



## Accurate Clinic

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OIH

## Accurate Education

Naltrexone for Pain

# Understanding Opioid-Induced Pain and Naltrexone

If you have chronic pain and have been taking opioid medications (like oxycodone, morphine, or fentanyl patches) for a long time, you may have heard about Opioid-Induced Hyperalgesia (OIH), Opioid Analgesic Tolerance and Central Sensitization (CS). This handout explains what these terms mean, who is most at risk to have them and what new treatment options are available—including ultra-low-dose naltrexone (ULDN) and low-dose naltrexone (LDN).

### Opioid-induced Hyperalgesia, Opioid Analgesic Tolerance, and Central Sensitization

- **Opioid-induced hyperalgesia (OIH)** is a condition where your body becomes more sensitive to pain because of long-term opioid use. Instead of helping, opioids can sometimes make pain worse or cause new pain in different areas. The prevalence of OIH in patients on long-term opioid therapy is likely in the range of 5% to 15%.
- **Opioid Analgesic Tolerance (OAT)** means your body gets used to the opioid, so you need higher doses to get the same pain relief. This is different from OIH, but both can occur together. The expected prevalence of clinically significant opioid analgesic tolerance is very high—likely >50% and approaching 100% of patients with increasing duration of therapy.
- **Central Sensitization (CS)** is when your nervous system becomes extra-sensitive, making you feel pain more easily or more intensely (hyperalgesia), even from things that shouldn't hurt at all (allodynia). This is common in conditions like migraines, chronic back pain, neuropathy and fibromyalgia and it can be worsened by long-term opioid use.

### You are most likely to have OIH and OAT if you:

- Have been on high doses of opioids for a long time (months to years)
- Have needed to increase your opioid dose over time for the same pain relief
- Notice that your pain is spreading to new areas, getting worse, or not responding well to higher opioid doses
- Have a history of conditions like migraines, chronic back pain, fibromyalgia or other "centralized" pain syndromes

### How are these problems treated?

Traditional painkillers (like NSAIDs, acetaminophen, or even more opioids) are generally not effective for OIH or central sensitization, and may even make things worse. New treatments focus on restoring the nervous system's natural pain control (endorphins).

**Naltrexone** is a medication that at standard doses (50 mg), blocks opioid effects. At much lower doses, it works differently: it helps "reset" your body's pain system, reduces inflammation in the nervous system, and can restore your natural pain-blocking compounds (endorphins).

## Ultra-Low-Dose Naltrexone (ULDN) and Low-Dose Naltrexone (LDN)

### How are ULDN and LDN Naltrexone used?

- **ULDN** is naltrexone given at ultra-low doses (starting at 0.001 mg twice daily) along with your current opioid. It helps prevent or reverse OIH and OAT by protecting your body's pain-blocking system without interfering with your current opioids.
- **LDN** is naltrexone given at low doses (1.5–4.5 mg once daily) along with your current opioid. It is especially helpful for people with centralized pain (like fibromyalgia) and can improve pain, sleep, and quality of life without interfering with your current opioids.

**How long does it take to work?** Many people notice improvement in pain and function within 2–4 weeks, but it may take longer for some.

**How long do I need to take it?** If you respond well, you may continue as long as you are on opioids or have ongoing pain. If you stop and your pain returns, restarting is safe.

**What are the side effects?** ULDN and LDN are generally well tolerated. Some people on LDN may have mild stomach upset, headache, or vivid dreams.

**What are the benefits?** Studies show that ULDN and LDN can:

- Significantly improve pain tolerance (sometimes quadrupling it in OIH)
- Reduce pain and improve quality of life
- Help lower opioid doses over time, if desired.

**How much does it cost?** \$1- 2/day at compounding pharmacies (not covered by insurance)

### What else can help with OIH and OAT and Central Sensitization?

- Reducing opioid doses, if possible, can also help reverse OIH and tolerance.
- Acupuncture, physical therapy and exercise are important for long-term pain management.
- Supplements like Omega-3's (Lovaza), Magnesium (citrate or glycinate), Resveratrol, NAC, alpha-Lipoic Acid, and Acetyl-L-Carnitine have substantial preclinical evidence and some clinical support for chronic pain and CS, with limited but promising data for OIH/OAT.
- Non-opioid medications (gabapentin, pregabalin (Lyrica), or duloxetine (Cymbalta) may help with central sensitization.
- *Buprenorphine*: Butrans transdermal patches (Micro-Dose) & Belbuca buccal strips (Low Dose) may help OIH and OAT without interfering with current opioid therapy.
- *Buprenorphine*: Subutex (Standard Dose: 2-32mg/day) may help OIH and OAT but requires substitution of current opioid therapy. Micro-dosing Rotation protocol recommended.

### Talk to your pain specialist about whether ULDN or LDN might be right for you

These treatments are not yet FDA-approved specifically for chronic pain, but growing evidence supports their use, especially when other options have not worked.

**References available upon request**