Statement of the American Society of Addiction Medicine Consensus Panel on the Use of Buprenorphine in Office-Based Treatment of Opioid Addiction

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Objectives: Opioid addiction affects over 2 million patients in the United States. The advent of buprenorphine and the passage of the Drug Addiction Treatment Act in 2000 have revolutionized the opioid treatment delivery system by granting physicians the ability to administer office-based opioid treatment (OBOT), thereby giving patients greater access to treatment. The purpose of this consensus panel was to synthesize the most current evidence on the use of buprenorphine in the office-based setting and to make recommendations that will enable and allow additional physicians to begin to treat opioid-addicted individuals.

Methods: Literature published from 2000 to 2009 was searched using the PubMed search engine and yielded over 375 articles published in peer-reviewed journals, including some that were published guidelines. These articles were submitted to a consensus panel composed of researchers, educators, and clinicians who are leaders in the field of addiction medicine with specific expertise in the use of OBOT. The panel discussed results and agreed upon consensus recommendations for several facets of OBOT.

Results: On the basis of the literature review and consensus discussions, the panel developed a series of findings, conclusions, and recommendations regarding the use of buprenorphine in office-based treatment of opioid addiction.

Conclusions: Therapeutic outcomes for patients who self-select office-based treatment with buprenorphine are essentially comparable to those seen in patients treated with methadone programs. There are few absolute contraindications to the use of buprenorphine, although the experience and skill levels of treating physicians can vary considerably, as can access to the resources needed to treat comorbid medical or psychiatric conditions—all of which affect outcomes. It is important to conduct a targeted assessment of every patient to confirm that the provider has resources available to meet the patient's needs. Patients should be assessed for a broad array of biopsychosocial needs in addition to opioid use and addiction, and should be treated, referred, or both for help in meeting all their care needs, including medical care, psychiatric care, and social assistance. Current literature demonstrates promising efficacy of buprenorphine, though further research will continue to demonstrate its effectiveness for special populations, such as adolescents, pregnant women, and other vulnerable populations. Since the time of this review, several new studies have provided new data to continue to improve our understanding of the safety and efficacy of buprenorphine for special patient populations.

Key Words: buprenorphine, office-based treatment, opioid addiction

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Since 2002, a large body of evidence has become available, reflecting the experience of US researchers and

clinicians. This evidence is reflected in articles published in peer-reviewed journals, as well as in guidelines issued by various organizations and agencies (Health Resources and Services Administration, 2004; McNicholas, 2004; Wedam et al., 2007; Center for Substance Abuse Treatment, 2006a; Center for Substance Abuse Treatment, 2006b; Gordon and Krumm, 2008; Baxter, 2009).

To make this information more readily available to practicing physicians, as well as to encourage additional physicians to begin treating opioid-addicted persons, members of the American Society of Addiction Medicine consensus panel engaged in a critical examination of the scientific literature and employed their considerable clinical experience in reaching consensus as to recommended patient care practices. In doing so, panel members recognized that advice is not an adequate substitute for the knowledge and skills of practicing physicians who are engaged in developing treatment regimens tailored to the needs of individual patients.

The panel also recognized that not all treatment providers would be able to conform to each of the strategies recommended here. Instead, providers are encouraged to consider the panel's findings, conclusions, and recommendations in the context of the individual patient and their overall practice. Information and recommendations provided in this document are not intended to create a legal standard of care for any physician or to interfere with his or her clinical judgment or practice of medicine.

METHODS

Literature published from 2000 to 2009 was the subject of a PubMed search. The search yielded 376 articles published in peer-reviewed journals. Consensus reports from the federal Center for Substance Abuse Treatment and other authoritative sources also were included in the review.

Articles and published guidelines were submitted to a consensus panel composed of researchers, educators, and clinicians who have expertise in the use of buprenorphine. On the basis of the literature review and consensus discussions, the panel developed a series of findings, conclusions, and recommendations regarding the use of buprenorphine in office-based treatment of opioid addiction. Members agreed on the evidence for buprenorphine's overall efficacy and safety, as well as contraindications to its use.

Multiple drafts of the consensus panel's work were submitted to a national peer review panel, whose members were asked to evaluate the documents for scientific accuracy and clinical relevance. That work is presented here.

RESULTS

Patient Management With Buprenorphine

Induction

Patients who are currently physically dependent on opioids should be in moderate opioid withdrawal before the first buprenorphine induction dose. Patients are instructed to stop taking their opioid, and wait until they develop moderate spontaneous withdrawal. If a patient is not in withdrawal, and is given buprenorphine, precipitated withdrawal may occur. The Clinical Opioid Withdrawal Scale is a useful and validated assessment tool. The initial dose is 2 to 4 mg, and the total first day dose is up to 12 to 16 mg (Johnson et al., 2003; McNicholas, 2004; Batki, 2005; Marsch et al., 2006; Stephen, 2006; Baxter, 2009). During induction, patients should be frequently assessed for signs of overmedication. There is no data as to the specific time interval during which overmedication should be assessed. Therefore, it should be approached based on an individual patient basis.

Patients requesting transfer from methadone to buprenorphine should gradually taper their methadone dose to 30 to 40 mg and remain clinically stable on that dose before starting buprenorphine induction. Because methadone has a long and variable half-life, patients will need to discontinue methadone for at least 36 hours and often up to 72 hours to experience moderate withdrawal before proceeding with buprenorphine induction (McNicholas, 2008).

Patients should be advised to avoid driving or operating other machinery until their dose is stabilized and they are familiar with the effects of buprenorphine.

During induction and stabilization, patients should be assessed frequently for signs of overmedication or undermedication, and dose adjustments should be made accordingly (Johnson, 2003; McNicholas, 2004; Batki, 2005).

Consensus of the Panel

The buprenorphine/naloxone combination product should be used for induction as well as for stabilization and maintenance. The exception is pregnant women who are candidates for buprenorphine treatment, who should be inducted and maintained on the buprenorphine monoproduct (see the discussion of pregnancy).

In opioid dependent patients undergoing induction who exhibit signs of precipitated withdrawal, the physician has 2 options:

1. Continue with buprenorphine induction by continuing to give additional doses of buprenorphine up to 16 mg or until signs and symptoms of withdrawal abate;
2. Or to stop induction when the patient exhibits withdrawal symptoms, treat withdrawal symptomatically (eg, clonidine, antidiarrheals, nonsteroidal anti-inflammatory drugs) and instruct the patient to continue to abstain from opioids and return the following day for reassessment of induction.

The timing of buprenorphine induction requires care to avoid overdose (eg, in a patient who has been using central nervous system depressants such as alcohol or benzodiazepines in addition to opioids) or underdose (eg, triggering a re-emergence of opioid craving).

Stabilization

The stabilization phase is focused on finding the optimal dose for the individual patient. This dose should eliminate all withdrawal symptoms, decrease opioid craving, eliminate other opioid use, and provide maximal functional status (Joseph et al., 2000; Baxter, 2009).

Most patients stabilize on 8 to 24 mg/day (Comer et al., 2005a; Comer et al., 2005b). Rarely, there is a need to go up to 32 mg for the highly tolerant patient. The primary concern

in going to these larger doses is the much greater potential for diversion.

Certain medical factors may cause a patient's dosing requirements to change. These include (but are not limited to) starting, stopping, or changing the dose of other prescription medications; onset and progression of pregnancy; onset of menopause; progression of liver disease; and significant increase or decrease in weight (Baxter, 2009).

Relapse should always be ruled out as a reason for loss of stability. Continued or resumed use of short-acting opioids during treatment with buprenorphine may increase tolerance and render the buprenorphine dose inadequate (Stephen, 2008). If a short-acting opioid of abuse produces euphoria, the buprenorphine dose may be increased to block this effect. A dose increase also may help to suppress drug cravings (Leavitt et al., 2000). Ideally, receipt of opioids from multiple providers should be avoided. However, in cases where this is not so, coordination with other prescribing physicians to limit the number of short-acting opioids obtained by prescription is essential (Baxter, 2009).

Consensus of the Panel

There is no precise way to determine in advance the optimal dose for a particular patient. Because buprenorphine has a long plasma half-life and an even longer duration of action at the mu opioid receptor, 5 days should be allowed between dose adjustments to assess the effect. While most patients stabilize on a dose of 8 to 24 mg/day as demonstrated by the data, many will not need a dose higher than 16 mg/day. This is further supported by Comer et al. in their study noting that brain mu receptors are approximately 90% saturated at a dose of 16 mg/day demonstrated on neuroimaging.

Detoxification/Medically Supervised Withdrawal Management

Few studies have evaluated predictors, mediators, and moderators of treatment success for medically supervised withdrawal from opioids conducted in outpatient settings.

Consensus of the Panel

Detoxification using buprenorphine is not technically difficult, but long-term abstinence following such detoxification appears as difficult to achieve as with other medications. Arguably, detoxification is best conceptualized not as definitive treatment, but as a preparatory and stabilizing introduction to other forms of care.

The most effective withdrawal method involves stabilizing the opioid dependent patient with buprenorphine and then tapering the dose over time by 2 mg every 5 days until the taper is completed. Evidence comparing buprenorphine with methadone is limited, but it appears that completion of withdrawal may be more likely with buprenorphine and withdrawal symptoms may resolve more quickly with buprenorphine than with methadone (Gwoing et al., 2006; Gowing et al., 2009).

Maintenance Treatment

Except in patients whose addictive disorders are of brief duration, the best outcomes occur with long-term medication maintenance with methadone or buprenorphine accompanied by appropriate psychosocial interventions (Collins and McAllister, 2007; Kleber, 2007; Soeffing et al., 2009; Stotts et al., 2009; World Health Organization, 2009). The optimum duration of maintenance is unclear, but may involve long-term or even lifetime medication use (Kleber, 2007; World Health Organization, 2009). This is similar to the treatment of other chronic diseases, such as hypertension, diabetes, or asthma. In the maintenance treatment paradigm, the goal is not to "get off" the buprenorphine, but rather to achieve maximal function both at home and at work.

Generally 8 to 24 mg/day of buprenorphine will be an adequate maintenance dose. Some patients may require a higher dose up to 32 mg or a lower dose as noted above. In positron emission tomographic scan studies, approximately, 92% of mu opioid receptors were occupied by buprenorphine at a dose of 16 mg/day (Comer et al., 2005a; Comer et al., 2005b). It is unclear how positron emission tomographic scan images translate into clinical outcomes such as withdrawal, craving, and treatment retention (Johnson et al., 2003; Sporer, 2004). Doses higher than 24 mg should prompt a thorough review of the patient's rehabilitation status. To evaluate patient progress and success of maintenance therapy, physicians should assess patients regularly for relapse and instability. In managing these challenges, some of the consensus panel recommendations include:

- Increasing frequency of visits
- Adding additional psychosocial interventions
- Increasing drug dose (if not higher than the maximum daily dose already)
- Decrease prescription interval
- Increase level of care
- Initiate a unilateral involuntary taper toward medication discontinuation
- Consider switching medication management to methadone

Consensus of the Panel

As Kleber (Kleber, 2007) has noted, medications are available to treat opioid addiction although none are curative. Medications can, however, markedly diminish withdrawal symptoms and craving, and block opioid euphoric effects if patients relapse, and enhance the efficacy of psychosocial interventions.

Relapse Prevention

Among the major challenges confronting patients in treatment is the prevention of relapse, which is a risk even with successful treatment interventions (White, 2007).

Specific precipitants of relapse vary substantially from one experience to the next, even in the same individual (Connors et al., 1996). Attributing causality is even more complex in patients who have co-occurring medical or psychiatric disorders. In a survey, Daley and colleagues identified factors that contributed to relapse including inability to manage stress or negative emotional states (69%); interpersonal conflicts with family or others (29%); poor adherence to the treatment regimen (25%); negative thinking (11%); and insufficient motivation to change (10%) (Daley et al., 1998).

Consensus of the Panel

The following principles, which are common to many models of relapse prevention (Marlatt and Gordon, 1985; Tims and Leukefeld, 1987; Dimeff and Marlatt, 1995; Amato et al., 2008a; Amato et al., 2008b), can minimize the risk of relapse and attenuate the severity of a relapse episode:

1. Identifying environmental cues and stressors that act as relapse triggers.
2. Learning to identify and manage negative emotional states.
3. Working toward a more balanced lifestyle.
4. Developing skills to cope with stressful life events.
5. Understanding and managing craving.
6. Learning to identify and interrupt lapses and relapses.
7. Developing a recovery support network, such as joining a self-help group.
8. Utilizing clinical resources available to patients, such as counseling.

PATIENT SELECTION

Patient Assessment

The assessment should include:

1. Establishment of the diagnosis (such as, the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) of opioid dependence including the duration and severity of the illness.
2. Discussion of current opioid use history in terms of when, what and how much opioid the patient most recently used.
3. Documentation of the patient's substance use history, including alcohol and other drugs of abuse.
4. Identification and referral of patients who need medically supervised withdrawal management from alcohol, benzodiazepines, or other sedatives.
5. Identification of comorbid medical and psychiatric conditions and disorders and to determine how, when and where they will be addressed.
6. Screening for communicable diseases and address them as needed.
7. Assessment of the patient's access to social supports, family, friends, employment, housing, finances, and legal problems.
8. Evaluation of the patient's readiness to participate in treatment.

Laboratory tests should include; liver function tests, human immunodeficiency virus (HIV) and viral hepatitis serologies, pregnancy test for women and urine toxicology screening for naturally occurring opioids (eg, such as heroin which is detected as morphine), synthetic and semisynthetic opioids (methadone, oxycodone), and other commonly abused drugs such as cocaine, amphetamines, and benzodiazepines (Gordon and Krumm, 2008).

Consensus of the Panel

Consensus opinion is that an initial patient assessment is of higher quality when it includes a medical and psychiatric history, a substance abuse history, and an evaluation of family and psychosocial supports, as well as pregnancy testing for all women of childbearing age. The physical examination should be focused on evaluating neurocognitive function and identification of sequelae of opioid addiction or severe hepatic dysfunction (Gordon and Krumm, 2008). The decision to initiate medication-assisted therapy begins with an evaluation of the patient to confirm the diagnosis of opioid dependence. An ideal candidate for office-based treatment with buprenorphine is an individual who will comply with each issue noted in the patient consent form such as withdrawal symptoms, risks of combining buprenorphine with other medications, directions for taking medication, cost of medication, and potential side effects (McNicholas, 2004).

Relative Contraindications to the Use of Buprenorphine

Concurrent Use of Sedative-Hypnotics (Including Alcohol)

Individuals with current, active alcohol dependence rarely are appropriate candidates for office-based treatment with buprenorphine (Fishman et al., 2005; McNicholas, 2008).

The combination of buprenorphine with sedative-hypnotic medications has been associated with deaths (Lavie et al., 2005). If concomitant treatment is deemed necessary, the doses of both medications may need to be reduced.

Elevated liver function tests: patients with elevated liver function 3 to 5 times above normal should not be considered for buprenorphine.

Consensus of the Panel

Patients who are dependent or abusing sedative hypnotics, alcohol, or both are rarely appropriate for office-based opioid treatment (OBOT) with buprenorphine. These patients should undergo careful clinical evaluation and should be considered for OBOT only if all of the following apply: clinical indication; willingness to discontinue sedative hypnotics, alcohol, or both by undergoing medically supervised withdrawal; and success in discontinuing hypnotics, alcohol, or both. In addition, patients with elevated liver functions tests 3 to 5 times greater than normal should not be considered for treatment with buprenorphine. These patients may be considered if they are willing to and have successfully discontinued sedative hypnotics, typically through medically supervised withdrawal.

Adolescents

Few studies have systematically evaluated buprenorphine in the treatment of adolescents, although there is good evidence that patients younger than 18 years are at particularly high risk for serious complications of addiction, including overdose deaths, suicide, HIV and other infectious diseases (Levy et al., 2007; Fiellin, 2008). Woody and colleagues (Woody et al., 2008) conducted 12-week clinical trials at 6 community programs for patients aged 15 to 21 years who were randomized to either 12 weeks of buprenorphine/naloxone treatment or a 14-day taper. Adolescents in the treatment group remained in counseling/ancillary treatment longer than those that were rapidly tapered (70 vs 20.5%, $P = 0.001$). Woody and colleagues concluded that continuing treatment with buprenorphine/naloxone improved outcomes compared with short-term detoxification, although further research is needed to assess the

efficacy and safety of longer-term treatment with buprenorphine for adolescents.

Consensus of the Panel

Buprenorphine/naloxone may be considered in adolescents for whom the balance of risks/benefits is considered favorable, considering such factors as: severity of addiction, previous failure, or low likelihood of success of other treatment approaches and overall risk of relapse. Furthermore, risks and benefits of using buprenorphine in adolescents should be discussed between providers and patients (and parents or guardians if patient is less than 18 years of age) on an individual basis.

Pregnant Women

Until recently, in the United States, methadone was the standard of care for pregnant women addicted to opioids. Since this review was conducted, however, new research has demonstrated promising safety and efficacy data for use of buprenorphine in pregnant women (Jones et al., 2009). Pregnant women should be offered either methadone or buprenorphine. Methadone has been shown to be safe and effective for both the pregnant woman and the neonate (Anderson and Kearney 2000; Jones et al., 2005; Vavrinková and Binder 2007). Buprenorphine (as is methadone) has been labeled as a Category C because there was insufficient evidence to establish its safety during pregnancy. Since the release of the 2009 study, buprenorphine monotherapy is a reasonable choice and appears to be as safe as methadone in pregnancy.

Buprenorphine maintained pregnancies also suggest that there is a lower severity of neonatal abstinence syndrome. Several studies have recently been published that have demonstrated that buprenorphine offers a substantial efficacy advantage over the current standard of care with oral morphine (Kraft et al., 2011; Unger et al., 2011). Other potential treatment of neonatal abstinence syndrome is methadone (Bio et al., 2011). This consensus panel review did not evaluate alternative delivery forms other than sublingual tablets (Note: more information and data maybe found in the references cited).

Breast-feeding

The safe use of buprenorphine during breast-feeding is not clearly delineated. However, the benefits of breast-feeding are multiple, including a natural strengthening of the maternal-child bond, which is of particular importance for this patient population. Further research will continue to clarify details regarding the use of buprenorphine in breast-feeding but until then the risks and benefits should be discussed and balanced on an individual patient basis (Lejeune et al., 2005; Briggs et al., 2008).

Consensus of the Panel

Short-term data on pregnancy and neonatal outcomes at the time of this review may indicate buprenorphine monotherapy for treatment of opioid dependent pregnant women is safe. Studies released since this review demonstrate promising safety and efficacy for the use of buprenorphine in pregnant women.

Although the available data are insufficient to firmly establish the safety of breast-feeding for mothers maintained on buprenorphine, the low theoretical risk should be balanced against the well-documented benefits of breast-feeding to both mother and neonate.

Pregnant patients require extensive counseling and community resources for recovery and parenting success. Integration of services and communication among all providers is essential for office-based treatment. The buprenorphine provider should work with the obstetric and pediatric providers to plan all aspects of care within the community. Since these consensus statements were written, additional research has been published that has demonstrated and supported the safety of buprenorphine in pregnant patients. Initial outcomes from these studies are positive demonstrating good outcomes for both mothers and neonates. A full discussion of this research is beyond the current scope of these guidelines, but readers should refer to the referenced literature to obtain further details (Jones et al., 2010).

Patients with Acute and Chronic Pain

In the United States, the parenteral formulation of buprenorphine is approved by the Food and Drug Administration for pain but not addiction treatment, while the sublingual formulation is approved for addiction but not pain treatment. Small studies in Europe and Asia demonstrate analgesic efficacy of the sublingual formulation (0.2-0.8 mg q 6-8 h) in opioid naïve postoperative pain (Edge et al., 1979; Moa and Zetterstrom, 1990). Parenteral analgesic potency is about 30 times that of morphine.

Consensus of the Panel

Several possible approaches exist for treating acute pain requiring opioid analgesia in the patient on buprenorphine therapy. With such limited clinical experience, mutiple treatment approaches based on pharmacologic principles have been published (Alford et al., 2006). The most effective approach will be elucidated with increased clinical experience. Currently there are insufficient data to recommend sublingual buprenorphine for the treatment of acute or chronic pain in patients with a history of opioid dependence.

Patients with HIV Disease

Buprenorphine should be used cautiously in combination with HIV antiretroviral medications that may inhibit, induce, or be metabolized by the cytochrome P450 3A4 enzyme system. Protease inhibitors inhibit cytochrome P450 3A4. Metabolism of buprenorphine, the antiretroviral medications, or both may be altered when they are combined. In some cases, therapeutic blood levels of antiretrovirals may need to be monitored (McCance-Katz, 2005; McCance-Katz et al., 2006a; McCance-Katz et al., 2006b).

Consensus of the Panel

While buprenorphine may be effectively used to treat patients with HIV, its use should be with caution concerning possible but as yet not clinically relevant drug-drug interactions. While drug/drug interactions remain a consideration with buprenorphine, they are likely less of a concern than when treating patients with methadone. Furthermore, successful use

of buprenorphine to treat HIV-infected, opioid-addicted patients has been demonstrated in multiple studies (Moatti et al., 2000; Berson et al., 2001; McCance-Katz, 2005).

Patients With Hepatitis and Other Liver Disorders

Viral hepatitis (especially infection with hepatitis B virus or hepatitis C virus) is common among individuals with up to 60% to 90% of injection drug users being infected with hepatitis C (Berson et al., 2001; Cazorla et al., 2005; Bruce and Altice, 2006). Therefore, patients with viral hepatitis who have opioid dependence and should be evaluated and treated appropriately (Backmund et al., 2001).

Consensus of the Panel

Buprenorphine treatment is not contraindicated by mildly elevated liver enzymes, although liver enzyme levels should be monitored. The threshold for elevated liver function for starting or discontinuing buprenorphine therapy is an elevated liver enzyme level of 3 times above normal. Patients with a history of injection drug use should be strongly encouraged to undergo immunization for hepatitis A and B, taking into account individual patient factors and appropriateness for vaccination.

Patients With Other Medical Conditions and Complications

Buprenorphine may be superior to methadone for the treatment of opioid dependence for patients with underlying cardiopulmonary disease or at risk for respiratory compromise, as it is less likely to cause respiratory depression (Gordon and Krumm, 2008).

Consensus of the Panel

Medical comorbidities may complicate the treatment of opioid addiction. Buprenorphine may be preferrable to methadone for specific medical conditions, though the evidence does not necessarily support which specific conditions.

Patients With Psychiatric Comorbidities

Coexisting psychiatric disorders are present in 20% to 60% of the persons entering addiction treatment, especially older individuals, those living in urban areas, patients who are incarcerated, or patients of a lower socioeconomic status (Robins et al., 1991; Kessler et al., 1994; Room, 1998; Sacks and Ries, 2005).

Patients with co-occurring psychiatric disorders have more difficulty engaging in, participating in, and completing addiction treatment, and generally have poorer prognoses than patients with diagnoses of either substance use or mental disorder alone (Kessler et al., 1994; Dausey and Desai, 2003). Untreated or inadequately treated psychiatric disorders can interfere with the effective treatment of addiction (Ziedonis et al., 2003; Khalsa et al., 2008. Patients with major depression or dysthymia are more likely to use illicit drugs during treatment than patients who do not suffer from depression (Sacks and Ries, 2005).

The presence of comorbid psychiatric disorders should not exclude patients from admission to office-based treatment with buprenorphine if outpatient treatment of both diseases can be accomplished (Sacks and Ries, 2005).

Consensus of the Panel

It is important to determine whether psychiatric symptoms are independent of the substance use or are substance-induced as this may inform treatment approach. Regardless, all patients with psychiatric symptoms should be evaluated and adequately treated. In the latter case, stability in the addiction treatment regimen should be the first therapeutic step (Ziedonis et al., 2003).

However, in patients with very severe psychiatric disease, the reverse treatment sequence may be more reasonable. In these patients, treatment using maintenance buprenorphine should be considered following stabilization of illness.

DISCUSSION

Although almost 2 million persons in the United States abuse or are addicted to opioids—prescription and illicit-–recent data suggest that nearly 80% do not receive treatment for their disorder (Kleber, 2007; Becker et al., 2008; Tetrault et al., 2008).

The use of buprenorphine and buprenorphine/naloxone combination in office-based primary care has improved access to care. Multiple studies have shown that buprenorphine treatment of addiction can be successfully integrated into office practice by physicians who are not addiction specialists (Fiellin et al., 2008).

In most cases, treatment is required for a long period or even throughout life (Kleber 2007; World Health Organization, 2009). Such long-term care, which is common to many medical conditions, should not be seen as a failure of treatment but as a cost-effective way to prolong life and improve quality of life by supporting the natural and long-term process of change and recovery. While the consensus panel did not make a formal recommendation on the frequency of monitoring and the use of varying methods for monitoring patient progress, we agreed that this is often dependent on physician preference as well as the individual patient. Therefore, urine toxicology, prescription supply/interval, etc, may be considered for each individual patient case.

Recent studies indicate that buprenorphine can be used safely and effectively to treat people with specialized needs, such as persons with co-occurring psychiatric conditions, adolescents, older adults, and persons with HIV and liver disease. Each of these conditions imposes specific requirements that must be addressed through careful patient selection, monitoring, and adjunctive services. There is little data on efficacy and safety to support the use of buprenorphine monotherapy to treat breast-feeding women. However, the benefits of breast-feeding are multiple, including a natural strengthening of the maternal-child bond, which is of particular importance for this patient population. The decision to place breast-feeding women on buprenorphine requires a balance of the risks and benefits and a discussion between provider and the individual patient, as a lack of data does not necessarily imply a risk of harm to the neonate. Populations not discussed by this panel remain of importance in treating opioid dependence, including

homeless populations, homosexual and bisexual populations, as well as patients with other medical comorbidities. Though beyond the scope of this review, these populations should be considered individually regarding treatment plans for opioid addiction.

CONCLUSIONS

Based on a review of the available evidence by a consensus panel with considerable clinical expertise and experience in the use of buprenorphine, the following recommendations are offered:

1. Medication-assisted therapies such as buprenorphine have been shown to be more effective than any other type of treatment for opioid dependence, particularly when used in concert with psychosocial interventions, such as counseling and other psychosocial therapies.
2. As in the treatment of most chronic diseases, pharmacotherapy of opioid dependence should be expected to take place over an extended period of time to achieve continued effective management of the underlying disorder. Most successful patients receive maintenance medication for years, whereas only a minority successfully taper off medication.
3. Therapeutic outcomes for patients who self-select office-based treatment with buprenorphine are essentially comparable to those seen in patients treated with methadone programs. While data thus far demonstrate that buprenorphine is almost as effective as methadone at promoting treatment retention, reducing illicit use of heroin and prescription opioids, reducing risky behaviors that transmit HIV and hepatitis, and is superior to methadone in terms of safety, further clinical data are still needed.
4. There are few absolute contraindications to the use of buprenorphine. However, the experience and skill levels of treating physicians can vary considerably, as can access to the resources needed to treat comorbid medical or psychiatric conditions—all of which may make the use of buprenorphine more complex.
5. Some patients who could benefit from treatment with buprenorphine may face challenges to successful treatment through office-based care, either because they require the structure afforded by a methadone program or because they lack access to office-based treatment or such care is not covered. It is important to conduct a targeted assessment of every patient to confirm that the provider has resources available to meet the patient's needs.
6. Patients should be assessed for a broad array of biopsychosocial needs in addition to opioid use and addiction, and should be treated, referred for help, or both in meeting all their care needs, including medical care, psychiatric care, and social assistance. In addition to the benefit they obtain directly from medication, patients should be encouraged to develop relapse prevention skills and to make active changes in their life circumstances to reduce relapse risk.
7. Most patients are likely to stabilize on 8 to 24 mg of buprenorphine per day, although some may need doses of up to 32 mg/day. In the absence of specific contraindications, the buprenorphine/naloxone combination is preferred to the monoproduct.
8. Although drug interactions with buprenorphine do occur, they are not always clinically relevant in a particular patient and do not necessarily prohibit the concomitant administration of buprenorphine with other drugs (although adjustment of the buprenorphine dose may be necessary). In any case, patients should be informed of the potential for drug interactions.
9. Physicians who wish to use buprenorphine should seek a level of comfort with this treatment approach. This encompasses knowledge of applicable practice standards and guidelines, familiarity with the evidence supporting recommended treatment strategies, protocols for treatment or referral of patients with complicating conditions (eg, severe depression, pain, or pregnancy), and an understanding of applicable federal, state, and local laws and regulations.
10. Physicians who treat opioid-dependent patients with buprenorphine should engage in continued medical education and other professional activities to keep current with the evolving knowledge base regarding optimal use of medication-assisted therapies in general with a particular focus on buprenorphine.

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