



## **PCSS Guidance**

**Topic:** Treatment of opioid dependent adolescents and young adults using sublingual buprenorphine

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**Guideline Coverage:**

None current

**Clinical Questions:**

1. What is the research evidence for the treatment of opioid dependent youth with buprenorphine?
2. What special issues should be considered when treating adolescents with buprenorphine?

**Background:**

While the use of heroin has remained low and stable (at approximately 1%), the use of non-heroin opioids, the second most commonly used illicit drug among youth has almost doubled over the past decade. (5 to 9%)<sup>1</sup>. Correspondingly, there has been a ten-fold increase in adolescent admissions to publicly funded substance abuse treatment programs for non-heroin opioid use problems during the same period (0.2 to 2.2%)<sup>2</sup>. Further, treatment-seeking opioid dependent youth, with short histories of dependence on any type of opioid, present with complex co-occurring treatment issues such as psychiatric disorders, injection-drug use and sexual behavior related HIV risk, abscesses, Hepatitis-C infection, school-drop out, legal problems, etc.<sup>3,4</sup>. Currently, most youth who enter treatment receive usual care consisting of brief detoxification followed by psychosocial treatments, commonly in outpatient and sometimes in residential settings, even though these interventions have not been well studied.

Buprenorphine, a partial opioid agonist, with Food and Drug Administration (FDA) approval for the treatment of opioid dependence for those 16 years and older has been well established as an effective treatment of opioid dependent adults. However, the empirical evidence for treatment of opioid dependent youth with buprenorphine is emerging and it has been shown to be effective when combined with psychosocial treatments. In one study, 36 opioid dependent adolescents ages 13-18 years were randomly assigned to a 28-day outpatient treatment with

either sublingual buprenorphine or oral clonidine; both groups received 3 times weekly behavioral counseling and incentives contingent on opiate abstinence. Those who received buprenorphine compared to those on clonidine had higher rates of treatment retention, opiate negative urines and higher rates of transfer to oral naltrexone<sup>5</sup>. In the second study (a NIDA Clinical Trials Network sponsored multisite study), 152 opioid dependent youth aged 15-21 were randomized to either sublingual buprenorphine/naloxone (longer treatment condition) for 12-weeks or a 14-day buprenorphine/naloxone taper (detoxification condition), with each arm being offered weekly group and individual drug counseling. During weeks 1-12, those in the longer treatment condition compared to the detoxification condition had significantly fewer opioid-positive urines, better retention, less self-reported opioid use and less injection drug use. Buprenorphine/naloxone was well tolerated (up to a maximum dose of 24mg/day) and no medication-related serious adverse effects were reported in either study.

### **General Principles:**

The following general principles are based on clinical experiences guided by current research with youth and the information available from the use of buprenorphine/naloxone in the treatment of opioid dependent adults. Most adolescents that have developed opioid dependence will be not able to remain abstinent without treatment. No single approach is suitable for all individuals; treatment should be comprehensive, and tailored to meet individual needs. In most cases, treatment should include both opioid agonist medication as well as behavioral therapies.

Prior to beginning medication-assisted therapy, all adolescents should have a complete evaluation including a thorough substance use history to confirm the diagnosis of opioid dependence, medical, mental health, vocational and psychosocial histories and physical exam, and all active problems should be addressed so that they do not interfere with recovery. Routine laboratory tests, particularly urine toxicology tests to confirm opioid use and to evaluate concomitant benzodiazepine dependence (because of its potential for death from overdose), and liver enzymes to assess hepatic function are recommended. Clinicians treating adolescents should take advantage of the availability of parents or guardians for authority and structure whenever possible to improve adolescent treatment adherence, allow for prompt intervention when a relapse occurs and minimize diversion risk.<sup>6</sup> However, most states have laws that allow adolescents to seek treatment for substance use disorders without parental consent; in these cases the adolescents confidentiality should be respected.<sup>7</sup>

### **Induction, Dosing and Duration of Treatment:**

We recommend observed induction for adequate dosing, education regarding adherence and parental monitoring of medication adherence and adverse effects of sedation, drowsiness, etc. The relative long half-life of buprenorphine permits once- daily dosing, though, if preferred, doses may be given 2-3 times a day. In studies, maintenance dosing has ranged from 2-24mg/day with 59% of patients

stabilized on 9-16 mg/day.<sup>4</sup> It is considered optimal to dose until the youth no longer reports withdrawal symptoms or craving for opioids. Since there is no scientific evidence on the optimal duration of buprenorphine treatment we recommend that there be no hurry to wean these youth off buprenorphine and that the length of treatment (up to a year or longer) be determined based on progress and in collaboration with patients and in the case of minors, their legal guardians. Medications should be tapered slowly to avoid withdrawal symptoms and/or resurgence of cravings.

### **Recommendations:**

Level of evidence: **Low - clinical experience and limited research**

1. Confirm the diagnosis of opioid dependence through history and urine drug testing. Screen for potentially confounding conditions such as benzodiazepine abuse or dependence, elevated liver enzymes, need for ongoing pain management, etc.
2. Provide education about the role and effectiveness of buprenorphine in the treatment of opioid dependence. Establish a set of expectations for patients beginning medication-assisted therapy, i.e. medication compliance, participation in psychosocial treatments, risks of concomitant alcohol and/or benzodiazepine abuse/dependence. Encourage patients to commit to abstinence from all psycho-active substances including alcohol which can be dangerous in combination with buprenorphine, and provide or refer ancillary treatments to patients who are unable to achieve abstinence.
3. The optimal length of opioid agonist treatment for adolescents with opioid dependence has not been well established. Available research suggests that continued sublingual buprenorphine/naloxone for at least 12 weeks significantly improves outcomes. Even patients with short histories of opioid dependence (i.e. 1-2 years) prior to starting medication may rapidly relapse after medication cessation.
4. Involve parents in treatment whenever possible. In many cases, parents may already be aware of their child's drug use and the adolescent may give permission to involve their parents. Ask the adolescent for permission to discuss diagnoses, treatment recommendations and progress with parents. In order to protect the therapeutic relationship with the adolescent, avoid sharing details that do not impact treatment. In some states written parental consent may be required prior to starting medication; prescribers should be cognizant of the laws in their state.
5. Follow patients regularly to monitor for side effects, adherence, lack of diversion and continued cravings and adjust the dosing accordingly.
6. Refer patients for psychosocial support to develop relapse prevention skills.
7. Monitor patients with random drug tests to assure that they are taking their medication and evaluate the risk from use of other illicit substances.

8. Screen for co-occurring psychiatric disorders. Symptoms of mild depression or inattention may improve with abstinence and can be monitored if not debilitating; more significant co-morbidities should be treated simultaneously using pharmacological and non-pharmacological treatments.
9. Address or refer to the appropriate agencies/provider for concomitant social issues that may hinder the progress of treatment such as unstable living arrangements, conflicts and/or substance use within the family home, academic disengagement, employment issues and legal problems, etc.
10. Be aware that buprenorphine and buprenorphine/naloxone are approved by the Food and Drug Administration for individuals aged 16 and up, due to lack of data available in those younger than 16.

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PCSS Guidances use the following levels of evidence\*:

**High** = Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate** = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low** = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low** = Any estimate of effect is very uncertain.

**Type of evidence:**

Randomised trial = **high**

Observational study = **low**

Any other evidence = **very low**

\* Grading quality of evidence and strength of recommendations

*British Medical Journal*, 2004;328;1490-

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