



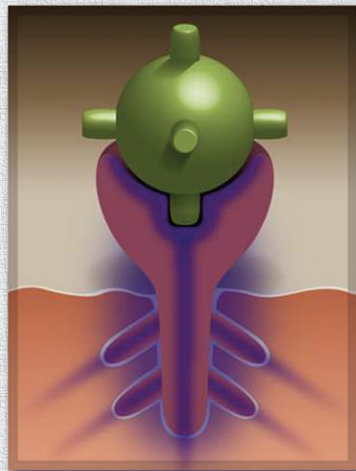
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The National Alliance of Advocates for Buprenorphine Treatment
Precipitated Withdrawal. What it is. How to avoid it.

What Is Precipitated Withdrawal?

It is a **rapid and intense onset** of withdrawal symptoms initiated by a medication. In the case of Buprenorphine, because it has a higher binding strength at the opioid receptor, it competes for the receptor, “kicks off” and replaces existing opioids. If a significant amount of opioids are expelled from the receptors and replaced, the opioid physically dependent patient will feel the rapid loss of the opioid effect, initiating withdrawal symptoms.

More precisely, precipitated withdrawal can occur when an antagonist (or partial agonist, such as Buprenorphine) is administered to a patient who is physically dependent on full agonist opioids. Due to the high *affinity* but low *intrinsic activity*



Full Agonist Opioid.
Perfect receptor fit. Maximum intrinsic activity (opiate effect).



Partial Agonist Opioid (Buprenorphine). Imperfect Fit. Less intrinsic activity (opiate effect).

of Buprenorphine at the μ -receptor, the partial agonist displaces full agonist opioids from the μ -receptors, but activates the receptor to a *lesser* degree than full agonists which results in a net *decrease* in agonist effect, thereby precipitating withdrawal.¹

A common misconception is that the naloxone in the buprenorphine/naloxone combination medication initiates precipitated withdrawal. Naloxone may only initiate withdrawal if *injected* into a person physically dependent on opioids. Taken sublingually, as directed, naloxone is clinically

insignificant and has virtually no effect. (Except in rare cases of an allergic reaction or naloxone hypersensitivity.²)

Avoiding Precipitated Withdrawal

Patient education and developing realistic expectations are essential before beginning treatment.

To **avoid** precipitated withdrawal, physically dependent patients must no longer be experiencing the agonist effects of an opioid. One way to gauge this is to observe objective symptoms of withdrawal sufficient to score a minimum of 5 to 6 on the COWS (Clinical Opioid Withdrawal Scale). Scores of >10 are preferable. Due to patient individuality, required abstinence times may vary considerably from patient to patient. Only use the time since last use as an estimate to anticipate the onset of withdrawal symptoms.⁴

The **induction begins** by assessing last use of all opioids, short and long acting, objective and subjective symptoms and a COWS score calculation. If not in sufficient withdrawal (mild to moderate: COWS of 5 to 24), it is in the patient's best interest to wait. Long-acting opioids will require a longer period of abstinence, than short-acting opioids.

Short-acting Opioids

(*Heroin, Crushed OxyContin®, Percocet®, Vicodin®, Oxycodone and others*)

Prior to induction, patients must abstain from all short-acting opioids for 12 to 24 hours **and/or** have objective withdrawal symptoms sufficient to produce a score of 5 to 24 on the COWS.¹

Long-acting Opioids

OxyContin® (Taken Orally)

Discontinue use for at least 24 hours prior to induction. A minimal score of at least 5 on the COWS is recommended, although some physicians prefer scores of 15 or higher.⁵

Methadone

It is recommended that patients transitioning from methadone to Buprenorphine slowly taper to 30 mg./day of methadone, for at least one week. Last dose must be no less than 36 hours prior to induction, and may be 96 hours or more. A minimal score of at least 5 on the COWS is recommended, although some physicians prefer scores of 15 or higher.⁵

Patients transferring from methadone or another long-acting opioid to Buprenorphine may experience discomfort for several days and dysphoria for up to 2 weeks.³

The **goal of induction** is to safely suppress opioid withdrawal as rapidly as possible with adequate doses of Buprenorphine. Failure to do so may cause patients to use opioids or other medications to alleviate opioid withdrawal symptoms or may lead to early treatment dropout.³ To achieve this, some physicians have found they may need to dose as high as 32 mgs. the first day with some methadone to Buprenorphine transfers.⁵

¹Center 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://naabt.org/links/TIP_40_PDF.pdf

²FDA. Full Prescribing information on Subutex® (buprenorphine)/Suboxone® (buprenorphine/naloxone) www.fda.gov/cder/foi/label/2002/20732lbl.pdf

³*Dosing Guide Maintenance therapy for Opioid Dependence.* Suboxone®/Subutex® www.suboxone.com/pdfs/DosingGuides.pdf

⁴*Practical Considerations for the use of Buprenorphine* Hendrée E. Jones, Ph.D., Johns Hopkins University School of Medicine, Baltimore, MD

⁵Physician Clinical Support System: www.pcsmmentor.org *Transfer from Methadone to Buprenorphine*, Paul P. Casadonte, MD, PCSS guidance paper. 8/9/2006 http://www.pcsmmentor.org/pcss/documents/2/PCSS_MethadoneBuprenorphineTransfer.pdf

Clinical Opiate Withdrawal Scale (COWS)

Flowsheet for measuring symptoms over a period of time during buprenorphine induction.

For each item, write in the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example: If heart rate is increased because the patient was jogging just prior to assessment, the increased pulse rate would not add to the score.

Patient Name: _____		Date: _____			
Buprenorphine Induction: _____					
Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.		Times of Observation:			
Resting Pulse Rate: Record Beats per Minute					
Measured after patient is sitting or lying for one minute					
0 = pulse rate 80 or below					
1 = pulse rate 81-100					
2 = pulse rate 101-120					
3 = pulse rate 121-140					
4 = pulse rate greater than 120					
Sweating: Over Past 1/2 Hour not Accounted for by Room Temperature or Patient Activity					
0 = no report of chills or flushing					
1 = subjective report of chills or flushing					
2 = flushed or observable moistness on face					
3 = beads of sweat on brow or face					
4 = sweat streaming off face					
Restlessness Observation During Assessment					
0 = able to sit still					
1 = reports difficulty sitting still, but is able to do so					
3 = frequent shifting or extraneous movements of legs/arms					
5 = Unable to sit still for more than a few seconds					
Pupil Size					
0 = pupils pinned or normal size for room light					
1 = pupils possibly larger than normal for room light					
2 = pupils moderately dilated					
5 = pupils so dilated that only the rim of the iris is visible					
Bone or Joint Aches if Patient was Having Pain Previously, only the Additional Component Attributed to Opiate Withdrawal is Scored					
0 = not present					
1 = mild diffuse discomfort					
2 = patient reports severe diffuse aching of joints/muscles					
4 = patient is rubbing joints or muscles and is unable to sit still because of discomfort					
Runny Nose or Tearing Not Accounted for by Cold Symptoms or Allergies					
0 = not present					
1 = nasal stuffiness or unusually moist eyes					
2 = nose running or tearing					
4 = nose constantly running or tears streaming down cheeks					
GI Upset: Over Last 1/2 Hour					
0 = no GI symptoms					
1 = stomach cramps					
2 = nausea or loose stool					
3 = vomiting or diarrhea					
5 = multiple episodes of diarrhea or vomiting					
Tremor Observation of Outstretched Hands					
0 = no tremor					
1 = tremor can be felt, but not observed					
2 = slight tremor observable					
4 = gross tremor or muscle twitching					
Yawning Observation During Assessment					
0 = no yawning					
1 = yawning once or twice during assessment					
2 = yawning three or more times during assessment					
4 = yawning several times/minute					
Anxiety or Irritability					
0 = none					
1 = patient reports increasing irritability or anxiousness					
2 = patient obviously irritable/anxious					
4 = patient so irritable or anxious that participation in the assessment is difficult					
Gooseflesh Skin					
0 = skin is smooth					
3 = piloerection of skin can be felt or hairs standing up on arms					
5 = prominent piloerection					
Score: 5-12 = Mild		Total score			
13-24 = Moderate					
25-36 = Moderately Severe		Observer's initials			
More than 36 = Severe Withdrawal					

