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 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.)

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 gage 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 abstinent 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. ¹

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 Oxycodone® Percocet® Vicodin® Oxycodeone 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

Oxycodone® (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.⁶

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.²

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.


²FDA. Full Prescribing information on Subutex® (buprenorphine)/ Suboxone® (buprenorphine/naloxone)


³FDA. Full Prescribing information on Subutex® (buprenorphine)/

Suboxone® (buprenorphine/naloxone)


⁴FDA. Full Prescribing information on Subutex® (buprenorphine)/

Suboxone® (buprenorphine/naloxone)


⁵Practical Considerations for the use of Buprenorphine Hendel S. Jones, Ph.D., Johns Hopkins University School of Medicine, Baltimore, MD

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Clinical Opiate Withdrawal Scale (COWS)

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.

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine Induction:</td>
<td>Times of Observation:</td>
</tr>
</tbody>
</table>

**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 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
- 2 = frequent shifting or extraneous movements of legs/arms
- 3 = 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
- 3 = pupils 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
- 3 = 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
- 3 = 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
- 4 = 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
- 3 = 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
- 3 = yawning several times/minute

**Anxiety or Irritability**
- 0 = none
- 1 = patient reports increasing irritability or anxiousness
- 2 = patient obviously irritable/anxious
- 3 = patient so irritable or anxious that participation in the assessment is difficult

**Gooseflesh Skin**
- 0 = skin is smooth
- 1 = skin is rough
- 2 = piloerection of skin can be felt or hairs standing up on arms
- 3 = prominent piloerection
- 5 = prominent piloerection

**Score:**
- 5-12 = Mild
- 13-24 = Moderate
- 25-36 = Moderately Severe
- More than 36 = Severe Withdrawal

<table>
<thead>
<tr>
<th>Total score</th>
<th>Observer’s initials</th>
</tr>
</thead>
</table>