



# Indiana Medicaid Drug Utilization Review Board Newsletter

Volume 12 Issue 2

June 2009

## Indiana Medicaid DUR Board

Room W382

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## Office-Based Treatment of Opioid Dependence Doug Brink, Pharm.D., BCPP

### Introduction

The disease of opioid dependence has been described as a hidden epidemic in the United States, and the incidence appears to be increasing. Americans, while constituting only 4.6% of the world's population, have been consuming 80% of the global opiate supply.<sup>1</sup> The 2007 National Survey on Drug Use and Health found that approximately 12 million Americans over the age of 12 years had used prescription analgesics for nonmedical purposes in the past year.<sup>2</sup> That number reflected an increase from around 5 million in the 2002 survey. In addition, according to the same 2007 survey, just over 33 million teens and adults reported having used prescription opioids for nonmedical purposes at least once in their lifetime. These numbers do not include the use of the illicit drug heroin. In fact, the nonmedical use of prescription opioids is approximately 10 times higher than the reported incidence of heroin abuse. In the 2007 survey, it was found that heroin had been used by 3.8 million individuals at least once in their lifetime with 400,000 having used it in the past year.

The high frequency of nonmedical use of opioids correlates with an increasing need for substance abuse treatment. In the same 2007 survey, there were over 23 million people, almost 9.5% of the population, who needed treatment for a drug or alcohol use problem.<sup>2</sup> This included 7.5 million people (3% of the total population) who needed treatment not related to alcohol abuse, with another 3.6 million needing treatment for both illicit drug and alcohol use problems.

Of the 7.5 million individuals who needed treatment specifically for a drug-related problem, only 1.3 million reported receiving it. Thus, there were 6.2 million persons (2.5% of the total population) who needed treatment for a drug use problem independent of alcohol but did not receive it in 2007.

### Opioid Dependence Treatment

Opioid dependence is a brain disease and, like other brain diseases such as depression or schizophrenia, should be treated as such. Specifically, it is a dopamine-related disorder. The human brain rewards behaviors conducive to survival (e.g. eating) by stimulating dopamine activity to create a reinforcing, pleasurable sensation. Similarly, opioids increase dopamine activity in the nucleus accumbens (the "reward center" of the brain) which reinforces drug-taking behavior.<sup>3</sup> Excessive or prolonged use of opioids can lead to physiologic changes in brain chemistry and receptor function that makes stopping the drug difficult and, depending on genetic and other factors, predisposes to abuse and addiction. Individuals who seek opioid dependence treatment often describe different reasons for their dependence. Many inadvertently become dependent after being appropriately prescribed painkillers that were continued after the need for pain relief had passed. Other individuals become dependent when recreational drug use spirals out of control.

The treatment of opioid dependence has traditionally involved both nonpharmacologic and pharmacologic interventions.<sup>4</sup>

### Resources to Treat Opioid Dependence

- Free Resource Kits: [turntohelp.com](http://turntohelp.com) or 1-866-455-TURN
- Physician locator: [turntohelp.com](http://turntohelp.com), [naabt.org](http://naabt.org), or [buprenorphine.samhsa.gov](http://buprenorphine.samhsa.gov)
- Certification & other information for doctors: [DocOptIn.com](http://DocOptIn.com), 1-877-782-6966, [suboxone.com](http://suboxone.com), or [opioiddependence.com](http://opioiddependence.com).

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Nonpharmacologic interventions typically include counseling and involvement in 12 Step programs such as Narcotics Anonymous. The primary pharmacological treatment options for opiate dependence were opioid receptor blockers (e.g. naltrexone) or substitute opioids (e.g. methadone). Historically, substance abuse treatment has primarily occurred in specialized treatment centers. Such an approach is expensive, limits availability, and may increase the perceived stigma associated with seeking treatment.<sup>5</sup> In 2007, not being able to afford the cost of treatment was cited by 34% of the respondents who identified a need but did not receive treatment for illicit drug use.<sup>2</sup> In addition, over 30% did not receive treatment due to fear of stigma either in the community or at their place of employment. Another 14% said they were not sure where to go. Having more private office based treatment options available might alleviate some of these issues.

### The Drug Addiction Treatment Act of 2000

The laws governing the treatment of substance abuse with controlled substances changed in 2000 when the U.S. Congress passed the Drug Addiction Treatment Act (DATA 2000).<sup>6</sup> DATA 2000 allows physicians, who meet certain qualifications, to prescribe narcotic medications that have been specifically approved by the Food and Drug Administration (FDA) for the treatment of opioid dependence. For the first time such treatment was allowed outside of specially licensed treatment facilities (so-called methadone clinics) and can be done in a variety of settings, including a private physician's office. At the present time, buprenorphine is the only medication that is specifically approved by the FDA for this purpose. It is available as sublingual tablets in two different formulations for this indication: Subutex<sup>®</sup> (buprenorphine alone) and Suboxone<sup>®</sup> (buprenorphine plus naloxone).<sup>7</sup>

To provide buprenorphine as a deterrent to opioid abuse a waiver must be obtained as described at the DATA 2000 website.<sup>6</sup> In order to receive the waiver, a physician must hold addiction certification or complete eight hours of CME training. This training is provided by the American Society of Addiction Medicine, the American Academy of Addiction Psychiatry, the American Medical Association, the American Osteopathic Association, and the American Psychiatric Association. The guidelines also allow for other training or experience that is considered appropriate by individual State medical licensing boards (of the State in which the physician will provide maintenance or detoxification treatment). After meeting these requirements, an application is submitted to the Drug Enforcement Administration (DEA) who will assign a special identification number. DEA regulations require this ID number to be included on all buprenorphine prescriptions for opioid addiction therapy, along with the physician's regular DEA registration number. After registering to provide buprenorphine as a deterrent to opioid abuse, physicians are limited to treating a maximum of 30 patients at any one time for the first year. One year after the date on which a physician submitted the initial notification, they may submit a second notification of the need and intent to treat up to 100 patients.

### Buprenorphine Treatment of Opioid Dependence

Buprenorphine is a semi-synthetic opiate with partial agonist activity at the mu-opioid receptor and antagonist activity at the kappa-opioid receptor with a long duration of action.<sup>7,8</sup> It was first developed in the 1980s as an analgesic. In 2002, the sublingual versions, Subutex<sup>®</sup> and Suboxone<sup>®</sup>, were FDA approved for the treatment of opioid dependence. Both Subutex<sup>®</sup> and Suboxone<sup>®</sup> are Schedule III (C-III) controlled substances under the Controlled Substances Act. Subutex<sup>®</sup> (buprenorphine HCl) is recommended for use only during the induction phase of opioid dependence treatment, the first 1 to 3 days, or in patients who are hypersensitive to naloxone. Suboxone<sup>®</sup>, the combination of buprenorphine and naloxone, is recommended to be initiated as rapidly as possible after the risk for precipitating withdrawal has passed. There are no documented differences in the clinical effects of Subutex<sup>®</sup> and Suboxone<sup>®</sup> and they are considered interchangeable. The naloxone present in Suboxone<sup>®</sup> has no effect when the medication is given orally. It is present so that if the medication is abused by the injectable route, full narcotic antagonism will occur rather than the partial agonist effects seen after oral administration.<sup>7,8</sup>

There are three phases of opioid dependence treatment: induction (up to one week), stabilization (up to two months), and maintenance (two months or greater).<sup>8</sup> When initiating induction, patients should have taken their last dose of an opiate at least four hours prior to starting buprenorphine. To avoid precipitating acute withdrawal symptoms, it is preferable that patients already show early symptoms of acute opiate withdrawal (sweating, lacrimation, dilated pupils, etc.). On day one, 8 mg of buprenorphine (Subutex<sup>®</sup> or Suboxone<sup>®</sup>) is recommended and supervised administration should be considered. When used as a deterrent to opioid abuse, buprenorphine is recommended to be given as a single daily dose. On day two, the patient should be evaluated for withdrawal symptoms and 12 – 16 mg of buprenorphine administered. If Subutex<sup>®</sup> is used for induction, a switch to buprenorphine plus naloxone (Suboxone<sup>®</sup>) should be considered beginning on day two and be initiated as soon as possible (when withdrawal symptoms are not present). The dose should be titrated as rapidly as possible to the target as clinical studies found a higher drop-out rate associated with more gradual induction.<sup>7</sup> The target dose of buprenorphine is 16 mg/day with doses in the range of 12 to 16 mg/day being common.<sup>8</sup> The dosage range recommended by the manufacturer is 4 – 24 mg/day.<sup>7</sup> The maximum recommended dose is 32 mg/day, and it should be remembered that as the dose of buprenorphine increases the agonist effect decreases as the antagonist properties proportionately increase.

Common adverse effects of buprenorphine are similar to those of other opioid agonist agents and include constipation, nausea, itching, dry mouth, and sedation.<sup>7</sup> Orthostatic hypotension is possible and hepatic toxicity has been reported, especially after the intravenous use of crushed tablets.

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Impairment in concentration and coordination may be seen, especially during induction and following dose increases, therefore, caution should be exercised during those periods. Respiratory depression has also been reported, but is generally only seen following intravenous administration. The risk for this adverse event is substantially reduced by the presence of naloxone in Suboxone®.

The safety and efficacy of buprenorphine as a deterrent to opioid abuse was established in three controlled trials prior to FDA approval for this indication. Almost 5,000 patients were studied using the drug or placebo in combination with psychosocial counseling. Efficacy has not been assessed as a sole component of treatment without any counseling provided. When used as part of a comprehensive program in controlled studies, significantly more individuals were retained in treatment and had negative urine drug screens on active drug compared to placebo.<sup>7</sup> Similar results have been documented in a "real-world" setting with treatment retentions rates of over 60% and evidence of misuse of drugs or alcohol during treat-

ment documented at less than 25%.<sup>9</sup> Clinical trials comparing buprenorphine to methadone have shown comparable efficacy.<sup>8,10</sup>

### Conclusion

Buprenorphine, when combined with counseling and/or 12 Step programs, can be effectively used as a deterrent to opioid abuse and dependence. Under the provisions of the DATA 2000, office-based providers now have the opportunity to provide assistance to patients struggling with opiate use problems without having to refer them to a specialized treatment center. Buprenorphine possesses relatively low abuse potential, especially when combined with naloxone, and appears safe and effective when used as a deterrent to opioid abuse. To provide buprenorphine as a deterrent to opioid abuse a waiver must be obtained.<sup>6</sup> In order to receive the waiver, a physician must hold addiction certification or complete eight hours of CME training. For more information, interested doctors can use the following resources: DocOptIn.com, 1-877-782-6966, suboxone.com, or opioiddependence.com.

### References

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**Program Assistance**

All prior authorization requests or questions regarding the PDL should be directed to the ACS Clinical Call Center at 1-866-879-0106.

**PDL Listing**

The fee-for-service PDL listing may be found at the following Web site:  
<http://www.indianapbm.com/>

**Top 20 Drugs for 1Q 2009**

Top 20 Drugs 1 <sup>st</sup> Quarter 2009 Ranked by Total Amount Paid		
Drug	Total Claims	Total Paid
Aripiprazole	10,429	\$4,264,454.94
Quetiapine Fumarate	11,824	\$3,543,616.15
Olanzapine	6,184	\$3,158,338.88
Antihemoph.FVIII Plas/ Alb Free	98	\$3,015,032.05
Risperidone	14,086	\$2,739,535.27
Antiheoph. Factor, Hum. Rec.	71	\$1,993,469.18
Topiramate	6,218	\$1,901,801.41
Insulin	10,038	\$1,626,716.42
Lamotrigine	7,280	\$1,568,094.37
Ziprasidone HCL	4,392	\$1,421,841.18
Oxycodone HCL	5,309	\$1,420,848.23
Levetiracetam	5,035	\$1,331,640.66
Divalproex Sodium	10,709	\$1,267,213.18
Fluticasone/Salmeterol	5,604	\$1,136,628.75
Duloxetine HCL	7,165	\$980,857.23
Amphet. Asp/Amphet./ D-Amphet.	7,437	\$980,612.75
Atorvastatin Calcium	7,973	\$941,579.97
Palivizumab	475	\$938,453.14
Methylphenidate HCL	9,062	\$931,733.19
Clopidogrel Bisulfate	5,873	\$862,818.19

Top 20 Drugs 1 <sup>st</sup> Quarter 2009 Ranked by Total Number of Claims Paid		
Drug	Total Claims	Total Paid
Hydrocodone/APAP	44,268	\$346,726.46
Aspirin	39,556	\$34,788.72
Docusate Sodium	35,707	\$72,660.41
Alprazolam	33,106	\$190,029.25
Calcium Carb/Vit D	32,124	\$65,822.51
Acetaminophen	31,011	\$77,153.23
Multivitamins	27,664	\$39,106.64
Loratadine	25,423	\$237,272.83
Clonazepam	23,620	\$109,086.56
Lorazepam	20,501	\$112,722.04
Albuterol	20,172	\$606,189.14
Multivitamins with Minerals	15,705	\$42,691.48
Omeprazole	15,123	\$458,390.63
Lisinopril	14,114	\$52,129.30
Risperidone	14,086	\$2,739,535.27
Levothyroxine Sodium	13,508	\$93,251.13
Ferrous Sulfate	13,453	\$14,697.26
Amoxicillin Trihydrate	12,370	\$81,985.10
Diazepam	12,109	\$322,419.14
Quetiapine Fumarate	11,824	\$3,543,616.15