What is the recommended initial dose of oral Suboxone® in an intravenous heroin drug abuser?

There are several pharmacologic treatment options for addiction involving opioid use: methadone, buprenorphine (or buprenorphine with naloxone), and naltrexone.[1,2] Buprenorphine is a partial agonist at the mu-opioid receptor and is available alone or in combination with naloxone, an opioid antagonist. The combination product was designed to be less subject to diversion and injection misuse, compared to the mono-product – when taken orally or sublingually, naloxone has little effect on the efficacy of buprenorphine, but when injected, naloxone significantly attenuates the effects of buprenorphine and may lead to acute withdrawal. Thus, the combination is preferred to buprenorphine monotherapy for all patients, except those who are pregnant or with hypersensitivity to naloxone.[2]

There are several buprenorphine-containing products (see Table 1).[3-12] The combination products contain buprenorphine and naloxone in differing ratios and strengths.[9-12] All of the combination products and the generic mono-product are approved for treatment of opioid dependence.[6,9-12] The monotherapy implant (Probuphine®) is also approved for treatment of opioid dependence.[8] All other branded mono-products are approved for management of pain.[3,4,7]

Table 1. Buprenorphine-containing products and approved uses.[3-12]

Products	Dosage form	FDA-approved uses
Buprenorphine		
Belbuca®	Buccal film	Management of pain severe enough to require daily, around-the-clock, long-term opioid treatment, for which alternative therapy is inadequate
Buprenex®	Injection solution	
Butrans®	Transdermal film	
Buprenorphine HCl (generic)	Injection solution	
	SL tablet	Treatment of opioid dependence; preferred for induction
Probuphine®	Implant	Maintenance treatment of opioid dependence in patients who are clinically stable on low-to-moderate doses of a transmucosal buprenorphine-containing product (≤8 mg per day)
Buprenorphine/naloxone		
Bunavail®	Buccal film	Maintenance treatment of opioid dependence
Buprenorphine HCl + naloxone HCl (generic)	SL tablet	
Suboxone®	Buccal or SL film	Treatment of opioid dependence
Zubsolv®	SL tablet	Treatment of opioid dependence

FDA=Food and Drug Administration; HCl=hydrochloride; N/A=not applicable; SL=sublingual
[a]For alternative therapy, non-opioid analgesics, immediate-release opioids, or opioid combination products are listed in product labeling. Options considered inadequate are those that are not tolerated or not sufficient for management of pain.
[b]In treatment of opioid dependence, manufacturers recommend that the medications be used in addition to counseling and psychosocial support

Multiple guidelines have been published with recommendations on use of buprenorphine to treat opioid dependence.[1,13,14] Though not specific to intravenous heroin abuse, these recommendations are applicable to heroin users. Both the American Society of Addiction Medicine (ASAM) and the Substance Abuse and Mental Health Services Administration (SAMHSA) suggest that treatment begin with an induction phase, followed by stabilization and maintenance.[1,13] Only the generic buprenorphine mono-product and Suboxone® are approved for induction; however, the ASAM notes that other forms of the combination

product have been used by clinicians in patients addicted to short-acting opioids without other complications.[1] In patients transitioning from long-acting opioids and patients with hepatic impairment, the ASAM recommends the mono-product for initial treatment due to concerns for an increased risk of withdrawal with sublingually-absorbed naloxone.

The ASAM recommends initiation of therapy when patients are experiencing mild to moderate opioid withdrawal (at least 6-12 hours after the last use of heroin or other short-acting opioids, or 24-72 hours after the last use of long-acting opioids).[1] Use of the Clinical Opiate Withdrawal Scale (COWS), an 11-item scale designed to be administered by a clinician in both inpatient and outpatient settings,[15] is advised to determine severity of withdrawal, and scores of 11-12 or more are considered appropriate for safe induction of buprenorphine.[1] Induction is recommended in the prescriber's office, to reduce the risk of precipitated opioid withdrawal, but home-based induction may be recommended if the patient or prescriber is experienced with use of buprenorphine.

The initial dose of buprenorphine recommended by the ASAM is 2-4 mg.[1] The patient should be monitored for signs of precipitated withdrawal. If 60-90 minutes have passed without onset of withdrawal, additional doses may be administered in increments of 2-4 mg. Repeated assessment using COWS is recommended. Once it is established that the initial doses are well tolerated, the doses may be increased fairly quickly to a dose that provides stable effects for 24 hours and is clinically effective. After induction and titration, the ASAM asserts that the average buprenorphine dose is usually at least 8 mg per day. If patients are continuing to use opioids, the ASAM recommends considering a dose increase by 4-8 mg to a daily dose of 12-16 mg or more. The maximum recommended dose is 24 mg per day; there is limited evidence demonstrating the relative efficacy of higher doses. Table 2 lists target doses recommended for maintenance treatment.

Table 2. Recommended maintenance treatment doses for buprenorphine-containing products.[2] Adapted from the SAMHSA 2016 Advisory.

Products	Available strengths	Recommended once-daily maintenance dose	
		Target	Range
Generic mono-product	2 mg 8 mg	16 mg	4 mg to 24 mg
Generic combination product	2 mg/0.5 mg 8 mg/2 mg	16 mg/4 mg	4 mg/1 mg to 24 mg/6 mg
Bunavail®	2.1 mg/0.3 mg 4.2 mg/0.7 mg 6.3 mg/1 mg	8.4 mg/1.4 mg	2.1 mg/0.3 mg to 12.6 mg/2.1 mg
Suboxone®	2 mg/0.5 mg 4 mg/1 mg 8 mg/2 mg 12 mg/3 mg	16 mg/4 mg	4 mg/1 mg to 24 mg/6 mg
Zubsolv®	1.4 mg/0.36 mg 2.9 mg/0.71 mg 5.7 mg/1.4 mg 8.6 mg/2.1 mg 11.4 mg/2.9 mg	11.4 mg/2.9 mg	2.9 mg/0.71 mg to 17.2 mg/4.2 mg

Dosing recommendations from the manufacturer of Suboxone® are aligned with the ASAM recommendations.[11] The manufacturer suggests that patients with short-acting opioid dependence and experiencing moderate withdrawal should receive an initial buprenorphine/naloxone dose of 2 mg/0.5 mg or 4 mg/1 mg and titrate upwards in 2 or 4 mg increments of buprenorphine, at approximately 2-hour intervals, under supervision, to 8 mg/2 mg. On Day 2 of induction, a single dose of up to 16 mg/4 mg of Suboxone® is recommended. For maintenance, the dose should be adjusted in increments of 2 mg/0.5 mg or 4 mg/1 mg to a level that suppresses opioid withdrawal and retains the patient in treatment with a target in the range of 4 mg/1 mg to 24 mg/6 mg.

Notably, the manufacturer of Suboxone® states that patients who are dependent on heroin or other short-acting opioids may be inducted with either Suboxone® or with the generic sublingual mono-product, and that the first dose should be administered when objective signs of moderate opioid withdrawal appear, within 6 hours of the patient's last dose opioid dose.[11]

In a recently published review of sublingual and transmucosal buprenorphine for opioid use disorder, SAMHSA states that induction strategies vary depending on individual patient variables and type of opioids used.[2] They refer to the Providers' Clinical Support System for Medication Assisted Treatment (PCSS-MAT), which suggests a similar strategy to the approach outlined by the ASAM (see above) for office-based induction.[16] The PCSS-MAT also discusses strategies for home-based induction. In 1 model, they describe administration of the Subjective Opioid Withdrawal Scale (SOWS), a 16-item scale, prior to initiation of therapy to determine severity of withdrawal, with a minimum recommended score of 17 or more. The initial recommended dose is 1-2 mg, then increased by increments of 1-2 mg in approximately 2-hour intervals to a target of 8 mg in the first day or 16 mg if approved by phone. On Day 2, the total dose from the previous day is recommended as a starting dose, then titrated in 2 mg increments in 2-hour intervals to a maximum of 16 mg or 24 mg if approved by phone. The patient is advised to follow-up with an office visit between Days 3 and 7.

The ASAM recommends frequent (weekly, at a minimum) visits until patients are stable; once deemed stable, patients may be seen less often but at least monthly.[1] Urine drug testing is advised, to monitor for adherence to buprenorphine and to address use of prescription and illicit substances (e.g., opioids, benzodiazepines, amphetamines). They note that there is no recommended length of treatment and state that tapering and discontinuing buprenorphine is a slow process that may require several months. SAMHSA also states that the optimal duration of buprenorphine treatment is unclear, and discontinuation of therapy should be based on clinical judgment and a mutual agreement between the prescriber and patient.[2]

References:

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