulted in a better high than other prescription opioids while 63 percent indicated that they had previously used diverted buprenorphine.[53,54] As a partial opioid agonist, buprenorphine is not widely used recreationally because it does not offer the euphoria of other opioids. Buprenorphine has been consistently shown to reduce the risk of opioid overdose in all settings of care[55] and less than 5 percent of all opioid overdose deaths involve buprenorphine.[56,57] Buprenorphine diversion is, therefore, likely a means to facilitate self-medication rather than recreational use and is also unlikely to result in overdose or significant harm. This is neither an endorsement of buprenorphine diversion

nor an encouragement for community pharmacists to facilitate buprenorphine diversion. Rather, it is a clarification that buprenorphine diversion is often for very different reasons than the diversion of other opioid analgesics. It is also important to recognize that buprenorphine diversion would be largely prevented by addressing financial, clinical, and administrative barriers to treatment. While pharmacists are required to fulfill their corresponding responsibility when dispensing controlled substances, they should also recognize that denying buprenorphine prescriptions may force patients to rely on diverted medication to fill their treatment needs. Preventing buprenorphine diversion starts with filling buprenorphine prescriptions.

Dispensing to new patients

It is unreasonable to expect that all patients presenting with a prescription for buprenorphine will have a history of buprenorphine use. Furthermore, not all patients initiating treatment with buprenorphine will have a record in the state's PDMP. In one cohort of patients initiating treatment with buprenorphine identified from the Texas Prescription Monitoring Program dispensation database, less than half had a history of prescription opioid use at baseline.[58] The majority of patients entering treatment for OUD will not have an active opioid prescription at the time of treatment initiation. It is, therefore, unreasonable for pharmacists to expect that all patients have a PDMP profile when they start treatment. Conversely, observable recent prescription opioid use in the PDMP is likely an indication to initiate treatment, rather than a reason to deny. Denying a patient's initial prescription is inappropriate in almost all circumstances and will unnecessarily delay treatment initiation, leaving patients at risk of opioid related morbidity and mortality. Buprenorphine is indicated for the treatment of opioid use disorder which may involve use of both prescription and non-prescription opioids. For this reason, if pharmacists detect recent high-risk prescription opioid use (e.g., extended durations of treatment, high daily opioid dosages, concomitant use of opioids and benzodiazepines) in the PDMP profile, they should consider this a reason to fill buprenorphine rather than a reason to deny the prescription. Pharmacists should discuss continuing high-risk prescription opioid use with the prescriber and patient if it persists after treatment initiation.

Buprenorphine dosing and titration

It is normal for patients to increase their buprenorphine dose frequently early in treatment. Pharmacists should expect that patients initiating treatment with buprenorphine will rapidly increase their dose.[59] Current practice guidelines suggest that a target daily dose of 24 mg be reached early in treatment to prevent cravings and treatment discontinuation.[60] Patients with a history of fentanyl or higher baseline opioid tolerance may require more rapid titration or higher daily doses.[60,61] For this reason, ASAM and the Center for Substance Abuse Treatment (CSAT) both support the use of buprenorphine at daily doses of up to 32 mg for maintenance treatment of opioid use disorder.[39,60,62] Bridge to Treatment, an organization that assists health systems with the implementation of emergency department buprenorphine induction protocols, offers an evidence based protocol that involves rapidly titrating the dose to 32 mg on the first day of treatment prior to discharge from the emergency department.[63] Higher doses may be recommended as the evidence surrounding synthetic opioid use continues to evolve. High doses of buprenorphine and rapid titration are both supported by evidence and representative of an acceptable standard of care. It is worth noting that buprenorphine's package insert was developed and approved by FDA before the widespread, non-medical use of fentanyl.[24] It is now evident that daily doses above the labeled maximum dose of 24 mg are useful for the management of opioid use disorder. At the time of publication, there is insufficient evidence to support a maximum effective daily dose of buprenorphine. Instead, pharmacists are strongly recommended to rely on current consensus guidance from ASAM and CSAT to guide clinical decision making and to evaluate the appropriateness of each prescription on an individual basis.[26,39,60,62] Pharmacists should not decline to dispense buprenorphine due to the prescribed dose. Rather, patients prescribed a high dose of buprenorphine may benefit from enhanced clinical monitoring. If a

pharmacist observes that the patient is experiencing sedation or other adverse effects at any point in treatment or is concerned that buprenorphine may lead to drug-drug or drug-disease interactions, the pharmacist should contact the prescriber to discuss their concerns prior to dispensing.

Filling potentially outdated buprenorphine prescriptions

To ensure that patients in treatment remain adherent to their plan of care, it is critical that they fill their most recent prescription. Patients prescribed buprenorphine often visit their treatment prescriber at least monthly early in treatment. Visit frequency may decline for patients on long-term maintenance treatment. If a patient presents a new prescription that was not written recently, this may not be their most recent prescription. The pharmacist should contact the prescriber to clarify before dispensing. It is important to remember, however, that Schedule III controlled substance prescriptions are valid for six months after the written date and that patients are entitled to use the balance of a prescription before filling a new prescription. If a prescriber issues an identical prescription as a renewal of a previously approved prescription, the patient should be allowed to complete the older prescription before beginning the new prescription. Forcing patients to use a new prescription preemptively may lead to lapses in care coordination or require that the patient visit their prescriber to renew their prescription earlier than necessary. This could cause lapses in adherence.

Multiple prescriber episodes

Multiple concurrent buprenorphine prescriptions or prescriptions from multiple buprenorphine prescribers from different practice groups may indicate misuse or diversion. Patients prescribed buprenorphine may occasionally receive prescriptions from different prescribers in the same practice, however, due to the organizational structure of telehealth or community-based treatment programs. If the plan of care appears to be consistent, this is not a cause for concern. Because buprenorphine is not universally available in community pharmacies, patients may frequently change pharmacies to maintain access to treatment.[32] When multiple prescriber use or multiple pharmacy use is detected, pharmacists may fulfill their corresponding responsibility by contacting the treatment organization or patient to clarify the reason that the patient has changed prescribers and documenting their discussion.

Travel distance to prescriber

Patients with OUD often struggle to identify a local source of care. West Virginia Medicaid enrollees residing in metropolitan areas lived an average of 7.1 miles from their nearest buprenorphine prescriber.[64] Those in non-metropolitan areas lived an average of 14.5 miles from their nearest prescriber.[64] Distance to the nearest prescriber, however, is likely an under-estimate of distance to actual prescriber. In Pennsylvania, persons prescribed buprenorphine lived a median of 4.2 miles from their nearest potential prescriber but traveled 48.8 miles to their actual treatment prescriber.[65] Locating a buprenorphine prescriber is difficult, particularly in socioeconomically disadvantaged areas.[66,67] The MAT Act, signed into law in December 2022, enables all prescribers with an active DEA registration to prescribe buprenorphine for the treatment of OUD.[12] Whether this legislation will reduce travel burden, however, remains unknown.

The scarcity of buprenorphine prescribers means that patients may need to travel further to access treatment for OUD. Limited availability of buprenorphine in community pharmacies may also mean that patients have to range further from their homes to fill their prescription.[3] In either case, distance may be inappropriately interpreted as a potential indicator of nontherapeutic dispensing. Within the context of substance use disorder treatment, however, the evidence suggests that this is just as likely to indicate limited and inequitable access to care. It is also unreasonable to expect that patients using telehealth reside within a certain distance, or even within the same state, as their prescriber. Pharmacists should not rely on traditional distance-based decision rules to determine whether a buprenorphine prescription should be dispensed. Rather, pharmacists should discuss

concerns about travel distance with the patient and prescriber before deciding to decline to dispense buprenorphine. In any case, travel distance alone should not dictate whether a pharmacist decides to dispense. If a prescription is otherwise legitimate, the pharmacist can fulfill their corresponding responsibility, and the patient has no known contraindications to buprenorphine, the pharmacist should dispense regardless of how far the patient traveled to receive the prescription, how far they traveled to fill the prescription, or how far the prescriber is from their pharmacy. Accordingly, pharmacies should exclude buprenorphine from policies that include distance-based thresholds. There is simply no evidence to support a maximum distance from patient to prescriber or patient to pharmacy. These policies diminish access for patients with OUD and potentially more so for patients living in disadvantaged areas.

Self-payment

Patients prescribed buprenorphine may prefer to use cash payment, rather than insurance benefits, for a variety of reasons. In the 2019 National Survey on Drug Use and Health, 15.9 percent of all patients with OUD[68,69] and 20 percent of adolescent patients in need of treatment for OUD were uninsured.[70] If approximately one in five patients do not have insurance, it is unreasonable to expect that all patients prescribed buprenorphine use insurance at the pharmacy counter. Even for patients with insurance, insurance coverage of substance use disorder treatment services is not always adequate. Simply put, cash prices for buprenorphine may be lower than the patient's copay or co-insurance. Patients with OUD are regularly exposed to stigma from prescribers, employers, and even friends and family members.[71–73] Fear of stigma in the workplace is common among persons with OUD.[74–76] Patients in treatment may be concerned that their employer will terminate their employment should they use their employer sponsored health insurance to pay for substance use disorder treatment services or medication.[76–78]

Privacy concerns in the workplace are not unwarranted. First, insurance plans may provide aggregate, deidentified summaries of benefits utilization to employer sponsors. Employees of smaller companies may feel threatened by the sharing of sensitive information, even if deidentified. Additionally, the Coronavirus Aid, Relief, and Economic Security (CARES) Act of 2020 diminished the effectiveness of measures laid out in 42 CFR Part 2 intended to protect the privacy of persons receiving treatment for substance use disorder.[45,79] Although 42 CFR Part 2 requires that patients in treatment must approve of all information transmittal between Health Information Privacy and Portability Act (HIPPA) covered entities, a provision of the CARES Act (the Protecting Jessica Grubb's Legacy Act) permits an initial consent to apply to future disclosures.[79,80] This means that if patients consent to share their information once, future disclosures do not always require consent. Finally, if the Affordable Care Act were amended to remove protection for pre-existing conditions, a history of addiction treatment would likely disqualify individuals from receiving future coverage.[81]

Other patients may need to purchase buprenorphine out of pocket due to unexpected changes in therapy. In the first several weeks of treatment, a patient's daily buprenorphine dose is likely to change frequently as their prescriber attempts to find the dose that most effectively limits cravings without causing adverse effects.[59] If a patient fills their initial prescription using their employer sponsored prescription benefit for a seven-day supply and is then asked to titrate their dose upwards, they may deplete their supply earlier than expected leading to an early refill. This refill would not necessarily be eligible for reimbursement under the patient's prescription benefit. Efforts to amend the previous claim or to obtain authorization for an early refill may delay care. If patients are traveling an extended distance to the pharmacy, they may be unable to return the next day. This is an example of a circumstance when it may be perfectly rational for a patient to wish to pay for their prescription out of pocket. With these circumstances in mind, pharmacists should allow patients to purchase buprenorphine out of pocket particularly if no other potential indicators of nontherapeutic dispensing are present. As allowing an insured patient to purchase a controlled substance prescription out of

pocket may occasionally indicate nontherapeutic dispensing, the pharmacist should document their rationale for dispensing in the profile to provide evidence that they fulfilled their corresponding responsibility prior to releasing the prescription.

Avoiding delays or interruptions in care

Note that in each of these circumstances, pharmacists should contact the prescriber and patient before making a dispensing decision rather than denying the prescription outright. The pharmacist's priority in each case is to fulfill their corresponding responsibility while establishing the legitimacy of the prescription and the appropriateness of continuing or initiating treatment with buprenorphine. If the prescription is legitimate and the pharmacist can fulfill their corresponding responsibility, they should dispense. In each scenario, the pharmacist should weigh the risks of delaying treatment against the benefits of waiting for the prescriber to respond to the pharmacist's query. If the prescriber is not available to clarify, the pharmacist should dispense a partial fill, 1-3 day supply, as allowed by state law, to avoid potentially harmful disruptions in treatment.

Regardless of their decision, it is critical that pharmacists openly and transparently discuss the rationale for their decision with the patient. Dismissing the patient without explanation or telling the patient that the medication is not in stock without offering to order it is not ethical and diminishes trust. Patients with OUD should be treated with the same level of dignity or respect afforded to others living with non-substance related chronic diseases. Along these lines, patients should also have the opportunity to explain the presence of red flags and pharmacists should be receptive to their explanation. Stigma from health professionals, including pharmacists, often leads individuals to use diverted buprenorphine to sustain their recovery.[82,83] Addressing stigma in the pharmacy most fundamentally means fostering an environment of mutual trust and respect between pharmacy staff and patients.

Recommendation 3 | Early refills

Recommendation: Occasional requests to refill buprenorphine early are unlikely to indicate misuse of buprenorphine but may instead indicate that a patient has been asked to change their dose, lost or damaged a dosage unit, or is attempting to refill their medication in advance of a change in home address or insurance benefits. Before making a dispensing decision, pharmacists should discuss the context of the request with the patient, contact the prescriber, and document their rationale for dispensing or declining the prescription.

Supporting recommendations

- A pattern of early refill requests for a single patient or among patients under the care of the same prescriber is more indicative of potential misuse or diversion than a single request for an early refill. Pharmacists should still discuss their decision to decline the prescription with the prescriber and document the nature and content of this discussion prior to deciding whether to dispense or decline the prescription.
- Pharmacies should provide guidance on early buprenorphine refills to employee pharmacists. Guidance should be tailored to patients receiving buprenorphine for the treatment of OUD rather than a general controlled substance refill policy. The early refill policy should be communicated to patients when they initiate buprenorphine pharmacotherapy. Pharmacists should be allowed to use their professional judgement to dispense buprenorphine earlier than allowed by employer policy.

Rationale

When early refills may be needed

Short gaps in medication possession at any point in treatment have been shown to markedly increase risk of mortality.[17,29] Any number of reasonable scenarios may lead patients to request an early buprenorphine refill. Persons prescribed buprenorphine may need to refill their prescription early for the same reasons as individuals living with other chronic conditions. They may need to travel for work, leave town for a funeral, or take a vacation. Additionally, patients may be entering a residential treatment facility and need to bring their medication with them. Most pharmacists would allow an early refill, where allowed by state law, of other medications in each of these circumstances. Patients living with substance use disorder deserve the same level of care. If a patient occasionally requests an early refill, the pharmacist should generally accommodate the patient. Concerns should be addressed through discussion with the prescriber and documentation. In most cases, however, occasional requests for an early refill are not a reason for concern.

It is worth noting that most insurers will not reimburse the pharmacy for refills dispensed before the supply of the previous prescription has ended. Many payers will authorize a “vacation override” if the patient is traveling. An early refill may even be authorized by the payer if the patient is entering a treatment facility. Early refill policies will vary by insurer. Regardless, payer approval or denial is not a substitute for clinical judgement. If the pharmacist believes that an early refill is needed to promote continuity of care and the patient can pay for their medication out of pocket, the pharmacist should dispense.

Considerations for early refills during induction and stabilization

Buprenorphine pharmacotherapy is subject to frequent dose modification. In the first few weeks of treatment, buprenorphine is rapidly titrated as the treatment prescriber and patient work to find the lowest effective dose that controls cravings and minimizes withdrawal symptoms.[59] Patients may rapidly titrate their daily dose to 24 mg or higher within the first week of treatment.[26,39,59,63] Steady state plasma concentrations are reached after approximately 7 days.[84,85] At a daily

buprenorphine dose of 16 mg, approximately 80-85 percent of Mu opioid receptors are bound.[86] Patients with a history of fentanyl use may benefit from higher doses. In a cohort of 6,499 patients initiating buprenorphine between 2016 and 2020, patients prescribed 16 mg of buprenorphine were found to have a greater risk of treatment discontinuation within 180 days of initiation (aHR: 1.20, 95 percent CI: 1.06-1.37) than those prescribed 24 mg daily.[61]

Prevailing guidelines recommend that patients are seen frequently early in the course of buprenorphine treatment to ensure that withdrawal symptoms are adequately managed and to modify the buprenorphine dose as needed.[26,59] For patients who are capable of assessing their own withdrawal symptoms or those with experience with buprenorphine, at-home induction may be considered.[26,59,87] In some cases, unobserved induction is performed by issuing the patient a prescription for an approximate one-week supply of buprenorphine (e.g., a quantity of 14, 8 mg/2mg buprenorphine/naloxone dosage units).[87] The duration and intensity of the initial prescription for unsupervised home induction may vary depending on the patient's expected treatment needs, prescriber preference, and the patient's treatment history.[88] In either case, it is difficult to predict buprenorphine needs early in treatment. It is conceivable, however, that patients may deplete their initial prescription earlier or later than expected causing the pharmacist to perceive their next refill as early or delayed, respectively. Refusing to dispense buprenorphine early in treatment significantly increases the patient's risks of withdrawal as described previously. Rather than refuse to dispense due to early or delayed refill requests, the pharmacist is strongly recommended to contact the treatment prescriber, explain their concerns about the patient's refill timing, and ask for clarification. They should document this discussion to fulfill their corresponding responsibility and make their dispensing decision accordingly.

Patient reports of damaged dosage units

Additionally, patients at any point in therapy[87] may need to cut transmucosal buprenorphine/naloxone films into sections.[38] While this is not recommended in the product labeling, prescribers may recommend cutting films to achieve the patient's needed dose efficiently. Despite the current labeling, Suboxone films may be safely cut with a ruler and a razor blade and doing so has been shown to yield sections with 97.7 percent dose stability relative to initial strength.[38] It is reasonable to observe, however, that this process may lead to error. A patient may incidentally damage a film while cutting, misplace the reserved half, or expose the reserved half to moisture damaging the film. In this case, the patient may need an early refill to avoid disruptions in treatment.

Considerations to prevent misuse and diversion

Pharmacists should, in these scenarios, be mindful of patients stockpiling buprenorphine or accumulating a surplus of medication through sustained early refill requests as this may be a sign of non-medical use or diversion.[89,90] Stockpiling, however, does not always indicate that the patient is diverting buprenorphine. Patients may stockpile buprenorphine to prevent treatment interruption and withdrawal if their pharmacy is unable to fill their prescription. Being able to refill prescriptions in a timely manner is likely to give patients the confidence needed to not stockpile medication. Pharmacists should consider allowing sporadic, early buprenorphine refills if the circumstances necessitating an early refill are reasonable, the prescriber is informed, and the pharmacist documents their decision and rationale for dispensing. If the patient continues to routinely request early refills, appears to be stockpiling buprenorphine, or frequently reports theft, loss, or damage of medication, the pharmacist should consider declining to fill the prescription early. Prior to making their dispensing decision, however, the pharmacist should discuss their observations of a sustained pattern of early refill requests with the prescriber and patient and document the discussion. In any case, refusal to fill should only be considered if the pharmacist has reason to believe that the patient's prescription was not issued for a legitimate medical purpose, the patient is not using buprenorphine as directed, or the

patient is diverting their medication. In each case, the pharmacist should cautiously weigh the risks and benefits of declining to dispense buprenorphine.

Pharmacy policy on early buprenorphine refills

From the above, it follows logically that corporate policies that prohibit pharmacists from using their clinical judgement to dispense buprenorphine early are unacceptable. Arbitrary restrictions on the timeliness of refills are far from patient-centered and likely contribute to harmful interruptions in buprenorphine pharmacotherapy. For this reason, it is strongly recommended that pharmacies modify their controlled substance refill policies to allow pharmacists to use their clinical judgement when determining if buprenorphine may be dispensed early as allowed by state law or state board of pharmacy rules. As long as a persistent pattern of early refill requests is not present, pharmacists should prioritize facilitating uninterrupted access to buprenorphine.

Recommendation 4 | Providing care to persons utilizing telehealth

Recommendation: Pharmacists should dispense buprenorphine prescriptions issued by virtual health, or telehealth, prescribers if the prescription is legitimate, and the pharmacist can fulfill their corresponding responsibility.

Supporting recommendations

- Pharmacists are encouraged to evaluate telehealth prescriptions in the same manner and to the same standard that they would prescriptions originating from in-person encounters.
- Pharmacists have the right to inquire about the nature of the patient-prescriber relationship formed regardless of the place of service. If pharmacists are concerned about the quality of the patient-prescriber relationship, they should contact the prescriber rather than deny the prescription.
- Pharmacists should continue to dispense buprenorphine to telehealth patients even if they change prescribers.

Rationale

Quality and cost effectiveness of telehealth services for people with OUD

In March of 2020, DEA and HHS exempted DEA registered prescribers from requiring an in-person visit prior to prescribing Schedule III-V controlled substances, thus allowing prescribers to initiate patients on buprenorphine products indicated for the treatment of OUD through an audio only or audio-visual telehealth encounter. After initiation, prescribers may continue to prescribe buprenorphine without an in-person encounter as allowed by state law. It is important to note that current telehealth flexibilities do not mandate a minimum visit frequency and that no in-person assessment is needed to provide care. There is also no evidence to support a minimum visit frequency or mandated in-person assessments. Though these flexibilities were initially temporary, DEA and HHS have repeatedly extended telehealth flexibilities. Under their current extension, telehealth flexibilities will not expire until Dec. 31, 2024.[11] [10]

Emerging evidence suggests that access to telehealth has led to improved treatment outcomes for persons with OUD. Among individuals with OUD, receipt of telehealth services has been shown to significantly reduce risk of overdose mortality (aOR, 0.67; 95 percent CI, 0.48-0.92).[91] Telehealth encounters are both more convenient and potentially less stigmatizing than in-person encounters for persons with OUD. Patients are 3.34 times more likely to complete a scheduled telehealth encounter compared to a scheduled in-person encounter.[92] As discussed in earlier sections, travel distance to care is a salient barrier to OUD treatment, particularly in rural and socioeconomically disadvantaged areas.[65,67] Telehealth effectively addresses distance to prescriber as a barrier to care.

The available evidence suggests that telehealth encounters are non-inferior to in-person visits. In a comparative analysis of patients treated by clinicians with low, moderate, and high use of telemedicine in their practice, there was no difference in the rate of MOUD initiation, days' supply of MOUD, or OUD related clinical events between patients treated within high and low telemedicine practices.[93] Furthermore, buprenorphine has been shown to improve patient satisfaction, accessibility, and treatment adherence.[94,95] Widespread implementation of substance use disorder telehealth programs is expected to avert upwards of 20,000 overdose deaths annually. Implementing telehealth programs as a part of a comprehensive approach to buprenorphine treatment is expected to contribute to a total gain of 517,045 quality adjusted life years and a total cost savings of over $621,000,000 in the U.S. annually, providing evidence of the cost effectiveness of telehealth interventions for OUD.[96]

The first three and a half years of buprenorphine treatment via telehealth have provided sufficient evidence to support the quality and cost effectiveness of treatment through this modality. Still, pharmacists report reluctance to dispense buprenorphine prescriptions issued by telehealth prescribers.[97] Pharmacists may feel that that they should not dispense buprenorphine to telehealth patients due to the distance from the pharmacy or patient to the telehealth prescriber, the perceived legitimacy of the prescription or prescriber/patient relationship, or distributor thresholds. None of these are absolute reasons to deny telehealth prescriptions. DEA has repeatedly extended their exemption of the in-person office visit requirement allowing for the continual issuance of buprenorphine prescriptions without an in-person encounter. It is highly unlikely that DEA expected patients to only use local telehealth prescribers as this would defeat the practicality of the in-person visit exemption and limit access. Most telehealth agencies will use secure, electronic prescribing systems to transmit prescriptions. The likelihood of prescription fraud is, therefore, extremely minimal.[98] There is also no reason to suspect that telehealth encounters are of inferior quality when compared to in-person visits. While additional evidence is still emerging, that which is available to date indicates that patients prescribed buprenorphine via telehealth experience similar outcomes to those who have received in-person care indicating that a high quality patient-prescriber relationship is formed. Finally, concerns that dispensing telehealth prescriptions may cause pharmacists to breach distributor thresholds on buprenorphine purchase should not deter pharmacists from filling legitimate telehealth prescriptions. As mentioned earlier in this document, DEA has encouraged distributors to modify distributor thresholds for buprenorphine and recognizes that MAT Act implementation will result in increased demand for buprenorphine.[14] If pharmacists do see an influx of buprenorphine patients from a single telehealth practice and are concerned that extending access may interfere with wholesale acquisition, they should work closely with their distributor to ensure that thresholds are amended to allow their pharmacy to continue purchasing buprenorphine.[99,100]

If pharmacists are concerned about the legitimacy, appropriateness, or veracity of a telehealth prescription, they should contact the prescriber and document their discussion to alleviate their concerns as they would for in-person encounters. When evaluating the legitimacy of a prescription, pharmacists are encouraged to rely on the definitions of legitimacy established by the DEA and their state board of pharmacy.[16] Rarely will a state have separate standards for medically necessary telehealth and in-person prescriptions issued by prescribers in good standing with DEA and their state licensing board. Pharmacists are encouraged to evaluate telehealth prescriptions in the same manner and to the same standard that they would prescriptions originating from in-person encounters. The evidence available suggests that buprenorphine treatment is likely to benefit patients with OUD regardless of the patient's source of care. Use of a telehealth prescriber is not a sufficient reason to be denied care if the prescription is otherwise legitimate.

Evaluating multiple prescriber use in telehealth patients

Patients who use telehealth may change prescribers occasionally due to the organizational structure or process of care in the telehealth practice. If the patient's plan of care remains unaltered or does not drastically change under a new prescriber, a prescriber change alone is not cause for concern. Once again, the risks of abruptly discontinuing treatment greatly outweigh the risks of dispensing. If a pharmacist is concerned due to a change in prescriber, they should contact the prescriber and ask them to verify the reason for the change in prescriber. The nature and outcome of the call should be documented in the patient profile before dispensing the prescription to fulfill their corresponding responsibility.

Recommendation 5 | Buprenorphine monoproduct

Recommendation: Current clinical evidence supports the safety and efficacy of buprenorphine monoproduct for the treatment of OUD.

Supporting recommendations

- Buprenorphine monoproduct may be preferred for pregnant patients, those with dental lesions, and those who cannot afford combination products. Use should not be limited to these populations.
- Pharmacists may discuss the rationale for monoproduct with the prescriber but should not prefer buprenorphine/naloxone combination products to buprenorphine monoproduct.

Rationale

Potential reasons for buprenorphine monoproduct

There are several potential reasons that buprenorphine monoproduct, or buprenorphine products formulated without naloxone, may be preferred for certain groups of patients. For pregnant and breastfeeding individuals with OUD, buprenorphine formulations without naloxone are preferred to combination products due to concerns about naloxone's potential to cross the placenta and cause harm to the developing fetus.[26] A recent systematic review, however, demonstrated that pregnant individuals undergoing treatment with buprenorphine/naloxone were no more likely to experience adverse maternal fetal outcomes than those treated with other forms of opioid agonist treatment.[101] Transmucosal buprenorphine/naloxone products are thought to increase patients' risk of dental caries and oropharyngeal adverse events.[102] It is important to note that the life-saving benefits of buprenorphine pharmacotherapy outweigh the risks to oropharyngeal health. Transdermal or long-acting injectable products may be considered in patients suffering from dental caries or other oropharyngeal adverse effects associated with the use of buprenorphine transmucosal products.[103] It is important to advise patients that good oral hygiene and regular dental examinations may reduce the risk of dental caries associated with buprenorphine pharmacotherapy. At higher doses, there is potential for systemic naloxone absorption. This is supported by the fact that naloxone is detectable on liquid chromatography and mass spectroscopy analyses of the urine of individuals taking buprenorphine.[104] Although rare, a small number of case reports exist of precipitated opioid withdrawal after administration of oral naloxone.[105–107] There is at least one case report of precipitated withdrawal in a patient treated with buprenorphine monoproduct presumably caused by transition to buprenorphine/naloxone.[107] Although precipitated withdrawal is highly unlikely, prescribers may transition patients on higher daily doses of buprenorphine to buprenorphine monoproduct to prevent potential adverse effects associated with high doses of oral naloxone. Potentially most relevant to pharmacists and patients, single ingredient buprenorphine is less expensive than buprenorphine/naloxone.[108] Some pharmacies only stock brand name formulations of transmucosal combination products due to Medicaid formulary management practices. In states where Medicaid will only reimburse for brand name buprenorphine/naloxone, locating generic transmucosal combination products may be difficult, leading to delays in care. Importantly, the above scenarios should be interpreted as examples of reasons where buprenorphine monoproduct may be preferred. Prescriptions for buprenorphine monoproduct issued for the treatment of opioid use disorder should generally not raise concern.

Safety and appropriateness of buprenorphine monoproduct

Buprenorphine monoproduct and naloxone containing formulations have comparable clinical safety profiles in patients with OUD in that there is no difference in the risk of mortality between patients treated with buprenorphine monoproduct and those treated with buprenorphine/naloxone.[109] Additionally, there is conflicting evidence regarding the ability of naloxone coformulation to prevent parenteral misuse.[110,111] Pharmacodynamic evaluations show no difference in buprenorphine

bioavailability if buprenorphine is administered with or without naloxone.[111] This is potentially because buprenorphine has up to 10-fold greater binding affinity for the Mu opioid receptor than naloxone which diminishes the ability of naloxone to act as an antagonist in the presence of buprenorphine.[112] Finally, patients with a history of buprenorphine insufflation reported no difference in preference for buprenorphine products formulated with or without naloxone in a blinded experiment.[111] Still, evidence based practice guidelines from ASAM recommend the use of buprenorphine/naloxone combination products for the first-line management of OUD.[59] If a patient cannot afford combination products, combination products are not available, or the patient is experiencing adverse effects related to combination therapy, transitioning to buprenorphine monoproduct is a reasonable clinical action. Pharmacists should work closely with prescribers and patients to ensure that the most appropriate buprenorphine product is used to support the patient's recovery. These discussions should be guided by the principle that the option that is available and affordable to the patient is preferrable to delays or disruptions in care.

Injunctive relief and buprenorphine monoproduct

Buprenorphine is a controlled substance and buprenorphine products formulated without naloxone are classified as a high-risk formulation in the injunctive relief agreement between distributors and the states.[9] Distributors are obliged to "analyze ordering of highly diverted controlled substances to identify customers with significant ordering of high-risk formulations." Notably, buprenorphine/naloxone combination products are not classified as high-risk formulations in the agreement. This classification does not mean that pharmacists should not dispense buprenorphine. Rather, pharmacists should recognize that distributors are likely to monitor buprenorphine orders for indicators of nontherapeutic dispensing. Sudden, aberrant changes in dispensing volume may lead to breech of thresholds and order cancellation. As described in the introduction to this document, pharmacists may request their distributors to modify their thresholds if thresholds interfere with their ability to meet the medical needs of their patients. Pharmacists should follow the threshold change request process outlined by their distributor.

Recommendation 6 | Optimizing the safety and effectiveness of buprenorphine pharmacotherapy

Recommendation: Pharmacists and pharmacy technicians should do the following to optimize the quality of care for persons prescribed buprenorphine:

- Pharmacists should counsel patients on buprenorphine's potential adverse effects and encourage patients to report adverse events if they emerge.
- Pharmacists should offer to dispense naloxone to patients prescribed buprenorphine for the management of OUD.
- As with any medication, pharmacists should educate patients about the dangers of certain drug combinations (particularly full opioid agonists, benzodiazepines, and sedative hypnotics) and the risks associated with alcohol use while taking buprenorphine.
- Pharmacists should provide counseling on the safe storage and disposal of buprenorphine products.
- Pharmacy technicians can provide valuable support to the process of care. Where not otherwise prohibited by state law, technicians can improve the efficiency of care by extracting information from prescription monitoring programs, contacting prescribers, reminding patients to refill their prescriptions, and assisting with reimbursement issues.

Rationale

Counseling and routine therapeutic monitoring

The Omnibus Budget Reconciliation Act of 1990 required that pharmacists provide counseling to Medicaid patients in all 50 states.[113] Shortly thereafter, all 50 states and the District of Columbia enacted policy requiring that pharmacists provide counseling to all patients, regardless of insurance status. Pharmacists should not, however, limit their counseling to the patient's initial encounter but should continue to monitor therapy for all patients, including those prescribed buprenorphine, by regularly assessing patient wellbeing and safety over the course of treatment. At the first encounter, pharmacists should counsel patients on the proper use of buprenorphine products. Many patients initiating treatment will have no experience with transmucosal medications. It is important to counsel patients to let their film or tablet dissolve slowly under their tongue or between their cheek and gum as swallowing the dose will likely reduce effectiveness and increase gastrointestinal irritation. Although the adverse event profile of buprenorphine resembles that of other opioids (constipation, sedation, nausea, etc.), some adverse events of buprenorphine therapy may not appear acutely. Dental caries, for instance, may take months to appear. Pharmacists should periodically monitor patients for emergent adverse events. If adverse events occur, the pharmacist should inform the prescriber as soon as possible and work with the patient and prescriber closely to modify the plan of care to avoid harm. A full explanation of the adverse events associated with buprenorphine may be found in the medication labeling.

- https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8a5edcf9-828c-4f97-b671-268ab13a8ecd.

Preventing dental caries and oropharyngeal lesions

Some patients prescribed transmucosal buprenorphine products may develop oral lesions or dental caies. The benefits of treatment exceed the risk to oral health. Oral lesions and tooth decay can be prevented with the implementation of simple oral hygiene practices. Pharmacists should counsel patients on preventive oral health practices when transmucosal buprenorphine is initiated. Patients should be reminded to swish with water after allowing their buprenorphine dose to dissolve completely and should brush their teeth an hour after taking their dose. Patients should also be

encouraged to receive preventive dental care with scale and polish cleaning every six months. Patients without a dentist should be referred to one at the time of treatment initiation. Pharmacists should refer patients to dental care if oral lesions or dental caries emerge. [24]

Access to naloxone and harm reduction supplies

Pharmacists should also counsel patients prescribed buprenorphine on steps to prevent overdose. The FDA recommends that all individuals in treatment for OUD be prescribed naloxone.[114] While filling a naloxone prescription should not be a prerequisite to receive buprenorphine, pharmacists should encourage patients to procure naloxone. Prescription only and over the counter naloxone preparations are effectively interchangeable. It should be noted that there are currently no known benefits to higher dose, 8 mg naloxone preparations compared to conventional 4 mg preparations.[115] Additionally, there is no clear advantage to the use of nalmefene over widely available and less costly 4 mg naloxone preparations.[116] High-dose naloxone and nalmefene may both increase the severity of precipitated withdrawal symptoms, including severe acute pain, and introduce other health risks.[115,116] Four mg naloxone preparations are preferred. Pharmacists should counsel patients and others in the home on how to identify an opioid overdose and appropriate use of naloxone. Pharmacists should be able to clearly describe how to differentiate overdose from intoxication to avoid inappropriate naloxone administration which may lead to unnecessary precipitated withdrawal. Pharmacists are encouraged to consult training materials and guidance available from SAMHSA if they are unclear on naloxone administration or use.[117]

In addition to naloxone, pharmacists should provide access to other harm reduction supplies as allowed by state and federal law. Pharmacists can be a point of access for safe injection and drug checking supplies for all patients, including those in treatment. It is a reality that a minority of patients will have recurrent non-medical opioid use, or relapse, at some point in therapy.[118] This is not a reason to discontinue treatment. As a competitive partial opioid agonist, buprenorphine prevents other opioids from exerting many of the positively reinforcing aspects of non-medical opioid use, including the feelings of euphoria that often motivate use.[119] Buprenorphine's affinity for the Mu opioid receptor also prevents other opioids from binding, reducing the risk of respiratory depression and adverse sequelae in the event of relapse.[120] Pharmacists should acknowledge the risk of relapse and commit to providing supplies for safe use regardless of treatment status. A request for clean needles or drug checking supplies, such as fentanyl or xylazine test strips, should not disqualify that patient from continuing treatment with buprenorphine but may indicate a pressing need for therapy modification. First, the requested supplies may not even be for the patient. In the event that the patient is purchasing supplies for themselves, this may be an indicator that they have ongoing cravings and are in need of a higher dose of buprenorphine or other supportive care.[59] This should lead to a patient-centered discussion with the patient and their care team to determine if dose escalation or another modification to the care plan is warranted. It is crucial to remember that severe cravings are a symptom of inadequate chronic disease state management. Pharmacists should carefully avoid the use of stigmatizing language when discussing recurrent opioid use with the patient and prescriber and should make every effort to continue providing access to buprenorphine to patients with a recent relapse. Discontinuing treatment after a relapse increases the risk of mortality.

Concomitant use of buprenorphine and CNS depressants

Overdoses involving buprenorphine are rarely due to the use of buprenorphine alone. In a series of 2,369 postmortem examinations of opioid overdose victims, buprenorphine was only involved in 55 (2.3 percent).[56] Of these, 51 involved another substance.[56] Like any other opioid, buprenorphine may interact synergistically with benzodiazepines, alcohol, other opioids, and other central nervous system (CNS) depressants. Patients should, therefore, be counseled to avoid using buprenorphine with non-prescribed CNS depressants, including alcohol. It should be noted that the supervised, neither medical use of benzodiazepines, sedative hypnotics, nor short courses of opioid

analgesics are contraindicated with buprenorphine.[121,122] Guidance from ASAM, SAMHSA, and FDA all agree that use of CNS depressants alone should not be a reason to withhold or discontinue treatment with buprenorphine.[26,59,121] Withholding treatment due to concomitant use of CNS depressants will not prevent patients from using illicit opioids, leaving them at a substantially increased risk of overdose. Rather, pharmacists should work closely with prescribers to ensure that patients are using CNS depressants as prescribed. Pharmacists should also educate patients on the risk of overdose associated with the continued use of CNS depressants and the potential risks associated with abrupt disruption of long-term benzodiazepine treatment. Patients who wish to stop taking benzodiazepines should only do so under medical supervision and should be referred back to their primary care or treatment provider.

Buprenorphine storage and disposal

Pharmacists should also discuss buprenorphine storage and disposal at the point of care. Approximately 56 percent of individuals who misuse prescription drugs obtain them from a friend or family member.[123] Improperly stored medications pose a significant risk to others in the home, including children and older adults. Poor storage may also increase the risk of theft and diversion. Pharmacists should, therefore, counsel all patients prescribed buprenorphine on safe medication storage and disposal. Buprenorphine should be stored in a secure, preferably locked, location out of reach of children or others susceptible to harm. Where available, pharmacists should provide a single use drug disposal system to patients prescribed buprenorphine. In 2022, the FDA announced the planned implementation of a Risk Evaluation and Mitigation Strategy (REMS) requiring pharmacists to provide a mail-back drug disposal system with each opioid medication dispensed.[124,125] A REMS program is a drug safety program that the FDA can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks. The REMS program is expected to be fully implemented in calendar year 2024 with financial support from opioid manufacturers. Until that time, it is highly recommended that pharmacists consider supplying a drug disposal system to patients or, when not available, advising on safe disposal. Several compliant disposal products exist and may be available through publicly funded state or federal programs.[126] In the absence of availability, pharmacists should recommend that patients deposit unused medication in a public medication takeback box (locations available here: https://safe.pharmacy/drug-disposal/) or return medications through an organized, local drug takeback event. If neither option is available, pharmacists may recommend removing buprenorphine products from their packaging, placing them in a sealable plastic bag, and mixing with unpalatable substances (coffee grounds, saw dust, or dirt) before disposing of them in the household trash.[127] Flushing unused medication, including buprenorphine, down the toilet is environmentally deleterious and should be avoided.

Involving pharmacy technicians in the care of persons with OUD

Pharmacists are well equipped to ensure that patients prescribed buprenorphine receive appropriate counseling and supportive care in the community setting. To ensure that pharmacists have ample time to counsel patients prescribed buprenorphine, it is highly recommended that pharmacists work closely with pharmacy technicians to ensure that they can focus on the cognitively demanding aspects of care delivery outlined above. Pharmacy technicians can play a key role in promoting adherence and safety for persons prescribed buprenorphine. At the most fundamental level, pharmacy technicians may improve efficiency of access by proactively working to address reimbursement issues, monitoring pharmacy inventory, and contacting prescribers for prescription renewals. In many states, pharmacy technicians may act as PDMP delegates and assist pharmacists in downloading the patient's PDMP profile for review.[46] Finally, pharmacy technicians are capable of communicating directly with patients to remind them to refill or retrieve prescriptions from the pharmacy. In addition to improving efficiency, involving pharmacy technicians in the process of team-

based care for persons with OUD fosters a cooperative culture of compassion in the pharmacy, thus limiting stigma toward persons in treatment.

Recommendation 7 | Care coordination and prescriber communication

Recommendation: Pharmacists can meet the comprehensive care needs of their patients and prevent interruptions in pharmacotherapy for OUD by doing the following:

- Pharmacists should extend the same level of medication therapy management, immunization, and point-of-care testing services to patients with OUD as they do to other patients.
- Implementing collaborative practice agreements could potentially enable pharmacists to monitor buprenorphine pharmacotherapy, provide supportive care, and potentially create opportunities to bill for cognitive services provided.
- Pharmacists can promote adherence to treatment for OUD by being willing and able to refer patients in treatment to local primary care, mental health, and peer support providers upon patient request.
- If a pharmacist needs to clarify a buprenorphine prescription for whatever reason, they should make every effort to promptly contact the prescriber through direct communication via phone, email, or pager rather than fax while following state and federal privacy rules.
- If pharmacists cannot promptly reach a prescriber to renew or clarify a buprenorphine prescription, they should consider dispensing a partial quantity of the prescription to prevent interruptions in care.

Rationale

Access to pharmacist delivered supportive care

Seamless transitions of care from prescriber to pharmacy and a focus on comprehensive care delivery are critical to ensure that patients prescribed buprenorphine receive high quality pharmaceutical care without unnecessary interruptions. In many pharmacies, this can start with vaccination. In a 2015 review of electronic medical records, 67.9 percent of individuals with OUD were found to lack immunity to Hepatitis B. Of those, 43.5 percent had no documentation of completing their primary Hepatitis B vaccine series.[128] In another cohort of 1,127 syringe exchange participants, only 57.1 percent reported having received an MMR vaccine, 45.9 percent Hepatitis A, 47.5 percent Hepatitis B, and 47.6 percent seasonal influenza.[129] Pharmacists are prolific vaccinators. As of 2024, more than 60 percent of influenza vaccines in the United States are administered in community pharmacies.[130] Given the relative accessibility of community pharmacies and the frequency with which patients prescribed buprenorphine visit community pharmacies, pharmacists should routinely assess vaccination status and offer to vaccinate patients with OUD. This would unquestionably benefit patients, particularly those without a routine source of primary care.[131]

In addition to vaccination, eligible individuals prescribed buprenorphine may be expected to benefit from Medication Therapy Management (MTM) services. In a cohort of 12,179 individuals prescribed buprenorphine and at least one other medication for a non-substance related chronic disease state, adherence to buprenorphine was associated with adherence to other maintenance medications.[132] Adherence to buprenorphine is also associated with both lower healthcare utilization and lower healthcare expenditures among individuals in treatment.[133,134] Pharmacy based interventions aimed at improving medication adherence are, therefore, highly likely to be beneficial for patients in treatment. In the United States, over 140,000 Medicare enrollees received treatment with buprenorphine in 2022.[135] While this represents a small fraction of the total number of Medicare enrollees with OUD, those with other conditions that qualify for MTM would be expected to benefit from MTM services delivered by the pharmacist. Part D drug plans currently cover MTM services for an annually-determined list of conditions, such as chronic heart failure, diabetes, end-stage renal disease, and hypertension. Note that substance use disorder alone is not a qualifying condition at this time. The complexity of buprenorphine pharmacotherapy, the prevalence of comorbidities in patients

with OUD, and the risks associated with non-adherence all support delivering MTM services to Medicare enrollees with OUD. Pharmacists interested in providing MTM services should consult resources provided by the Centers for Medicare & Medicaid Services as well as the individual patient's Part D drug plan.[136] More resources may be found here:

- https://www.cms.gov/medicare/coverage/prescription-drug-coverage-contracting/medication-therapy-management

Collaborative practice models

In most states, pharmacists may enter into collaborative practice agreements with physicians that enable them to supervise and potentially modify therapy, provide point-of-care testing, or order laboratory tests and prescribe therapy according to their results.[137] In some states, where pharmacists may obtain a DEA registration, collaborative practice agreements may also grant pharmacists the ability to prescribe medication for opioid use disorder treatment. Patients with OUD are expected to benefit from comprehensive medication management services in the same way as those without problematic substance use and should be offered these services as allowed by state law. ASAM supports the development of physician-pharmacist collaborative practice agreements that allow specially trained pharmacists to initiate, modify, or discontinue medications for the treatment of substance use disorder pursuant to a physician's diagnosis.[138] More uniquely, however, emerging collaborative pharmacy practice models tailored to patients prescribed buprenorphine promise significant improvements in convenience of care, medication adherence, cost effectiveness, and potentially health outcomes for patients with OUD.[88,139–141] Most recently, results of a clinical trial published in the *New England Journal of Medicine* demonstrated that patients prescribed buprenorphine for unobserved induction by pharmacists working under a physician protocol were significantly more likely to remain adherent to treatment one-month later compared to those receiving standard of care (89 pervent vs 5 percent).[88]

Other successful practice models involve leveraging frequent pharmacist contact to minimize the cost of care.[141] In a small, single-arm analysis of 12 patients enrolled in a health department based collaborative drug therapy management program, patients prescribed buprenorphine received follow-up care from an outpatient pharmacist. The physician consulted as needed and reviewed the pharmacist's care plan. Involvement of a community pharmacist was shown to result in a $22,000 cost savings and yield 100 percent treatment retention at six months.[141] In another example, community pharmacists entered into an Operational Care Agreement with buprenorphine prescribers. Under the agreement, patients visited the pharmacist monthly and as needed for medication reconciliation and to complete a clinical assessment. The physician was responsible for initiating buprenorphine, issuing maintenance prescriptions, and reviewing the care notes taken by the pharmacist. In this sample, 88 percent of patients were retained at six months.[140] In patient satisfaction screenings completed after the six-month follow-up, 86 percent of participants reported that treatment delivered under the pharmacist-physician collaborative care model was better than their past healthcare experiences.[140]

Evidence to support components of collaborative care models is emerging, however, that which is available suggests that involving the pharmacist in care can maximize convenience and promote long-term retention in treatment. Pharmacy professional organizations should continue to advocate for expansion of payment models that support pharmacists motivated to provide services to patients with OUD while simultaneously educating the pharmacy workforce on the implementation of best practices in this area. Accessible templates for collaborative practice agreements and guidance on billing and reimbursement are needed to promote the widespread dissemination of collaborative practice agreements for OUD treatment.

Practical steps to improve the efficiency and quality of buprenorphine pharmacotherapy

The widespread dissemination and adoption of pharmacist collaborative practice models may not occur in the immediate future. There are, however, several things that pharmacists can do to work more closely with local treatment prescribers to improve access to buprenorphine. First, patients prescribed buprenorphine may see their pharmacist more frequently, or at least as frequently, as their treatment prescriber. Pharmacists have a tremendous opportunity to be a resource for individuals prescribed buprenorphine. Outside of being a source of medication information, pharmacists can help refer patients to care in their immediate community. This may be more important for persons receiving treatment with telehealth. Pharmacists should consider inquiring as to whether their patients have a local primary care provider and be prepared to refer them to, or help them locate, accessible physical and mental health resources. Community pharmacists are uniquely well positioned to do this as they are often familiar with providers in their area, see patients from a multitude of prescribers, and are often afforded a unique perspective on an individual's care needs in their role as medication use expert.

Finally, pharmacists can directly improve the quality of care for persons with OUD by simply leveraging patient-centered communication approaches. Poor communication between prescribers and pharmacists is a salient barrier to buprenorphine access.[142] Community pharmacists are often distrustful of buprenorphine prescribers and tend to rely on communication through the patient as a way of reaching prescribers.[142] This places burden directly on the patient and is an inefficient and error prone approach to clinical communication. Pharmacists and prescribers alike should be willing to communicate directly to avoid unnecessary delays in care. Rather than delaying care by using inefficient forms of communication, refill requests and prescription modifications should be managed telephonically, via email, or through an e-prescribing platform as allowed by state and federal privacy rules. Delays in care due to the inability of a pharmacist to quickly reach a prescriber are unacceptable in the current era of communication and are a direct threat to continuity of pharmacotherapy for OUD. Prescribers may not always be able to respond to communication quickly due to their clinical commitments. Pharmacies are also often open at night and on the weekend when many clinical practices are closed. If a pharmacist cannot reach a prescriber quickly, it is strongly recommended that they consider dispensing a partial quantity of buprenorphine (1-3 days, as allowed by state law) to ensure that the patient does not run out of medication. This is especially important for patients without access to personal transportation as these individuals may be more burdened by returning to the pharmacy later in the day or the next day to pick up their prescription.

Recommendation 8 | Stigma toward persons with OUD

Recommendation: Pharmacists, pharmacy technicians, and all pharmacy staff should approach persons living with OUD with empathy, compassion, and support, recognizing and addressing how their biases may impact their ability to provide care and make appropriate, patient-centered decisions.

Supporting recommendations

- Pharmacists should not require patients to transfer prescriptions for non-controlled substances to their pharmacy before dispensing buprenorphine.
- Pharmacists should not rely on a patient interview to attempt to identify patients who may misuse or divert buprenorphine.
- Pharmacists should model empathetic behavior and speech for other pharmacy staff when interacting with patients with opioid use disorder.

Rationale

The Oath of a Pharmacist and stigma toward persons with OUD

The way that patients are treated at the point of care can determine whether persons with OUD continue treatment. The American Pharmacists Association *Oath of a Pharmacist* states: "*I will consider the welfare of humanity and relief of suffering my primary concerns. I will promote inclusion, embrace diversity, and advocate for justice to advance health equity."*[143] Declining to fill legitimate prescriptions for persons in treatment violates both of these points. Denying a legitimate prescription would violate this ethical premise and be directly damaging to persons with OUD. For very practical reasons, grounded in the roots of pharmacy practice, it is therefore recommended that pharmacists fully embrace their role as relievers of human suffering and promoters of health equity by dispensing medication for OUD whenever possible. Stigma experienced in the pharmacy is a significant barrier to treatment. Upwards of 34 percent of persons who resorted to the use of diverted buprenorphine report adverse interactions with pharmacy staff as a primary reason for leaving traditional care.[144] In all settings of care, regardless of corporate policy and pressure, pharmacists alone are responsible for determining how they treat the patients in their practice.

Requiring patient interviews

Pharmacists may feel obligated to interview patients with OUD prior to dispensing buprenorphine to ensure that they are using buprenorphine for a legitimate medical purpose. Throughout this document, pharmacists are recommended to communicate directly with patients to monitor therapy and clarify potential indicators of misuse and diversion. These discussions are grounded in fact and observed patterns of medication use. It is impossible to know if a patient will divert or misuse a medication before dispensing their first prescription. This is especially true for patients with little observable history of controlled substance use in the PDMP. Requiring a patient interview or refusing to fill buprenorphine for a patient with no known history of treatment, or a limited PDMP profile may constitute unlawful discrimination as defined by the Americans with Disabilities Act and Section 504 of the Rehabilitation Act. There is no evidence to support this practice or to guide the interpretation of a patient interview in this manner. Any interpretation is likely to be biased by the interviewing pharmacist's preconceived negative assumptions, otherwise known as stigmatic beliefs, toward the person wishing to fill the prescription. Furthermore, this practice is completely abnormal in other chronic disease states. There are very few scenarios in which a pharmacist would feel the need to interview a person with diabetes prior to dispensing insulin, and buprenorphine is no different. If the patient does have a history of controlled substance use or buprenorphine use in the PDMP, the pharmacist may feel the need to inquire why the patient is changing pharmacies to fulfill their corresponding responsibility. If pharmacists do feel the need to inquire about past use as reflected in the PDMP profile, they should be as transparent as possible about why they are asking and from where they obtained their information. Patients may be reasonably paranoid if confronted by a

pharmacist who seemingly has detailed, undisclosed information about their treatment history. Because so few pharmacies stock buprenorphine, pharmacists should generally trust patients who are changing pharmacies due to limited medication availability and agree to fill the prescription. Transparency and fairness in this initial discussion is crucial for the development of a lasting, beneficial, and open pharmacist-patient relationship.

Forced prescription transfer

Pharmacists may require persons filling buprenorphine to transfer other prescriptions to their pharmacy. This practice is burdensome, discriminatory, and unnecessary. It is burdensome in that patients may already have a routine source of care and not wish to disrupt their relationship with their current pharmacist. Alternatively, patients may be un- or under-insured and, thus, shop around for their medication at the lowest cost.[145] Finally, patients prescribed buprenorphine may not have other maintenance medications to transfer. This practice is discriminatory in that patients in low-income areas may have reduced access to buprenorphine in otherwise convenient pharmacies.[67] A patient may wish to maintain their usual, convenient source of care even if their routine pharmacy does not stock buprenorphine. While patients should not be forced to transfer their prescriptions, pharmacists can discuss the relative advantages of filling all prescriptions at the same pharmacy with patients and may offer to transfer prescriptions from another pharmacy for the patient's convenience. Pharmacists may remind patients that filling all medications in one pharmacy is not only convenient but potentially safer as it allows the pharmacist to identify dangerous or unnecessary combinations of medication. Where already available, pharmacists may offer delivery services, unit dose packaging, medication synchronization services, or adherence packaging to further incentivize patients to fill all of their medications in the same place. Approaching prescription transfer in a patient-centered way may help to engender trust while motivating patients to transfer prescriptions for non-controlled medications with their buprenorphine prescription.

Distributor thresholds are not a reason to force prescription transfer

Pharmacists often force patients prescribed buprenorphine to transfer non-controlled substance prescriptions to their pharmacy before dispensing buprenorphine. This is believed to offset thresholds that evaluate the ratio between controlled and non-controlled substances dispensed.[49,97,146] Injunctive relief prohibits distributors from disclosing threshold quantities or ratios directly to pharmacy customers.[9] As discussed earlier, pharmacists should not attempt to guess their thresholds nor should they have any reason to believe that forcing patients to fill a certain number of non-controlled substance prescriptions for every buprenorphine prescription dispensed will prevent them from crossing a threshold. If every patient who fills a buprenorphine prescription fills a certain number of non-controlled substance prescriptions, for example two non-controlled prescriptions for every controlled prescription, this consistent dispensing pattern may be viewed as suspicious. Forcing patients to transfer prescriptions is not a patient-centered decision. The patient, not the pharmacist, should dictate their source of care.[147] Pharmacists have an ethical obligation to preserve patient autonomy within reasonable limits.[143] The freedom to choose a pharmacy is the most fundamental choice that a pharmacist can provide a patient. New patients, regardless of what they are prescribed, represent an opportunity for pharmacy growth and for pharmacists to provide care.

Creating a welcoming pharmacy environment

It cannot be overstated that all patients, including those prescribed buprenorphine, deserve to be treated with dignity and respect by all staff in community pharmacies. Persons prescribed buprenorphine report that they more frequently feel stigmatized from pharmacists and pharmacy technicians than other care prescribers.[148] Pharmacists with more stigmatized views of people with OUD report lower comfort dispensing it and are less likely to make decisions that prioritize maintaining treatment access for vulnerable patients.[149] Stigma is a learned pattern of behavior developed through the transmission of ritualized practices from members within a group.[150]

Furthermore, power gradients, such as those formed between pharmacists and pharmacy technicians, may serve to perpetuate stigma in the pharmacy.[151,152] In brief, pharmacy technicians and other pharmacy personnel may begin to mirror the stigmatizing behavior of pharmacists toward other groups in an effort to avoid being the object of stigma themselves. Pharmacists have an ethical obligation to treat all patients equally.[143] Fulfilling this obligation entails creating a practice environment where patients are accepted regardless of their medical, demographic, or socioeconomic status. If pharmacists treat patients with OUD negatively, other pharmacy employees are likely to follow suit to preserve their status within the power hierarchy of the pharmacy. If pharmacists address persons with OUD with dignity, respect, and trust as they would any other patient, their staff are likely to do the same.

Fostering a caring environment for persons with substance use disorder is no different than the approach pharmacists use toward persons with other chronic disease states. Pharmacists should be cautious of the language they use when communicating with persons with substance use disorder. Avoiding using terms such as “addict” and “substance abuser” in favor of person-first terms such as “person with substance use disorder” has been shown to directly impact the perceptions of prescribers toward patients in their care.[153] The National Institute on Drug Abuse offers an excellent guide on preferred language when discussing substance use disorder here:

- https://nida.nih.gov/research-topics/addiction-science/words-matter-preferred-language-talking-about-addiction

Being able to promptly fill buprenorphine prescriptions, rather than ordering buprenorphine or making patients unnecessarily wait in the pharmacy, has also been shown to make persons with substance use disorder feel more accepted in the pharmacy environment.[148] Finally, pharmacies should consider providing their staff opportunities to participate in stigma reduction training. An institutional commitment to creating a welcoming pharmacy environment sends a strong signal to staff that the pharmacy is committed to providing equitable access to effective treatment.[154]

Recommendation 9 | Employer oversight

Recommendation: Pharmacy policies for buprenorphine dispensing should prioritize flexibility, allowing individual pharmacists to exercise their professional judgment when deciding whether to dispense a prescription for buprenorphine.

Supporting recommendations

- Pharmacy policies defined by numerical thresholds, such as distance to prescriber, distance to home or days' supply, should not be used to guide clinical decision making. Numerical thresholds should not be used to deny buprenorphine prescriptions.
- Pharmacy corporations should prioritize appointing registered pharmacists to management positions responsible for establishing corporate controlled substance dispensing and purchasing policies.

Rationale

Impact of corporate policy on patient care

Multidistrict opioid litigation has led to an accumulated $13 billion in financial damages to community pharmacies nationwide, a number that is expected to grow as cases continue to enter settlement.[155] Corporate pharmacy policy developed in response to recent opioid settlements has become a salient barrier to buprenorphine and controlled substance dispensing in community pharmacies.[49,97] As reviewed elsewhere in this document, there is almost no empirical evidence to support the development of algorithmic dispensing rules to prevent buprenorphine misuse or diversion.[20,49] Policies that limit pharmacists' ability to dispense a buprenorphine prescription due to the distance between the patient's home and their prescriber, the distance between the patient's home and the pharmacy, or the distance between prescriber and pharmacy are arbitrary and highly likely to lead to adverse and discriminatory decisions against rural and minoritized patients. Similarly, restrictions on the duration of a buprenorphine prescription may eliminate any potential adherence benefit that accompanies providing longer duration prescriptions.[26] As patients enter maintenance treatment, longer duration buprenorphine prescriptions (e.g., 30 vs 14 days) may be used to limit travel to pharmacy, thereby optimizing the convenience of care. Policy limiting pharmacists to dispensing a fixed duration of buprenorphine for ambulatory use would directly defy the prescriber's plan of care.

Effective employer guidance on buprenorphine dispensing

Any policy that does exist should be guiding rather than dictatory. It is reasonable for pharmacy organizations to set clear expectations and to provide standard operating procedures for pharmacists at the point of care. This may include guidance on reimbursement, guidance on the use of PDMPs, guidance on naloxone dispensing, and guidance on documentation to ensure that pharmacists fulfill their corresponding responsibility. Such guidance from the organization may play a role in limiting liability to the corporation and employee pharmacists. Pharmacy corporations may also be able to make care more accessible by signaling their support for buprenorphine dispensing. Any guidance on buprenorphine dispensing developed by pharmacy corporations should be grounded in valid, clinical evidence and should allow pharmacists to use their clinical judgement to make dispensing decisions that optimize the safety and effectiveness of care. The autonomy and the expertise of practicing pharmacists must be maintained. Corporate policy is blind to individual patient circumstance and must, therefore, not interfere with the pharmacists' ability to provide care.

Engaging pharmacists in corporate decision making

The creation of flexible, patient-centered corporate policy and clinically meaningful guidance for pharmacists would allow for pharmacy corporations to serve persons with OUD more effectively. Appointing pharmacists familiar with the responsible clinical management of pain and opioid use

disorder to lead these initiatives within pharmacy corporations would ensure applicability to employee pharmacists and potentially lead to the creation of more practical corporate initiatives.

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