

# Best Practices in the Use of Buprenorphine

## Final Expert Panel Report

Prepared for Community Care Behavioral Health Organization

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The Institute for Research, Education, and Training in Addictions (IRETA) is a 501(c)3 organization that works with national, state, and local partners to improve recognition, prevention, treatment, research and policy related to addiction and recovery.

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## INTRODUCTION

This report describes the project “Development of Best Practice Guidelines for the Use of Buprenorphine in Opiate Maintenance Treatment,” which was conducted by the Institute for Research, Education, and Training in Addictions (IRETA) on behalf of and with support from Community Care Behavioral Health Organization (COMMUNITY CARE). The intent of this project was to develop a set of clinical guidelines that provide guidance for clinicians and payers in their efforts to improve the quality of treatment services for consumers with opiate addiction.

## BACKGROUND

**Summary of Issue:** Buprenorphine was approved by the U.S. Food and Drug Administration in 2002 to treat opiate dependence in outpatient settings. Buprenorphine possesses key advantages over methadone; especially, it can be administered in a less restrictive setting. Under the physician waiver program established by the Drug Addiction Treatment Act (DATA 2000), physicians can obtain a waiver to prescribe buprenorphine in primary care and other office-based settings. However, prescription of buprenorphine in office-based settings has led to substantive concerns regarding lack of coordination with concurrent behavioral health treatments and risk of diversion.

Clinical practice guidelines do exist for the use of buprenorphine in opiate addiction; however, they have limitations. The *Treatment Improvement Protocol (TIP) 40* “Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction” (Center for Substance Abuse Treatment, 2004), is the most comprehensive set of existing guidelines, but many of the clinical issues noted below have emerged since its publication. The *Technical Assistance Publication (TAP) 30* “Buprenorphine: A Guide for Nurses” (Center for Substance Abuse Treatment, 2009) was drawn primarily from *TIP 40* and is substantially similar in content. *Management of Substance Use Disorders* (VA/DoD, 2009) addresses the evidence base for the use of buprenorphine, but in a larger context of the management of substance use disorders more generally. Finally, the *Vermont Buprenorphine Practice Guidelines* (Vermont Department of Health, Division of Alcohol and Drug Abuse Programs (VDH/ADAP) and the Office of Vermont Health Access (OVHA), 2010) was a relatively recent effort to develop recommendations for the use of buprenorphine within a single state system.

This project sought to overcome some of these limitations by creating updated guidelines for the use of buprenorphine in the treatment of opiate dependence. Clinical and research evidence that has emerged since the publication of *TIP 40* and *TAP 30* were examined. This project utilized a unique expert panel methodology, the RAND/UCLA Appropriateness Method (RAM) (RAND, 2001). This method shares some characteristics with consensus panel methods, but differs in that experts rate indicators

in isolation and there is no explicit goal of reaching consensus. See Methods section for a full description of the RAM.

***Development of Project:*** The first major milestone of this project was a kickoff conference entitled “Improving the Quality and Outcomes of Buprenorphine Treatment,” held January 6, 2011 at the Marriott Hotel and Conference Center, Pittsburgh, PA.

Between January and April 2011, a comprehensive literature review was conducted on current issues in the use of buprenorphine. Existing guidelines as well as the literature review were utilized to compile a set of proposed guidelines. Following the RAM, these proposed guidelines were sent to the expert panel, and the first round of ratings was completed in May 2011. These initial ratings were analyzed and the expert panel discussion was completed on July 19, 2011 via webinar. Directly following the discussion, the expert panel completed the second round of ratings. Based on these ratings, a final list of suggested guidelines was compiled, and key recommendations are included in this report.

## **METHODS**

***Kickoff Conference:*** The kickoff conference for this project, entitled “Improving the Quality and Outcomes of Buprenorphine Treatment” was held on January 6, 2011 at the Marriott Hotel and Conference Center in Pittsburgh, PA. There were over 60 attendees, including Single County Authorities and state drug and alcohol representatives from Pennsylvania, treatment providers from Pennsylvania, New York, West Virginia, and Vermont, managed care representatives, and academics. The agenda included presentations titled “A Clinical Model of Integrated Care,” “Quality Issues and Risk Management,” “Concurrent Medical and Psychiatric Conditions and Concerns,” and “Evaluation of Buprenorphine in the NIDA Clinical Trial Networks.” Attendees were from a variety of backgrounds, including psychiatry, nursing, addiction counseling, and social work. The conference highlighted clinical questions and current practices around buprenorphine, and also generated excitement about and commitment to the guideline development project. At this conference, previously identified experts in the field were formally invited to join the expert panel.

***RAND/UCLA Appropriateness Method:*** The RAM was developed as a method that would combine the best available scientific evidence with the collective judgment of experts to yield a statement regarding the appropriateness of a given clinical practice (RAND, 2001). Given the proliferation of buprenorphine use in clinical practice in the context of relatively limited empirical evidence about several aspects of treatment, the RAM was seen as ideal for the current project. The remainder of the Methods section describes the major steps in the RAM process as they were executed in the current project.

**Expert Panel:** Potential expert panel members were compiled in collaboration between COMMUNITY CARE, IRETA and other stakeholders. Potential expert panel members were invited to give presentations at the kickoff conference, where they were officially tapped to participate in the expert panel process. Expert panel members were offered an honorarium for their participation in the project. The individuals who participated in the expert panel are listed below in alphabetical order.

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***Literature Review and Development of Proposed Guidelines: A***

comprehensive review of the literature on current issues in the use of buprenorphine was conducted between January and April 2011. The review led to the production of a Background Paper. Based on the literature review, a proposed set of clinical guidelines was developed for rating by the expert panel. The development of proposed guidelines was accomplished through several steps. First, the current available guidelines were compiled and synthesized. Second, clinical areas in which recent research had eclipsed the current guidelines were collaboratively identified by IRETA and COMMUNITY CARE, such as buprenorphine treatment for pregnant women or dosing guidelines. In these areas, a literature review was conducted and integrated into the Background Paper and development of proposed guidelines.

The proposed set of guidelines was organized into subgroups according to phases of treatment. These subgroups of guidelines are listed here:

- Guideline 1: Conduct assessments to determine candidacy for buprenorphine treatment
- Guideline 2: Select candidates for buprenorphine treatment
- Guideline 3: Require and have patients sign a treatment contract
- Guideline 4: Administer appropriate dosing of buprenorphine
- Guideline 5: Provide or refer to concurrent psychosocial counseling
- Guideline 6: Monitor treatment adherence and effectiveness
- Guideline 7: Provide buprenorphine treatment of appropriate duration
- Guideline 8: Treat co-occurring mild-to-moderate depression and anxiety

***Round 1 Ratings:*** The Background Paper and proposed guidelines were provided to the expert panel, along with instructions on how to rate the items according to the method. Experts were asked to rate each indicator for validity. A proposed guideline was defined as valid if a) adequate scientific evidence or professional consensus exists to support a link between that practice and a health benefit to the patient with opiate dependence; b) a provider with high rates of adherence to that practice would be considered a higher quality provider; and c) a majority of factors that determine adherence to the practice are under the influence of the provider, or are subject to influence. Experts rated each guideline on a 9-point Likert-type scale, where a rating of 1 represented “definitely not valid,” 5 represented “uncertain or equivocal validity” and 9 represented “definitely valid.” Experts also were given the opportunity to provide

comments on each guideline with respect to possible changes to the guideline as well as potential barriers to implementation of the guideline. Experts were given the option to return rated guidelines either electronically or by postal mail.

After all rating forms were returned, the expert panel ratings were compiled and basic descriptive statistics were obtained for each indicator. Each indicator was then evaluated with respect to “appropriateness” and “agreement.” Indicators with a median rating of 7 or higher, and with no more than two ratings outside of the 7-9 range (i.e., agreement), were deemed “appropriate.” Indicators with a median rating of 3 or lower, and with no more than two ratings outside of the 1-3 range, were deemed “inappropriate.” The remaining indicators, those with median rating in the 4-6 range regardless of agreement, or with any other median rating, but without agreement, were labeled “uncertain.” Hence, guidelines where a certain level of disagreement existed within the panel about the appropriateness of the guideline, and guidelines where the panel indicated a neutral stance overall with regard to whether the given practice was appropriate, both fell into the “uncertain” category.

The comments made by the panel with respect to proposed changes to the guidelines and potential barriers to implementation were also reviewed carefully. For each indicator in the “uncertain” category following Round 1, the comments were analyzed for common themes, organized according to these themes, and presented to the expert panel members as part of the expert panel meeting.

**Expert Panel Meeting:** The expert panel meeting was held on July 19, 2011 via webinar. Several materials were prepared prior to the date of the meeting. The moderator of the expert panel (Bradley Stein, MD of COMMUNITY CARE) was provided with a copy of the proposed guidelines with a frequency distribution of expert ratings and representative comments for the items that fell in the “uncertain” category based on Round 1 ratings. Additionally, each expert was provided with an individualized copy of the proposed guidelines, including the group distribution of ratings overlaid with his or her individual ratings. Finally, a set of slides was prepared that reflected the moderator document, but that were organized by themes for discussion.

**Round 2 Ratings:** Directly following the expert panel meeting, experts were asked to re-rate the guidelines that were rated uncertain during the first round of ratings and discussed during the expert panel meeting, as well as any modified or additional guidelines added during the expert panel meeting.

**Development of Final Guidelines:** The final set of clinical guidelines for the use of buprenorphine in opiate dependence was comprised of the indicators that were rated appropriate, either during Round 1 or Round 2 of rating.

## RESULTS

***Kickoff Conference Outcomes:*** Satisfaction surveys were distributed following the conference and 42 individuals returned these surveys. Nearly all the respondents (95.2%) stated they were “satisfied” or “very satisfied” with the overall quality of the meeting, the quality of the information, and the quality of the materials. Notably, 95.2% of respondents strongly agreed or agreed with the statement “I would recommend this training to a colleague.”

### ***RAND/UCLA Appropriateness Method Outcomes:***

***Round 1 Ratings:*** Of the 89 indicators rated during Round 1, 50 indicators were deemed “appropriate” by the panel; that is, the median rating was in the 7-9 range and no more than two experts rated the indicator outside that range. The remaining 39 indicators fell into the “uncertain” category and were discussed during the expert panel meeting. Finally, none of the indicators was rated “inappropriate” by the expert panel during the first round of ratings.

The indicators rated “uncertain” were not evenly distributed among the subgroups of proposed guidelines. Certain subgroups of indicators exhibited greater levels of disagreement or uncertainty among the expert panel members. For example, 69% (11/16) of the indicators within the subgroup having to do with dosing were rated “uncertain” by the panel. Similarly, 63% (5/8) of the indicators on providing or referring patients to concurrent psychosocial counseling, 57% (4/7) of the indicators on duration of buprenorphine treatment, and 54% (7/13) of the indicators on selection of buprenorphine candidates fell into the uncertain category following the first round of ratings. These initial results foreshadowed the issues that would trigger the most involved and fruitful discussions during the expert panel meeting. In contrast, only 15% (2/13) of the indicators on the importance of a treatment contract were deemed uncertain by the panel, and 29% of the indicators on assessment and co-occurring disorders fell into this category.

***Round 2 Ratings:*** Several of the guidelines were modified during the expert panel meeting, consistent with the procedures suggested by the RAM manual. Additionally, 3 of the guidelines (2.7, 4.8, 8.12) were expanded into “sub-guidelines,” netting 6 additional indicators for a total of 44 indicators that were rated during Round 2. The same criteria were utilized to categorize indicators as “appropriate,” “uncertain” or “inappropriate.”

Of the 44 indicators rated during Round 2, 16 indicators were rated “appropriate,” 25 indicators remained in the “uncertain” category, and 3 indicators (2.11, 4.10, and 7.6) were newly rated as “inappropriate.”

***Development of Final Guidelines:*** Table 1 summarizes the development of the final set of clinical guidelines for the use of buprenorphine in opiate maintenance treatment. The final set of guidelines was comprised of those indicators that were rated appropriate during either Round 1 or Round 2 of the process. The final set of clinical guidelines is provided in Appendix A.

## **DISCUSSION AND RECOMMENDATIONS**

The expert panel members for this project were incredibly generous with their time. They provided thorough, detailed feedback on the proposed guidelines, both individually and as part of a panel discussion, addressing a range of clinical questions, many of which had no easy answers. As evidenced by the palpable enthusiasm among presenters and attendees alike at the kickoff conference on January 6, 2011, best practices in buprenorphine treatment for opioid addiction is a timely topic. In his introductory presentation, COMMUNITY CARE chief medical officer James Schuster pointed out that within COMMUNITY CARE’s membership, between the third quarter of 2007 and the third quarter of 2009, there was a *203% increase* in the number of patients on buprenorphine. With utilization growing at such a rate, researchers, practitioners, and payers agree on the importance of synthesizing current guidelines, research evidence, and clinical experience into updated guidelines that will improve the quality and outcomes of buprenorphine treatment. The expert panelists’ dedication to this project is a testament to its value.

While the expert panelists did not always agree on clinical practices, there were several themes that emerged in their comments and during the expert panel discussion:

- *Guidelines should be practical.* The panel included a primary care physician who works from a private office in Scranton, PA as well as an internal medicine physician who works within the Veterans Affairs healthcare system in Pittsburgh, PA. Both prescribe buprenorphine, but in very different settings with very different resources readily available to them. Given the variety in provider settings, guidelines should strive to be widely applicable and offer specific suggestions to fit smaller providers (e.g. how to establish linkages and make referrals, how to conduct a thorough assessment with a small staff) to ensure high-quality clinical care regardless of the setting.

- *Guidelines should be flexible and promote access to buprenorphine to the wide range of patients who may benefit from it.* Expert panelists agreed that a patient's recovery is variable and treatment should therefore be individualized. Experts were hesitant to disqualify certain patients for not being "ideal," e.g. for having previous treatment episodes, for using other illicit substances concurrently, or for having co-occurring mental health disorders. They discouraged time limits on treatment and rigid dosing regulations. Expert panelists suggested many strategies to engage and reengage patients in buprenorphine treatment rather than limit access to it.
- *Guidelines should combine psychosocial counseling with buprenorphine.* While expert panelists held different viewpoints about the type and frequency of psychosocial counseling that best complements buprenorphine, they agreed that psychosocial counseling is an essential element in medication-assisted treatment.

Expert panelists expressed hope that buprenorphine could be an essential tool in helping to treat opioid dependence in pregnant women, HIV-positive patients, and individuals who were recently incarcerated. When asked about barriers to the implementation of the proposed guidelines, their responses often included lack of time, lack of resources, lack of training, and lack of research on particular practices.

Other recommendations in key domains include:

### ***Assessments***

A practitioner should conduct assessments to determine candidacy for buprenorphine treatment. In addition to assessing a patient's medical history and his or her psychosocial supports, practitioners should conduct assessments to:

*Determine opioid dependence by DSM-IV standards.*

*Assess substance use history and current substance use.* Assessing all drugs of abuse is important for effectively treating addiction.

*Assess treatment history – previous treatment episodes with buprenorphine or methadone.* Previous treatment experiences may provide an opportunity to adapt the physician's current approach to treatment.

*Assess pain.* Understanding a patient's pain status is important, but pain should not exclude a patient from buprenorphine treatment.

## **Candidacy**

Buprenorphine should be accessible, and patients with less-than-ideal characteristics should not be precluded from treatment. However, the panel agreed on a list of criteria for a “good candidate,” including:

*Expected to be reasonably compliant.* Although motivation may be developed over the course of treatment, increased compliance is associated with better treatment outcomes. Compliance may be improved if the physician and patient establish goals and objectives in the treatment agreement at the outset.

*Not dependent on CNS depressants, including benzodiazepines and alcohol.* The panel emphasized the potential danger of combining CNS depressants, particularly benzodiazepines, with buprenorphine.

*Interested in treatment.* Voluntary treatment may contribute to patient success.

*Current opioid dependence.* Buprenorphine treatment may be effective for patients with mild, moderate and more severe opioid dependence.

*If currently on methadone, unable/unwilling to receive treatment from a methadone clinic.* Some patients have difficulty going to methadone clinics daily. Even if a patient is noncompliant with aspects of treatment, he or she may fare better with buprenorphine than with methadone.

*Pregnant women may be good candidates.* It is important to offer as many treatment options as possible to pregnant patients trying to manage addiction. Positive treatment outcomes have been achieved for pregnant patients using buprenorphine.

## **Dosing**

The expert panel recommended guidelines for appropriate dosing of buprenorphine. Experts approached dosing schedules differently, which limited the number of guidelines that the panel could agree on overall. For example, regarding maximum daily dose, none of the guideline statements (32 mg/day, 24 mg/day, and 16 mg/day) were rated appropriate by the panel by the standards of the RAM. However, 16 mg/day was rated most highly, though experts noted that there is clinical variation in patients’ needs. The following dosing guidelines were deemed appropriate by the panel:

*Induction: Day 2 maximum between 8-16 mg.* Panelists varied in their approach to the first day dose of buprenorphine during induction (some preferred to begin more

gradually, others preferred to induce a patient closer to the stabilized dose that they anticipated). Their typical day 2 dose overlapped in the 8-16 mg range.

*Stabilization: adjust dose (as needed) in no more than 2-4 mg increments/week. If a patient's dose needs to be adjusted, an appropriate rate of adjustment should not exceed 2-4 mg increments/week.*

*Stabilization: Daily dose has been established when patient is not using illicit opioids, withdrawal symptoms are not present, and the patient is not experiencing cravings.*

*Maintenance: Once patient has remained compliant with counseling and physician visits, the physician may extend the prescription to 30 days. The time to achieve compliance varies with each patient. Month long prescriptions should be contingent on a patient's biopsychosocial stability.*

*Induction after methadone: Induction for patients coming off methadone should be managed by experienced physicians only. To induce a patient after methadone, monitor for withdrawal symptoms. If not observed within 24+ hours after last methadone treatment, wait prior to initiation.*

### ***Psychosocial Treatment***

Effective buprenorphine treatment should include a psychosocial component in the induction and stabilization phases, and perhaps also in the maintenance phase. Guidelines related to psychosocial treatment are:

*Patients starting buprenorphine should receive an evidence-based psychosocial treatment.* Evidence-based therapy is generally of higher quality and there are a range of effective therapies, such as cognitive-behavioral therapy and contingency management. These therapies can be referred or implemented in the prescriber setting.

*Early in treatment, patients should be contacted if the physician is aware they are noncompliant with psychosocial therapy.* New patients face a higher risk of relapse. The more support a new patient has, the more likely he or she is to succeed. However, it may be challenging for a physician to track patients who have missed counselor appointments.

*During the maintenance phase, psychosocial therapy can be less frequent than during stabilization.* Psychosocial therapy may or may not be a necessary component of buprenorphine treatment for patients in the maintenance phase. Although psychosocial therapy should be individualized, the panel agreed on the guideline that it can be less frequent than during stabilization.

## **Duration**

The duration of buprenorphine treatment should be individualized to meet patients' various needs. The guidelines that were rated "appropriate" using the RAM related to duration are:

*Before discontinuing buprenorphine, patients must express a desire to discontinue.* Discontinuation is ideally a mutual decision between the physician and patient.

*Before discontinuing buprenorphine, patients must have stable housing and income.*

*Before discontinuing buprenorphine, patients must have adequate psychosocial support.* Patients have a higher risk of relapse if they discontinue without adequate psychosocial support.

*Conditions for termination and contingencies for treatment should be outlined in the treatment agreement.*

## **Treatment for co-occurring mild-to-moderate depression and/or anxiety**

Co-occurring depression and anxiety are relatively common among opioid dependent patients seeking treatment. The panel recommended specific screening and assessment guidelines, including the patient's previous history of mental disorders and treatment with a focus on the temporal relationship of symptoms to substance use and response to previous treatment, as well as the following guidelines:

*Reassess symptoms of depression and anxiety with regularity.* It is important to reassess symptoms regularly, though a time frame was not specified.

*Consider alternatives to benzodiazepines.* Benzodiazepines have a high potential for abuse in the opioid-dependent population.

*Patients should be strongly advised against self-medicating with benzodiazepines.*

*Integrate treatment for opiate dependence and depression/anxiety to the greatest degree possible, as on-site integrated care is associated with better outcomes than referrals off-site.* The panel recognized that this integration may be difficult or impossible for physicians in certain settings. Off-site treatments should be carefully coordinated with the prescriber.

## REFERENCES

Center for Substance Abuse Treatment. *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction*. Treatment Improvement Protocol (TIP) Series 40. DHHS Publication No. (SMA) 04-3939. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2004.

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**Table 1.** Guideline statements rated as valid for the treatment of opioid dependence with buprenorphine with median score  $\geq 7.0$  and without disagreement among panelists during the first or second rounds of ratings\*

Domain	Median rating, agreement, and range	
	Round One	Round Two
<i>Assessments to determine candidacy for treatment</i>		
1.1. Determine opioid dependence by DSM-IV standards	9.0, A, 8-9	NR
1.2. Assess psychiatric history with attention to current compliance with medication	8.0, A, 3-9	NR
1.3. Assess medical history with attention paid to liver and cardiac status, medications, and seizures	8.0, A, 7-9	NR
1.4. Assess pregnancy status	9.0, A, 3-9	NR
1.5. Assess psychosocial supports – employment, family, housing, 12-step involvement	8.0, A, 5-9	NR
1.6. Assess substance use history and current substance use	9.0, A, 8-9	NR
1.7. Assess treatment history – previous treatment episodes with buprenorphine, methadone	8.5, A, 5-9	NR
1.8. Assess for potential contraindications through laboratory screening: ALT, AST, Hep B and C, HIV, gonorrhea, chlamydia, syphilis, TB	7.0, U, 3-9	3.0, U, 1-6
1.9. Assess for current opioid agonist treatment by conducting a witnessed urine screen (methadone, buprenorphine, benzodiazepines)	9.0, A, 5-9	NR
1.10. Assess withdrawal status	9.0, A, 6-9	NR
1.11. Assess readiness to change	6.5, U, 3-9	5.0, U, 2-6
1.12 Assess addiction severity (Suggested tool:	7.0, U, 4-8	NR

Addiction Severity Index)		
a. Assess addiction severity	NR	8.0, A, 7-9
1.13. Assess potential treatment needs in relation to the physician's ability to accommodate them (intensive monitoring, interactions with legal system, employers, others)	8.0, A, 4-9	NR
1.14 Assess pain	7.0, U, 5-9	8.0, A, 6-9
<i>Selection of candidates for treatment</i>		
2.1. Current mild-to-moderate opioid dependence	7.5, U, 1-9	NR
a. Current opioid dependence	NR	9.0, A, 3-9
2.2. If currently on methadone, unable/unwilling to receive treatment from a methadone clinic, but not in compliant with methadone treatment, or with a documented severe, uncontrollable adverse effect/true hypersensitivity to methadone	7.0, I, 5-9	NR
a. If currently on methadone, unable/unwilling to receive treatment from a methadone clinic	NR	8.0, A, 7-9
2.3. Have adequate psychosocial support	8.0, A, 1-9	NR
2.4. Do not have co-occurring mental disorder or co-occurring disorder is stable	8.0, A, 1-9	NR
2.5. Not suicidal	8.5, A, 4-9	NR
2.6. Not pregnant	4.0, U, 1-9	NR
a. Pregnant women may be good candidates	NR	8.0, A, 8-9
2.7. Have no or few failed treatment attempts	6.0, U, 2-9	NR
a. Have no prior treatment experiences	NR	5.0, U, 1-8
b. Have a few failed treatment attempts	NR	7.0, U, 1-8
c. Have previous responsive treatment experiences with buprenorphine	NR	8.0, U, 5-9

2.8. Expected to be reasonably compliant with treatment	8.0, A, 5-9	NR
2.9. Not dependent on CNS depressants, including benzodiazepines and alcohol	8.0, A, 1-9	NR
2.10. Not using other substances	6.5, U, 1-9	5.0, U, 2-8
2.11. Under age 65	6.0, U, 1-9	2.0, I, 1-7
2.12. Interested in treatment	8.0, A, 3-9	NR
2.13. Do not have the following medical conditions: seizure disorders, HIV, chronic severe pain	4.5, U, 1-9	2.0, U, 1-6
<i>Treatment Agreement</i>		
3.1. Voluntary participation	9.0, A, 7-9	NR
3.2: Pregnancy	7.0, U, 1-9	NR
a. Pregnancy: patients must agree to notify prescribing physician if they are or plan to become pregnant	NR	9.0, A, 8-9
3.3. Use of other medications	9.0, A, 7-9	NR
3.4. Use of alcohol and illicit drugs	8.5, A, 4-9	NR
3.5. Use of medications only as prescribed	9.0, A, 7-9	NR
3.6. Scheduled appointments	8.0, A, 6-9	NR
3.7. Compliance with required pill counts and drug tests	9.0, A, 7-9	NR
3.8. Counseling and other referrals	9.0, A, 7-9	NR
3.9. Appointments under the influence	8.0, A, 3-9	NR
3.10. Recovery and relapse	7.5, A, 3-9	NR
3.11. Diversion	9.0, A, 8-9	NR

3.12. Safe storage	9.0, A, 8-9	NR
3.13. Other safety issues	8.5, U, 5-9	7.0, U, 1-9
<i>Dosing</i>		
4.1. Induction: Begin induction early in the week.	6.0, U, 2-9	4.0, U, 1-4
4.2. Induction: Ensure that patient is experiencing objective signs of withdrawal.	8.5, A, 7-9	NR
4.3. Induction: Provide a dose daily.	7.0, U, 1-9	NR
a. During induction, provide a daily observed dose for the first three days (assuming a dose is indicated daily)	NR	4.0, U, 1-8
4.4 Induction: Assess withdrawal symptoms before each dose	8.0, U, 1-9	NR
a. Assess withdrawal and/or craving symptoms before each dose during induction	NR	8.0, U, 3-9
4.5 Induction: Day one dose between 2-8 mg.	7.5, U, 1-9	6.0, U, 5-9
4.6: Induction: Day two maximum dose between 8-16 mg	8.0, A, 1-9	NR
4.7 Induction: Day 3+ dose increments in 2-4 mg	7.0, U, 1-9	8.0, U, 2-8
4.8: Induction: Maximum daily dose 32 mg	5.0, U, 1-9	4.0, U, 1-6
a. 4.8b: Maximum daily dose of 24 mg	NR	8.0, U, 2-8
b. Maximum daily dose of 16 mg	NR	8.0, U, 2-9
4.9: Induction after methadone: Induction for patients coming off methadone should be managed by experienced physicians only.	8.0, A, 2-9	NR
4.10 Induction after methadone: Begin treatment 24 hours after last methadone treatment.	3.5, U, 1-7	2.0, I, 1-3
4.11 Induction after methadone: monitor for withdrawal symptoms. If not observed within 24+ hours after last methadone treatment, reevaluate	7.0, U, 1-9	NR

suitability for buprenorphine treatment.		
a. Induction after methadone: monitor for withdrawal symptoms. If not observed within 24+ hours after last methadone treatment, wait prior to initiation.	NR	8.0, A, 4-9
4.12 Stabilization: Adjust dose (as needed) in 2-4 mg increments/week.	6.0, U, 1-9	NR
a. Stabilization: Adjust dose (as needed) in no more than 2-4 mg increments/week.	NR	8.0, A, 2-9
4.13: Stabilization: Daily dose has been established when patient is not using illicit opioids, withdrawal symptoms are not present, and the patient is not experiencing cravings.	8.0, A, 7-9	NR
4.14 Stabilization: Prescribe 7 days' medication at a time for 2 months	7.0, U, 1-9	NR
a. Stabilization: Prescribe 7 days' medication at a time for 3 months	NR	4.0, U, 1-8
4.15 Maintenance: Once patient has remained compliant with counseling and physician visits, extend the prescriptions to 14 days for the next 2 months.	7.0, U, 1-9	7.0, U, 2-8
4.16: Maintenance: After a period of time that varies with each patient but should reflect compliance with treatment, a prescription for 30 days may be written.	8.0, A, 7-9	NR
<i>Psychosocial treatment</i>		
5.1: Patients receiving buprenorphine should receive simultaneous psychosocial counseling.	9.0, A, 7-9	NR
5.2: Physicians should establish linkages with a variety of psychosocial supports and be able to refer to qualified providers.	9.0, A, 7-9	NR
5.3 Patients starting buprenorphine should receive an evidence-based psychosocial treatment such as	7.5, U, 1-9	NR

Cognitive Behavioral Therapy.		
a. Patients starting buprenorphine should receive an evidence-based psychosocial treatment.	NR	8.0, A, 7-9
5.4 Patients should receive an evidence-based psychosocial treatment, such as Contingency Management Therapy.	7.5, U, 1-9	6.0, U, 4-9
5.5: Patients should receive weekly psychosocial therapy appointments during the stabilization phase.	8.0, A, 1-9	NR
5.6: Patients should be contacted after missing two consecutive psychosocial therapy appointments.”	7.5, U, 1-9	NR
a. Early in treatment, patients should be contacted if the physician is aware they are noncompliant with psychosocial therapy.	NR	8.0, A, 7-9
5.7 During the maintenance phase, psychosocial therapy should continue.	7.5, U, 6-9	7.0, U, 5-9
5.8: During the maintenance phase, psychosocial therapy can be less frequent (biweekly or monthly).	8.0, U, 3-9	NR
a. During the maintenance phase, psychosocial therapy can be less frequent than during stabilization.	NR	8.0, A, 5-9
<b>Monitoring</b>		
6.1: During induction and stabilization phases, urine screens to detect alcohol and other drugs of abuse and the presence of the buprenorphine metabolite should be conducted weekly.	7.0, A, 1-9	NR
6.2: During the maintenance phase, urine screens to detect alcohol and other drugs of abuse and the presence of the buprenorphine metabolite should be conducted biweekly or monthly.	8.0, A, 1-9	NR

6.3 During induction and stabilization phases, pill counts should be conducted weekly.	6.0, U, 1-9	3.0, U, 1-6
6.4: During the maintenance phase, pill counts should be conducted biweekly or monthly	6.5, U, 1-9	NR
a. During the maintenance phase, pill counts should be conducted randomly.	NR	7.0, U, 3-9
<b>Duration</b>		
7.1: Before discontinuing buprenorphine, patients must express a desire to discontinue.	9.0, A, 7-9	NR
7.2 Before discontinuing buprenorphine, patients must have achieved stability on buprenorphine.	9.0, U, 1-9	NR
a. Before discontinuing buprenorphine, patients must have achieved abstinence.	NR	8.0, U, 2-9
7.3: Before discontinuing buprenorphine, patients must have stable housing and income.	7.5, A, 1-9	NR
7.4: Before discontinuing buprenorphine, patients must have adequate psychosocial support.	8.0, A, 4-9	NR
7.5 Before discontinuing buprenorphine, patients must have no legal problems.	5.0, U, 1-9	NR
a. Before discontinuing buprenorphine, patients must have no new legal problems.	NR	4.0, U, 1-7
7.6 Buprenorphine tapering should occur over 5-7 days.	3.5, U, 1-7	1.0, I, 1-2
7.7 Involuntary termination of treatment should be rare; conditions for termination and contingencies for treatment should be outlined in the treatment contract.	8.0, U, 1-9	NR
a. Conditions for termination and contingencies for treatment should be outlined in the treatment agreement.	NR	9.0, A, 8-9
<b>Co-occurring Treatment</b>		

8.1: Screen for depression and anxiety (suggested tool: Mental Health Screening Form III, Mental Status Examination, Hamilton Depression Inventory, Hamilton Anxiety Inventory, Beck Depression Inventory, Beck Anxiety Inventory, PRIME-MD).	8.5, A, 7-9	NR
8.2: Assess previous history of mental disorders and treatment, focusing on temporal relationship of symptoms to substance use and response to previous treatment.	8.5, A, 7-9	NR
8.3: Assess type, quantity and frequency, and time of last use of illicit substances or prescribed psychotropic drugs.	9.0, A, 7-9	NR
8.4: Assess family history of mental disorders.	8.0, A, 6-9	NR
8.5: Assess severity of depression/anxiety.	9.0, A, 7-9	NR
8.6 Re-assess symptoms of depression and anxiety every two to four months.	7.0, U, 1-9	NR
a. Reassess symptoms of depression and anxiety with regularity	NR	9.0, A, 7-9
8.7 Refer to specialized behavioral health care.	7.0, U, 2-9	NR
a. Refer to specialized behavioral health care if patient fails to respond to treatment provided by prescribing physician.	NR	9.0, A, 8-9
8.8: Refer to concurrent evidence-based psychosocial treatment, such as Cognitive Behavioral Therapy, Motivational Interviewing, Relapse Prevention, Contingency Management, or supportive therapy.	8.5, A, 3-9	NR
8.9: Refer to Twelve-Step Facilitation, such as Dual Recovery Anonymous.	8.5, A, 2-9	NR
8.10 For patients without current psychotropic medication prescriptions, do not prescribe until the patient is stabilized on buprenorphine.	4.0, U, 1-8	3.0, U, 1-8

8.11: Once stabilized, if a patient continues to present symptoms of depression and anxiety, consider prescribing medications with low potential for abuse, such as SSRIs or tricyclic antidepressants.	8.0, A, 5-9	NR
8.12: Consider alternatives to benzodiazepines but if prescribing benzodiazepines, choose options with less potential for abuse, such as oxazepam. Patients should be strongly advised against self-medication with benzodiazepines.	7.0, U, 1-9	NR
a. Consider alternatives to benzodiazepines.	NR	9.0, A, 8-9
b. Patients should be strongly advised against self-medicating with benzodiazepines.	NR	9.0, A, 8-9
8.13: If a patient has a prescription for benzodiazepines at the outset of treatment, use caution taking him or her off of the benzodiazepines and do not discontinue abruptly.	9.0, A, 7-9	NR
8.14: Integrate treatment for opiate dependence and depression/anxiety to the greatest degree possible, as on-site integrated care is associated with better outcomes than referrals off-site.	9.0, A, 1-9	NR

\*A= Appropriate (panel median of 7-9 without disagreement); I= Inappropriate (panel median of 1-3 without disagreement); U= Uncertain (panel median of 4-6 OR any median with disagreement); NR = guideline statements that were not rated in Round One (guideline statements that were added to or modified from the proposed candidate indicators during the expert panel meeting) or in Round Two (guideline statements that were rated appropriate during Round One ratings or were modified during the expert panel meeting). For purposes of determining ratings, *agreement* means that no more than two panelists rate the indicator outside the 3-point region (1-3; 4-6; 7-9) containing the median.

## **Best Practices in the Use of Buprenorphine:**

### **Final Guidelines Rated Appropriate**

#### ***Assessments***

- 1.1. Determine opioid dependence by DSM-IV standards
- 1.2. Assess psychiatric history with attention to current compliance with medication
- 1.3. Assess medical history with attention paid to liver and cardiac status, medications, and seizures
- 1.4. Assess pregnancy status
- 1.5. Assess psychosocial supports – employment, family, housing, 12-step involvement
- 1.6. Assess substance use history and current substance use
- 1.7. Assess treatment history – previous treatment episodes with buprenorphine, methadone
- 1.9. Assess for current opioid agonist treatment by conducting a witnessed urine screen (methadone, buprenorphine, benzodiazepines)
- 1.10. Assess withdrawal status
- 1.12. Assess addiction severity
- 1.13. Assess potential treatment needs in relation to the physician's ability to accommodate them (intensive monitoring, interactions with legal system, employers, others)
- 1.14. Assess pain

#### ***Candidacy***

- 2.1. Current opioid dependence
- 2.2. If currently on methadone, unable/unwilling to receive treatment from a methadone clinic
- 2.3. Have adequate psychosocial support
- 2.4. Do not have co-occurring mental disorder or co-occurring disorder is stable
- 2.5. Not suicidal
- 2.6. Pregnant women may be good candidates
- 2.8. Expected to be reasonably compliant with treatment
- 2.9. Not dependent on CNS depressants, including benzodiazepines and alcohol
- 2.12. Interested in treatment

#### ***Treatment agreement***

- 3.1. Voluntary participation
- 3.2. Pregnancy: patients must agree to notify prescribing physician if they are or plan to become pregnant
- 3.3. Use of other medications
- 3.4. Use of alcohol and illicit drugs
- 3.5. Use of medications only as prescribed
- 3.6. Scheduled appointments
- 3.7. Compliance with required pill counts and drug tests
- 3.8. Counseling and other referrals
- 3.9. Appointments under the influence

- 3.10. Recovery and relapse
- 3.11. Diversion
- 3.12. Safe storage

### ***Dosing***

- 4.2. Induction: Ensure that patient is experiencing objective signs of withdrawal.
- 4.6: Induction: Day two maximum dose between 8-16 mg
- 4.9: Induction after methadone: Induction for patients coming off methadone should be managed by experienced physicians only.
- 4.11 Induction after methadone: monitor for withdrawal symptoms. If not observed within 24+ hours after last methadone treatment, wait prior to initiation.
- 4.12 Stabilization: Adjust dose (as needed) in no more than 2-4 mg increments/week.
- 4.13: Stabilization: Daily dose has been established when patient is not using illicit opioids, withdrawal symptoms are not present, and the patient is not experiencing cravings.
- 4.16: Maintenance: After a period of time that varies with each patient but should reflect compliance with treatment, a prescription for 30 days may be written.

### ***Concurrent psychosocial treatment***

- 5.1: Patients receiving buprenorphine should receive simultaneous psychosocial counseling.
- 5.2: Physicians should establish linkages with a variety of psychosocial supports and be able to refer to qualified providers.
- 5.3 Patients starting buprenorphine should receive an evidence-based psychosocial treatment.
- 5.5: Patients should receive weekly psychosocial therapy appointments during the stabilization phase.
- 5.6 Early in treatment, patients should be contacted if the physician is aware they are noncompliant with psychosocial therapy.
- 5.8 During the maintenance phase, psychosocial therapy can be less frequent than during stabilization.

### ***Monitoring***

- 6.1: During induction and stabilization phases, urine screens to detect alcohol and other drugs of abuse and the presence of the buprenorphine metabolite should be conducted weekly.
- 6.2: During the maintenance phase, urine screens to detect alcohol and other drugs of abuse and the presence of the buprenorphine metabolite should be conducted biweekly or monthly.

### ***Duration***

- 7.1: Before discontinuing buprenorphine, patients must express a desire to discontinue.
- 7.3: Before discontinuing buprenorphine, patients must have stable housing and income.
- 7.4: Before discontinuing buprenorphine, patients must have adequate psychosocial support.
- 7.7 Conditions for termination and contingencies for treatment should be outlined in the treatment agreement.

### ***Co-occurring Treatment***

- 8.1: Screen for depression and anxiety (suggested tool: Mental Health Screening Form III, Mental Status Examination, Hamilton Depression Inventory, Hamilton Anxiety Inventory, Beck Depression Inventory, Beck Anxiety Inventory, PRIME-MD).
- 8.2: Assess previous history of mental disorders and treatment, focusing on temporal relationship of symptoms to substance use and response to previous treatment.
- 8.3: Assess type, quantity and frequency, and time of last use of illicit substances or prescribed psychotropic drugs.
- 8.4: Assess family history of mental disorders.
- 8.5: Assess severity of depression/anxiety.
- 8.6 Reassess symptoms of depression and anxiety with regularity
- 8.7 Refer to specialized behavioral health care if patient fails to respond to treatment provided by prescribing physician.
- 8.8: Refer to concurrent evidence-based psychosocial treatment, such as Cognitive Behavioral Therapy, Motivational Interviewing, Relapse Prevention, Contingency Management, or supportive therapy.
- 8.9: Refer to Twelve-Step Facilitation, such as Dual Recovery Anonymous.
- 8.11: Once stabilized, if a patient continues to present symptoms of depression and anxiety, consider prescribing medications with low potential for abuse, such as SSRIs or tricyclic antidepressants.
- 8.12. Consider alternatives to benzodiazepines. Patients should be strongly advised against self-medicating with benzodiazepines.
- 8.13: If a patient has a prescription for benzodiazepines at the outset of treatment, use caution taking him or her off of the benzodiazepines and do not discontinue abruptly.
- 8.14: Integrate treatment for opiate dependence and depression/anxiety to the greatest degree possible, as on-site integrated care is associated with better outcomes than referrals off-site.