

Buprenorphine

in the Context of HIV—FACT SHEET

The Drug Addiction Treatment Act of 2000 opened the way for physicians to treat opioid addiction in their primary care patients by allowing them to prescribe opioid maintenance or detoxification with approved Schedule III, IV, or V medications. In 2002, the FDA approved buprenorphine for the treatment of opioid addiction.

ABOUT OPIOID ADDICTION

A history of drug use is common among HIV patients, as indicated by the fact that injection drug use is responsible for 30% of cumulative AIDS cases in the United States. National statistics indicate an estimated 750,000 and 1,000,000 regular heroin users and at least as many illicit users of prescription opioids. Though the development of addiction remains poorly understood, new evidence supports a physiologic basis for opioid addiction influenced by both genetics and environment. Studies have found that many persons with a history of addiction to opioids repeatedly relapse and require long-term maintenance to prevent morbidity and mortality. It is hypothesized that neuroadaptations to chronic drug exposure may lead to the long-term anhedonia that many opioid users experience; this may explain why many opioid users are unable to maintain long term abstinence.

OPIOID MAINTENANCE AND HIV

- When compared to untreated heroin users, *methadone* patients are:
 - 3-6 times less likely to become HIV infected.
 - If HIV-infected, more likely to access HIV treatment and less likely to be hospitalized.
- *Methadone* and *buprenorphine* have both been shown to substantially reduce the risk of heroin overdose.
- *Buprenorphine* has been shown to have a positive impact on adherence to HIV therapy.

BUPRENORPHINE VS. METHADONE

Safety: *Buprenorphine* is unlikely to cause respiratory depression and death in the case of overdose. These complications can occur with methadone.

Efficacy: Some studies suggest that persons requiring doses of methadone over 80mg continue to crave heroin on *buprenorphine* and will have a better outcome with methadone.

Accessibility: *Buprenorphine* has the potential to be far more accessible to patients than methadone (methadone is limited to highly-regulated clinics).

PHARMACOLOGY

Buprenorphine is a semi-synthetic derivative of thebaine, and acts as a partial opioid agonist. Like full agonists, it can produce typical opioid effects and side effects such as euphoria, pain relief, and respiratory depression. Yet unlike full agonists, *buprenorphine* is constrained by a “ceiling effect” (agonist effects increase linearly with increasing doses until they reach a plateau) thus respiratory depression is rare.

Buprenorphine is highly bound to plasma proteins. It is metabolized by the liver via the cytochrome P450 3A4 (CYP 3A4) enzyme system into norbuprenorphine and other metabolites. The half-life of *buprenorphine* is 24–60 hours. *Buprenorphine* has poor oral bioavailability and moderate sublingual bioavailability.

FORMULATIONS

- Suboxone[®], a sublingual tablet, comes in two dosage forms: 2 mg buprenorphine/0.5 mg naloxone and 8 mg buprenorphine/2 mg naloxone.
- Subutex[®], also a sublingual tablet, is available in 2 mg and 8 mg strengths.
- The naloxone is inactive when used sublingually as directed but will significantly attenuate euphoria if injected, lowering the potential for misuse.

INDICATIONS

Buprenorphine is indicated for the treatment of heroin and other illicit opioid addiction. It may be used both for maintenance and for managing withdrawal, in conjunction with appropriate psychosocial supports.

Buprenorphine:

- Alleviates and prevents withdrawal.
- Blocks the euphoric effects of opioids.
- Reduces the long term craving experienced by many persons with opioid addiction.

SIDE EFFECTS

Potential side effects are similar to those of other opioids and include nausea, vomiting, and constipation. Cases of liver enzyme elevations have been reported.

DRUG INTERACTIONS

Opioids

- Buprenorphine binds more tightly to opioid receptors than other opioids, thus:
- Buprenorphine precipitates opioid withdrawal syndrome if taken by an opioid dependent person who is not yet in withdrawal.
- Buprenorphine blocks the activity of other opioids, thus barring the use of opioids for pain management.

Benzodiazepines

There are case reports of deaths following the injection of buprenorphine with benzodiazepines. However, when benzodiazepines are taken as directed there is no contraindication.

HIV MEDICATIONS

Data are limited on interactions between buprenorphine and antiretroviral drugs. Studies have found no interaction with zidovudine. Efavirenz has been found to lower buprenorphine levels but with no clinical impact. Protease inhibitors may increase buprenorphine levels via CYP 3A4 inhibition; providers should be alert to the possible need for dose adjustment.

OTHER MEDICATIONS

As yet there is no data on interactions with CYP 3A4 inducers such as phenobarbital, carbamazepine, phenytoin, and rifampicin.

REQUIREMENTS

Only physicians may prescribe buprenorphine, and to do so, they must have specific qualifications:

- Certification in addiction medicine or addiction psychiatry, or completion of at least 8 hours of

authorized training, or previous participation in a clinical trial of buprenorphine.

- Prescribers must receive a waiver from the Substance Abuse and Mental Health Services Administration.
- Prescribers must have to the capacity to refer to appropriate psychosocial services.
- Each physician is permitted to treat a maximum of 30 patients at one time.

COST

Suboxone 16 mg/day costs \$9/day

RESOURCES

Buprenorphine and Primary HIV Care: Report of a Forum for Collaborative HIV Research Workshop: <http://www.hivforum.org/uploads/Buprenorphine.pdf>

Substance Use and Mental Health Services Administration <http://buprenorphine.samhsa.gov/>

The International Center for Advancement of Addiction Treatment <http://opiateaddictionrx.info/>

Pain Management/Addiction Management Medications and HIV Antiretrovirals: A Guide to Interactions for Clinicians (New York/New Jersey AETC, 06/2004): <http://www.aidsetc.com/pdf/p02-et/et-03-00/painmgmt.pdf>

New York State Department of Health AIDS Institute:

http://www.hivguidelines.org/public_html/center/clinical-guidelines/sub-gl/substance.htm

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.

<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat5.chapter.72248>

De Castro S, Sabate E. Adherence to heroin dependence therapies and human immunodeficiency virus/acquired immunodeficiency syndrome infection rates among drug abusers. *Clinical Infectious Diseases*. Dec 2003;15:37 Suppl 5:S464-7.

Lucas GM. Buprenorphine in primary HIV care clinics: a big pill to swallow. *Hopkins HIV Report*. 2004 Jul;16(4):5-7.

Johnson RE, Chutuape MA, Strain EC, Walsh SL, Stitzer ML, Bigelow GE. A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence. *N Engl J Med*. 2000 Nov 2;343(18):1290-7.

Joseph H, Stancliff S, Langrod J. Methadone maintenance treatment (MMT): a review of historical and clinical issues. *Mt Sinai Journal of Medicine*. 2000 Oct-Nov;67(5-6):347-64.

Mattick RP, Kimber J, Breen C, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews*. 2004;(3):CD002207.

Mattick RP, Ali R, White JM, O'Brien S, Wolk S, Danz C. Buprenorphine versus methadone maintenance therapy: a randomized double-blind trial with 405 opioid-dependent patients. *Addiction*. 2003 Apr;98(4):441-52.

McCance-Katz, E.F. Treatment of Opioid Dependence and Coinfection with HIV and Hepatitis C Virus in Opioid-Dependent Patients: The Importance of Drug Interactions between Opioids and Antiretroviral Agents. *Clinical Infectious Diseases* 2005;41:S89-S95.

The Medical Letter Vol. 45 (Issue W1150A) February 17, 2003. <http://www.medletter.com/freedocs/buprenorphine.pdf>

Moatti JP, Carrieri MP, Spire B, Gastaut JA, Cassuto JP, Moreau J. Adherence to HAART in French HIV-infected injecting drug users: the contribution of buprenorphine drug maintenance treatment. *AIDS*. 2000 Jan 28;14 (2):151-5.

Sambamoorthi U, Warner LA, Crystal S, Walkup J. Drug abuse, methadone treatment, and health services use among injection drug users with AIDS. *Drug and Alcohol Dependence*. July 1, 2000;60(1):77-89.

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