



Virginia DMHMRSAS Office of Substance Abuse Services
Guidance Bulletin No. 2004-01
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Title: Buprenorphine Products for the Pharmacologic Management of Opioid Addiction

Advisory (Evidence-Based Practice)

Mandate (Requirement)

RECIPIENTS:

- Community Services Boards (CSBs), Behavioral Health Authorities (BHAs), and Local Government Departments (LGDs) with Policy Advisory CSBs (Executive Directors, SA Services Managers and Physicians)
- Opioid Treatment Program (OTP) Directors

PURPOSE: To provide general information about buprenorphine products for pharmacological treatment of opioid addiction, and about the need for CSBs to work with community physicians to improve treatment outcomes for individuals receiving office-based treatment for opioid addiction.

Providing comprehensive services in conjunction with medication is the most effective method of treating opioid addiction. It is important that buprenorphine be administered in conjunction with behavioral therapy and psychosocial support to ensure medication compliance and to increase patient functioning.¹ The ultimate success of buprenorphine will depend on its integration into a broader continuum of health care services that includes counseling for patients with substance use disorders. CSBs may be called upon to work with community physicians to improve treatment outcomes by providing behavioral treatment and counseling.

BACKGROUND: Buprenorphine has been studied for over 20 years². Buprenex ® has been marketed in the United States as a Schedule V parenteral opioid analgesic. Recent enacted legislation permitted certain buprenorphine products (Subutex® and Suboxone®) to be utilized for detoxification or maintenance purposes, and made those medications available for use in settings that do not require specific Federal/State licensure (i.e., physician offices).³ Office-based pharmacological treatment of opioid addiction constitutes a unique opportunity for partnership among public and private providers to help to close the “treatment gap.” It is intended to address several needs in accordance with public health objectives. These include increasing access to treatment for opioid addiction, offering treatment to patients outside the traditional methadone clinic system, and “mainstreaming” the treatment of opioid addiction by coordinating it with treatment of other medical conditions.⁴

Integrating treatment for opioid dependence into the mainstream of the healthcare delivery system increases the likelihood other medical conditions such as tuberculosis, hepatitis C, HIV and sexually transmitted diseases will be addressed during addictions treatment.⁵ Office-based treatment offers patients greater flexibility in treatment

¹ NAADAC, The Association for Addiction Professionals. NAADAC Lauds Buprenorphine Launch: Association Supports Counselor Involvement in New Drug Therapy. Press Release 10/12/02. <http://naadac.org/pressroom/index.php?PressReleaseID=15>. (accessed 10/6/03).

² NASADAD, *op. cit.* December 2002.

³ National Association of State Alcohol and Drug Abuse Directors (NASADAD). NASADAD Policy Paper: The Use of Medications in Substance Abuse Treatment, December 2002. Washington, DC. www.nasadad.org.

⁴ Substance Abuse and Mental Health Services Administration (SAMHSA)-Center for Substance Abuse Treatment (CSAT). The Use of Buprenorphine in the Pharmacologic Management of Opioid Dependence: A Curriculum for Physicians. Strain, E., ed. January 2001.

⁵ SAMHSA-CSAT, *op. cit.* January 2001.

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scheduling, may promote recovery by limiting patients' contact with other drug-abusing individuals, and may be particularly useful in areas where methadone patients travel long distances to receive their opioid therapy. Treatment of patients in physicians' offices and in the same manner as patients with other chronic illnesses such as diabetes or high blood pressure may reduce the stigma associated with the disease and may make treatment more attractive for certain individuals.

LEGISLATIVE AUTHORITY: Buprenorphine is the first narcotic drug available for the treatment of opioid addiction that can be provided in physicians' offices as well as addiction treatment facilities. New legislation signed into law on October 17, 2000, known as **the Children's Health Act of 2000**, includes Sections 3501-3502 of **the Drug Addiction Treatment Act (DATA) of 2000**. Prior to the passage of this law, it was illegal for physicians to prescribe narcotics to patients for the purpose of treating opioid addiction. DATA 2000 allows "qualified physicians" (*see Provider Qualifications, below*) to treat patients for opioid addiction with Schedule III-V narcotic controlled substances that are approved by the **Food and Drug Administration (FDA)**. It permits physicians who meet certain qualifications to treat these patients with opioid medications in office-based settings without the requirement that they be referred to opioid treatment programs (OTPs), as previously required under federal law.⁶ In 2002, the **Drug Enforcement Administration (DEA)** reclassified buprenorphine from a Schedule V to a Schedule III narcotic, based on a re-evaluation of available evidence on its potential for abuse, diversion, dependence and side effects.⁷ The DEA assigns qualified physicians a special identification number, allowing them to dispense and/or prescribe under the authority of their DEA practitioner registration.^{8, 9}

In October 2002, **Reckitt Benckiser** received FDA approval to market two products for use in opioid dependence treatment: a buprenorphine monotherapy product (Subutex®) and a buprenorphine/naloxone combination product (Suboxone®).¹⁰ Subutex® and Suboxone® are the only Schedule III, IV or V medications to have received FDA approval for use in the treatment of opioid addiction. Other forms of buprenorphine (e.g., Buprenex®) are not approved for the treatment of opioid addiction. Neither the FDA approval nor the provisions of DATA 2000 affect the use of other Schedule III, IV or V medications that are not approved for the treatment of addiction.¹¹ Approval of buprenorphine products for office-based treatment does not affect the treatment standards of methadone which, per Title 42 Code of Federal Regulations Part 8 (42 CFR Part 8), must be dispensed for the treatment of opioid addiction only in the context of an opioid treatment program (OTP).¹²

Amendments to the Children's Health Act of 2000 (Public Law 106-310) and related regulations (Final Rule: 21 CFR Part 291, 42 CFR Part 8) created a new accreditation program managed by the **Substance Abuse and Mental Health Services Administration's (SAMHSA) Center for Substance Abuse Treatment (CSAT)** and replaced a 30-year old inspection program conducted by the Food and Drug Administration.¹³ CSAT's Division of Pharmacologic Therapies (DPT) is responsible for the day-to-day regulatory oversight of OTPs and manages

⁶ Federation of State Medical Boards of the United States, Inc. April 2002. <http://www.fsmb.org/policy.htm> (accessed 4/22/04).

⁷ Substance Abuse and Mental Health Services Administration (SAMHSA)-Center for Substance Abuse Treatment (CSAT) Buprenorphine Website, "About Buprenorphine Therapy", <http://www.buprenorphine.samhsa.gov/about.html> (accessed 6/2/04).

⁸ SAMHSA-CSAT Buprenorphine Website, "Physician Waiver Qualifications," http://buprenorphine.samhsa.gov/waiver_qualifications.html, (accessed 4/22/04).

⁹ Drug Enforcement Administration (DEA) Diversion Control Website, "Frequently Asked Questions (FAQs)," <http://www.deadiversion.usdoj.gov/drugreg/faq.htm> (accessed 6/2/04).

¹⁰ SAMHSA-CSAT About Buprenorphine Website, *op. cit.*

¹¹ SAMHSA-CSAT About Buprenorphine Website, *op. cit.*

¹² SAMHSA-CSAT About Buprenorphine Website, *op. cit.*

¹³ SAMHSA-CSAT Buprenorphine Website, "Legislation/Regulations," <http://www.samhsa.gov/centers/csat/content/dpt/regulations.htm>, (accessed 5/15/03).

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certification and accreditation processes. DPT approves waivers of the special registration requirements defined in the Narcotic Addiction Treatment Act and the Controlled Substances Act to allow qualified physicians (*see Provider Qualifications, below*) to practice opioid addiction therapy in office-based settings with Schedule III, IV or V narcotics.¹⁴ DPT also is responsible for training medical and substance abuse professionals on the use of medications such as buprenorphine.¹⁵

POLICY ISSUES:

PROVIDER QUALIFICATIONS: Under DATA 2000, prescription use of buprenorphine products (Suboxone ® or Subutex ®) for the treatment of opioid addiction is limited to physicians who meet qualifying requirements. Physicians' assistants (PAs) and nurse practitioners (NPs) may not prescribe buprenorphine products for the treatment of addiction even in states that allow them to prescribe Schedule III, IV or V drugs. Physicians may be considered qualified if they:¹⁶

- Meet one or more of the following training requirements:
 - Hold a subspecialty board certification in addiction psychiatry from the American Board of Medical Specialties;
 - Hold an Addiction certification from the American Society of Addiction Medicine;
 - Hold a subspecialty board certification in Addiction Medicine from the American Osteopathic Association;
 - Have completed not less than 8 hours of authorized training on the treatment or management of opioid-dependent patients. This training may include classroom situations, seminars at professional society meetings, electronic communications, or other media; (*See Resources for Buprenorphine Training Sessions, below*)
- AND meet both of the following criteria:
 - Have the capacity to provide or to refer patients for necessary ancillary services, such as psychosocial therapy;
 - Agree to treat no more than 30 patients at any one time in their individual or group practice (*unless treatment is provided through opioid treatment programs-OTPs*).

Before prescribing Suboxone ® or Subutex ®, qualified physicians must notify the Secretary of Health and Human Services (HHS) of their intent by submitting an application for a waiver. The agency within the HHS to be notified is the Substance Abuse and Mental Health Services Administration (SAMHSA); the Division of Pharmacologic Therapies (DPT) within the Center for Substance Abuse Treatment (CSAT) handles the notifications. For convenience, CSAT has developed a form that can be used for such notification (*attached*). **Questions may be directed to CSAT/DPT at (301) 443-7745.**

CSAT will communicate with the DEA, review the notification, and inform the DEA whether or not the physician is qualified as required by DATA. The DEA will issue a unique identification number that indicates that the physician is qualified under DATA. The physician then will be authorized to dispense and/or prescribe under the authority of his/her DEA practitioner registration. CSAT will send the physician a letter with the newly assigned DEA identification number. A new DEA registration

¹⁴ SAMHSA Fact Sheet: Frequently Asked Questions About Treatment for Opioid Addiction Using Buprenorphine. December 10, 2002.

<http://www.samhsa.gov/news/bupeFAQs.htm> (accessed 4/22/04).

¹⁵ SAMHSA-CSAT Buprenorphine Legislation/Regulations Website, *op. cit.*

¹⁶ Food and Drug Administration (FDA). 2002. Physician Information: Answers to Frequently Asked Questions, NDA 20-732, NDA 20-733, Page 36.

<http://www.fda.gov/cder/foi/label/2002/20732mdinfo.pdf>. (accessed 4/22/04).

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certificate will be issued to the physician that documents the new DEA number to be used in buprenorphine prescribing as well as the original DEA registration number assigned to the physician.

PROVIDING BUPRENORPHINE THERAPY THROUGH CSBs: For qualified CSB physicians to prescribe buprenorphine medications (Subutex® or Suboxone®), or for these medications to be supplied to the CSB through the Hiram W. Davis Medical Center Aftercare Pharmacy, patients must be admitted to and receiving treatment from the CSB. Subutex® and Suboxone® have been added to the state formulary. If CSBs choose to store small quantities of Suboxone® and Subutex® for induction dosing, or to fill prescriptions for CSB patients, they may order these products through the Aftercare Pharmacy. In addition to federal regulations, the CSB must adhere to the following **state regulations** regarding medication administration, storage or pharmacy operations remain in effect:

- Rules and Regulations for the Licensing of Providers of Mental Health, Mental Retardation and Substance Abuse Services & the Individual and Family Developmental Disabilities Support Waiver (12 VAC 35-105-790: Medication administration and storage or pharmacy operation);
- The Drug Control Act (§54.1-3400 et. seq. of the *Code of Virginia*);
- The Virginia Board of Pharmacy Regulations (18 VAC 110-20).
- Hiram W. Davis Medical Center Aftercare Pharmacy Policies (*attached*).

SUPPLY: Prescriptions written by qualified physicians will be valid at any pharmacy, but not all pharmacies carry these medications. If qualified CSB physicians treat patients with buprenorphine products but do not maintain supplies of tablets for induction, they must establish relationships with one or more specific pharmacies that can provide initial doses, with specific instructions for patients to return to the CSB for induction and follow-up prescriptions. For more information about state-specific requirements for maintenance of buprenorphine products in office settings, or for instructions on establishing relationships with suppliers of the medication for induction use, refer to the **Suboxone® website (www.suboxone.com) or call 1-877-SUBOXONE.**

COST: The cost of therapy could be a major limitation to the use of buprenorphine products (Suboxone® and Subutex®). For current pricing, refer to the most recent Hiram W. Davis Medical Center Aftercare Pharmacy price list. At present, it is not known if third party payers will reimburse for these medications. *There has been no increase in federal funds to allow for expansion of treatment capacity through the use of medications. However, there is no prohibition from using SAPT block grant funds to fund treatment for individuals found to meet the criteria for initiation of therapy.*

PREVENTING DIVERSION AND ABUSE: The following guidelines are suggested:¹⁷

- Initiate treatment with supervised administration, progressing to unsupervised administration as patients' clinical stability permits;
- Use Suboxone® exclusively unless contraindicated (e.g. pregnancy), when Subutex® can be used, but then only with supervision;
- Employ treatment contracts to make explicit what is expected of patients in terms of their cooperation and involvement in addiction treatment (*See Patient Responsibilities, below*);
- Avoid giving more than a two-week supply of buprenorphine medications, even for stabilized patients;

¹⁷ Food and Drug Administration (FDA). 2002. Physician Information: Answers to Frequently Asked Questions, NDA 20-732, NDA 20-733, Page 36. <http://www.fda.gov/cder/foi/label/2002/20732mdinfo.pdf>. (accessed 4/22/04).

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- Have plans in place to deal with patient requests for replacement of prescriptions or supplies of medication that are described as lost or stolen;
- Keep tight control of prescription pads and never sign incomplete prescription blanks;
- Write all numbers (quantity and strength) in both numbers and letters (similar to when writing checks);
- Request photo (or other) I.D. and Social Security number and maintain copies in the patient's record;
- When establishing relationships with pharmacies, discuss potential diversion problems and controls with them;
- Call the local police department if diversion of prescription medications is suspected.

CLINICAL GUIDELINES:

PHARMACOLOGICAL PROPERTIES: Buprenorphine is characterized pharmacologically as an *opioid partial agonist* with both agonist and antagonist properties, depending on dosage and clinical circumstances. Buprenorphine can be abused (i.e. its opioid agonist effects can produce euphoria and respiratory depression), particularly by individuals who are not physically dependent upon opioids, but its maximal effects are significantly less than those of full agonists such as heroin and methadone.¹⁸ Having both agonist and antagonist properties enhances the safety profile of buprenorphine, making it less likely to precipitate opioid overdose and reducing its potential for diversion.¹⁹ The combination of buprenorphine and naloxone (a pure antagonist) in Suboxone® deters patients dependent on *mu* opioid receptor agonists (heroin, methadone, hydrocodone, oxycodone, etc.) from injecting the tablets and further decreases the likelihood of diversion and abuse. At lower doses, buprenorphine acts as an opioid agonist, enabling opioid-dependent individuals to discontinue opioids without experiencing withdrawal. At moderate doses, the agonist effects reach a plateau (“ceiling effect”). At higher doses, the opioid antagonist properties dominate and, in certain circumstances, higher doses of buprenorphine can displace opioid agonists, precipitating withdrawal symptoms in acutely opioid-intoxicated individuals.²⁰ Buprenorphine is also a long-acting agent (it binds to the *mu* opioid receptors for a long time)²¹ so many patients may not need to take medication every day. These properties may offer some treatment advantages over the use of methadone.

PHASES OF TREATMENT: The three phases of buprenorphine therapy include induction, stabilization and maintenance.

- **Induction phase:** The induction phase is the medically monitored (supervised) startup of buprenorphine therapy; it should be initiated in the physician's office. Most patients can be inducted over 2-3 days using the combination product Suboxone®. During the induction phase, buprenorphine products are administered when an opioid-dependent individual has abstained from using short-acting opioids for at least six to eight hours, and when individuals on long-acting opioids have abstained for more than 24 hours and are in the early stages of withdrawal. Buprenorphine treatment cannot begin until patients are exhibiting objective signs and symptoms of opioid withdrawal. If patients are not in the early stages of withdrawal (i.e., when they have other opioids in the bloodstream), the administration of buprenorphine can precipitate withdrawal.^{22, 23}

¹⁸ SAMHSA-CSAT About Buprenorphine Website, *op. cit.*

¹⁹ NASADAD, *op. cit.* 2002.

²⁰ SAMHSA-CSAT About Buprenorphine Website, *op. cit.*

²¹ Opiate Medication Initiative for Rural Oregon Residents (OMIROR). November 2003. Treating Opiate Dependence in Rural Communities: A Guide for Developing Community Resources. Northwest Frontier Addiction Technology Transfer Center (ATTC). http://www.nfattc.org/Final_OMIROR_Report.pdf

²² Health Resources and Services Administration (HRSA) Bureau of Primary Health Care (BPHC). December 5, 2003. Use of Buprenorphine in Health Center Substance Abuse Treatment Programs, in Program Assistance Letter, Document # 2004-01.

²³ Food and Drug Administration (FDA). 2002. Physician Information: Answers to Frequently Asked Questions, NDA 20-732, NDA 20-733, Page 31. <http://www.fda.gov/cder/foi/label/2002/20732mdinfo.pdf>. (accessed 4/22/04)

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- **Stabilization phase:** The stabilization phase begins when patients who have discontinued or greatly reduced the use of their drug of abuse no longer have cravings and are experiencing few or no side effects. The buprenorphine dose may need to be adjusted during this phase. Once stabilization has been achieved, the long half-life of buprenorphine sometimes makes it possible to switch patients to alternate-day dosing.²⁴ Psychosocial counseling is a priority during the stabilization phase.²⁵
- **Maintenance phase:** The maintenance phase is reached when the patient is doing well on a steady dose of buprenorphine (preferably Suboxone®, the buprenorphine/naloxone combination product). There are few reasons other than pregnancy to use Subutex® (buprenorphine alone). The length of time of maintenance therapy is individualized and may be indefinite.²⁶ Patients should receive ongoing assessments and urine drug screens.²⁷

Initially patients should be seen daily while induction is being completed and at least weekly until well stabilized, when they may be seen no less frequently than every four weeks.²⁸ It is recommended that physicians determine the length of treatment for buprenorphine according to individual patients' needs and that patients be actively involved in the development of their treatment plan. The length of treatment may be as short as a few days for medical withdrawal (detoxification) services to as long as several years for maintenance therapy.

Medically-supervised withdrawal (formerly referred to as “**detoxification**”) is an alternative to maintenance therapy for some patients who have achieved stabilization.²⁹ The optimal rate at which buprenorphine should be reduced is a matter of ongoing research. However, the dose can be decreased by as much as 50% per day with a mild withdrawal syndrome that generally becomes manifest several days after the last dose and can be treated with over-the-counter symptomatic remedies. One approach might include medical withdrawal of compliant patients slowly at a rate that the physician determines to be therapeutic, and medical withdrawal of non-compliant patients by decreasing the dose of buprenorphine by 50% daily.³⁰

More detailed information will be available in “**Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction,**” SAMHSA’s Treatment Improvement Protocol (TIP #40), which will be available in 2004 through SAMHSA’s National Clearinghouse on Alcohol and Drug Information (NCADI) by calling 1-800-729-6686. The TIP covers screening, assessment and diagnosis of opioid dependence and its associated problems and contains detailed protocols for the use of buprenorphine under a variety of clinical scenarios including use of buprenorphine with patients with co-occurring pain, psychological disorders or chemical dependency involving more than one substance.

DOSING: Subutex® and Suboxone® are administered sublingually as a single daily dose, usually 8 to 16 mg per day. Dosages should be adjusted over several days.³¹ Initial prescriptions may be limited to one-day doses for the first several days of treatment before providing prescriptions for several days’

supply at one time (“take homes”). During the induction phase patients receive 2-4 mg sublingually, are monitored for 2 hours, then are administered another dose of 2-4 mg. The first day’s dose should not

²⁴ HRSA-BPHC, *op. cit.* 2003.

²⁵ HRSA-BPHC, *op. cit.* 2003.

²⁶ Food and Drug Administration (FDA). 2002. Physician Information: Answers to Frequently Asked Questions, NDA 20-732, NDA 20-733, Page 31. <http://www.fda.gov/cder/foi/label/2002/20732mdinfo.pdf>. (accessed 4/22/04)

²⁷ McCance-Katz E. Advances in the Treatment of Opioid Dependence: Office-based Buprenorphine Treatment. Virginia Commonwealth University Division of Addiction Psychiatry, lecture handout, June 8, 2004.

²⁸ McCance-Katz E. Buprenorphine Treatment Protocol. Virginia Commonwealth University Division of Addiction Psychiatry. March 2004.

²⁹ HRSA-BPHC, *op. cit.* 2003.

³⁰ McCance-Katz E. *op. cit.* March 2004

³¹ OMIROR, *op. cit.* 2003.

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exceed 8 mg.³² If a patient continues to complain of withdrawal symptoms following 8 mg, symptomatic management with over the counter medications can be discussed.³³ However, this is not a common clinical situation. Eight mg of buprenorphine alleviates the abstinence symptoms of most patients.

When patients return on day two their dose may be increased by up to 8 mg. By day three, most patients have achieved a stable dose and this should be the maintenance dose. Patients need several days to stabilize on 16 mg and they should not receive dose increases immediately, although they may not be completely comfortable for several days after induction. The average maintenance dose is 16 mg daily. Some patients may require higher doses of up to 32 mg but this is rare. *The treatment goal is stabilization on the lowest dose that achieves the optimal effects (reduced cravings and drug use).*³⁴

CONSULTATION: “Effective treatment of drug addiction requires comprehensive attention to all of an individual’s medical and psychosocial co-morbidities. Pharmacological therapy along rarely achieves long-term success. Thus, Suboxone® and Subutex® treatment should be combined with concurrent behavioral therapies and the provision of needed social services.”³⁵ Special attention should be given to patients who are at risk for misusing their medications and those whose living or work arrangements pose an increased risk for misuse or diversion. Management of addiction in patients with co-occurring psychiatric disorders requires extra care, monitoring, documentation and consultation with or referral to mental health professionals.³⁶ The need to coordinate counseling and the provision of needed ancillary services is of such importance that physicians must attest to their capacity to refer patients when they submit their waiver application to SAMHSA. Ongoing communication between the physician and consultants is necessary to help patients achieve their treatment plan objectives. The formal treatment agreement between the patient and the physician should include notification of this aspect of treatment.

SIDE EFFECTS: Side effects of buprenorphine are similar to those of other opioids and include nausea, vomiting and constipation. Buprenorphine and buprenorphine/naloxone can precipitate the opioid withdrawal syndrome. Signs and symptoms of withdrawal may be assessed using standardized instruments such as the COWS (Clinical Opiate Withdrawal Scale)³⁷, the OOWS (Objective Opiate Withdrawal Scale)³⁸ or the SOWS (Subjective Opiate Withdrawal Scale.)²⁴ Signs and symptoms of opioid withdrawal include:³⁹

- Dysphoric mood
- Nausea/vomiting/diarrhea
- Muscle aches/cramps
- Lacrimation (tears)
- Rhinorrhea (runny nose)
- Dilated pupils
- Piloerection (“goose flesh”)
- Yawning
- Mild fever
- Insomnia
- Craving
- Anxiety/irritability

SELECTION CRITERIA (PATIENT SELECTION): The selection of patients is very important for safe and appropriate treatment and positive outcomes. Patient selection criteria should be utilized in order to

³² McCance-Katz, E. *op. cit.* June 2004

³³ McCance-Katz E. *op. cit.* March 2004.

³⁴ McCance-Katz E. *op. cit.* March 2004.

³⁵ HRSA-BPHC, *op. cit.* 2003, page 6.

³⁶ Federation of State Medical Boards of the United States, Inc. April 2002. Model Policy Guidelines for Opioid Addiction Treatment in the Medical Office. <http://www.fsmb.org/policy.htm>, (accessed 4/22/04).

³⁷ Wesson DR and Ling W. The clinical opiate withdrawal scale (COWS). *Journal of Psychoactive Drugs* 35: 253-259, 2003.

³⁸ Handelsman, et al. Two new rating scales for opiate withdrawal. *American Journal of Drug and Alcohol Abuse* 13(3):293-308, 1987.

³⁹ SAMHSA-CSAT About Buprenorphine Website, *op. cit.*

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identify individuals who may be appropriate candidates for office-based buprenorphine treatment, including those who:

- Have a diagnosis of opioid addiction;
- Are interested in treatment for opioid addiction;
- Have no contraindication to buprenorphine treatment;
- Are expected to be reasonably compliant with treatment;
- Are capable of understanding the risks and benefits of such treatment;
- Are capable of following safety precautions for buprenorphine treatment; and
- Agree with treatment plan after a review of treatment options.

DRUG INTERACTIONS, CAUTIONS AND CONTRAINDICATIONS: *Please refer to the Subutex® and Suboxone® package inserts (attached) for a complete list of drug interactions, contraindications, warnings and precautions.*

- **In some instances, relapse to opioid drug use can be life threatening. A number of deaths have occurred when addicts have intravenously misused buprenorphine, particularly when there is concomitant use of benzodiazepines, alcohol or other opioids. Patients should be warned of the potential danger of self-administration of benzodiazepines or other depressants while under treatment with Subutex® or Suboxone®.**
- Patients should tell their family members and friends that, in the case of emergency, the treating physician or emergency room staff should be informed that the patient is physically dependent on narcotics and that the patient is being treated with Subutex® or Suboxone.
- In the case of overdose, primary management should be the re-establishment of adequate ventilation with mechanical assistance of respiration, if required. Naloxone may not be effective in reversing respiratory depression produced by buprenorphine.
- Patients with hepatic (liver) disease may not properly metabolize these drugs; their doses may need to be adjusted and these patients should be observed for opioid toxicity or precipitated opioid withdrawal.
- Drugs that require extra precautions and may require dosage adjustments include ketoconazole, an antifungal medication frequently used with patients with HIV/AIDS; certain antibiotics; HIV protease inhibitors and non nucleoside reverse transcriptase inhibitors; and certain barbiturates used to control epilepsy (seizures).
- Buprenorphine products should be administered with caution in elderly or debilitated individuals, and those with severe hepatic, pulmonary or renal function.
- Subutex® and Suboxone® should not be administered to patients who have been shown to be hypersensitive (“allergic”) to buprenorphine.
- Suboxone® should not be administered to patients who have been shown to be hypersensitive to naloxone. Hypersensitivity to naloxone must be medically documented. Many patients associate withdrawal symptoms experienced when naloxone may have been emergently administered to them in an overdose situation as “allergy” to naloxone, when in fact, this is the intended side effect of the drug (i.e., reversal of opioid toxicity). Allergy to naloxone may also be proffered by patients seeking treatment with Subutex® which can more easily be diverted and will have a higher street value than Suboxone®.

PATIENT RESPONSIBILITIES: To improve outcomes with pharmacologic therapies provided in office-based settings, providers should inform patients of clinic procedures and protocols, hours of operation, phone numbers, procedures for making appointments, fees, proper medication administration and storage, side effects and precautions, rights and responsibilities, and other CSB-specific or physician

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practice-specific protocols or guidelines. The following “red flag” behaviors should be addressed with patients immediately, and providers should support patients in making appropriate responses to them:⁴⁰

- Missed appointments
- Running out of medications too soon
- Taking medications off schedule
- Not responding to phone calls
- Refusing urine or breath testing
- Neglecting to mention new medication or outside treatment
- Appearing intoxicated or disheveled in person or on the phone
- Frequent or urgent inappropriate phone calls
- Neglecting to mention change in address, job or home situation
- Inappropriate outbursts of anger
- Lost or stolen medication
- Frequent physical injuries or auto accidents
- Non-payment of bills

Information about patient responsibilities should be clearly articulated in a “treatment contract” which should be signed by both the patient and the physician or staff witness. The treatment contract should include at least the following components:^{41, 42, 43}

- **Voluntary participation**—Patients should freely and voluntarily agree to receive buprenorphine products for the treatment of opioid addiction, provided that they accept the conditions of the treatment contract.
- **Pregnancy**—Female patients should tell the physician if they are pregnant, plan to become pregnant or are breastfeeding; it is not known whether Subutex® or Suboxone® can harm unborn children or infants.
- **Use of other medications**—Patients should agree not to obtain medications (prescription or non-prescription, including vitamins and herbal supplements) from physicians, pharmacists, or any other source without the approval of the physician who provides the buprenorphine therapy. Mixing buprenorphine with other medications, especially benzodiazepines such as Valium, Klonopin, Ativan, Librium, Xanax, Midazolam and other drugs of abuse can be especially dangerous and may cause death.
- **Only as prescribed**—Patients should take their medications on time, and should not adjust their dose on their own. If patients desire a dose change, they should call for an appointment to discuss this with their physician.
- **Scheduled appointments**—Patients should agree to keep and be on time for all scheduled appointments while taking buprenorphine products. Missed appointments result in not being able to get medication until the next scheduled visit.
- **Compliance with required pill counts and urine tests**—Urine testing is a mandatory part of office maintenance. Urine samples and pill counts should be required at each visit.
- **Counseling and other referrals**—Patients should agree to keep appointments for any recommended psychosocial counseling (including 12-step or other self help programs) and to accept referrals for other ancillary services as mutually agreed upon by the physician and the patient.
- **Recovery and relapse**—Relapse to opioid drug use can be life threatening. The physician should be informed about a relapse before it is detected with urine testing, and the treatment plan should be adjusted accordingly.
- **Under the influence**—Patients are not to come to the program intoxicated or under the influence of alcohol or drugs. If they do, they will not be medicated and may be discharged from buprenorphine treatment.
- **Diversion**—Patients should agree not to sell, share or give any medication to other persons. Such mishandling is a serious violation that results in discharge. Patients should notify the physician immediately in case of lost or stolen medication. If a police report is filed, the patient should bring in a copy for the record.
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⁴⁰ OMIROR, op. cit. 2003.

⁴¹ Reckitt Benckiser Suboxone® brochure: Important Information for Patients: What You Need to Know About Your Treatment.

⁴² OMIROR, op. cit. 2003.

⁴³ McCance-Katz E. op. cit. March 2004.

GUIDANCE BULLETIN ADVISORY # 2004-01

TITLE: Buprenorphine Products for the Pharmacological Management of Opioid Dependence

DATE: July 14, 2004

- **Safe storage**—Medication may be harmful to children, household members, guests and pets. Patients should be instructed to store the medication in a safe place, out of the reach of children, and to call the poison control center or 911 if anyone other than the patient ingests the medication. Lost medication will not be replaced.
- **Other safety issues**—Patients should not drive, operate heavy machinery or perform other dangerous activities until they know how the medication affects them. Dangerous or inappropriate behavior that is disruptive to the clinic and others will not be tolerated and may result in discharge from treatment.

SOURCES OF ADDITIONAL INFORMATION:**Center for Substance Abuse Treatment (CSAT) Buprenorphine Information Center:** <http://www.buprenorphine.samhsa.gov/>

Phone: 866-BUP-CSAT (866-287-2728); Live operators are available to answer calls M-F from 8:30 a.m. to 5:00 p.m. EST.

SAMHSA Buprenorphine Physician Locator Web Site: http://buprenorphine.samhsa.gov/bwns_locator/index.htmlEmail: info@buprenorphine.samhsa.gov.**Federation of State Medical Boards (FSMB):** Model Guidelines for Opioid Treatment in the Medical Office.<http://www.fsmb.org/policy.htm>**Food and Drug Administration (FDA)/Center for Drug Evaluation and Research (CDER):**

Phone: 888-INFO-FDA for consumer inquiries and 301-827-6242 for media inquiries.

http://www.fda.gov/cder/drug/infopage/subutex_suboxone/default.htm**Join Together:** National Poll of Physicians on Barriers to Widespread Buprenorphine Use.http://www.jointogether.org/sa/issues/hot_issues/bupe/**National Association of State Alcohol and Drug Abuse Directors (NASADAD):**

NASADAD Policy Paper: The Use of Medications in Substance Abuse Treatment

<http://www.nasadad.org/Features/SATx&Meds.pdf>**Northwest Frontier Addiction Technology Transfer Center (ATTC), Opiate Medication Initiative for Rural Oregon ‘****Residents (OMIROR).** November 2003. Treating Opiate Dependence in Rural Communities: A Guide for Developing Community Resources. http://www.nfattc.org/Final_OMIROR_Report.pdf**Physician Information—Answers to Frequently Asked Questions:**<http://www.nasadad.org/Departments/Buprenorphine/20732mdinfo.pdf>**Substance Abuse and Mental Health Services Administration (SAMHSA).**

“Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction,” Treatment Improvement Protocol (TIP #40), available in 2004 through SAMHSA’s National Clearinghouse on Alcohol and Drug Information (NCADI).

Phone: 1-800-729-6686. Web: <http://www.health.org/>**Suboxone® Clinical Information Hotline and Website:** Phone: 877-SUBOXONE (1-877-782-6966) Web: www.suboxone.com**Virginia Department of Mental Health, Mental Retardation and Substance Abuse Services:**

Managed Withdrawal Training Manual. January 2003. (Call the Virginia Office of SA Services at 804-786-3906)

RESOURCES FOR BUPRENORPHINE TRAINING SESSIONS: You may contact the Suboxone® helpline (1-877-782-6966) or visit the Suboxone® website (www.suboxone.com), or you may contact any of the following organizations:

The American Academy of Addiction Psychiatry
7301 Mission Road, Suite 252
Prairie Village, KS 66208
Telephone: (913) 262-6161
E-mail: info@aaap.org
Web site: www.aaap.org

The American Society of Addiction Medicine
4601 North Park Ave. Arcade Suite 101
Chevy Chase, MD 20815
Telephone (301) 656-3920
E-mail: email@asam.org
Web site: <http://asam.org>

The American Psychiatric Association
1400 K Street N.W.
Washington, DC 20005
Telephone (888) 357-7924
E-mail: apa@psych.org
Web site: <http://www.psych.org>

American Osteopathic Association
142 East Ontario Street
Chicago, IL 60611
Telephone (800) 621-1773
E-mail: info@aoa-net.org
Web site: <http://www.aoa-net.org/>

**DMHMRSAS OFFICE OF SUBSTANCE ABUSE SERVICES CONTACT:
Denise Clayborn, (804) 371-2193 or (804) 786-3906.**

COPY TO:

- DMHMRSAS Office of SA Services Contract Pharmacist (Hope Bolger, R. Ph.)
- DMHMRSAS Chief Pharmacist (Janice Dyson, R. Ph.)
- DMHMRSAS Clinical Pharmacy Services Manager (Michele Thomas, Pharm.D., BCPP)
- DMHMRSAS Medical Director (James Evans, MD)
- DMHMRSAS Office of Human Rights
- DMHMRSAS Office of Licensing
- DMHMRSAS Office of Mental Health
- DMHMRSAS State Facility Directors