COASTAL PHARMACY + Wellness

29 Marginal Way, Portland

FREE WEBINAR

You're Invited to Join

Prescribing Low-Dose Naltrexone (LDN): What We Know, Mechanisms and Evidence

Wednesday, March 17, 2021 | 6:00-7:30 pm ET

Individuals who suffer from symptoms of gastrointestinal, autoimmune, dermatological and pain conditions make up 80% of the patient population. The good news? Low-dose naltrexone (LDN) has been studied recently as a potential treatment option. Please join us for a free, live webinar that will provide insight into the science, physiology, and mechanisms of action of LDN, and answer your questions about the many conditions it may be beneficial for:

- Autoimmune disorders
- Chronic pain
- Fibromyalgia
- Arthritis
- Anxiety
- PTSD
- Inflammatory conditions of the skin
- Veterinary conditions
- Hashimoto's disease
- Crohn's disease
- And more!

A live Q&A session with the presenter is included.

FEATURED PRESENTER

Sebastian Denison, RPh, FAARM (candidate) | PCCA Clinical Compounding Pharmacist

Sebastian received his Bachelor of Science in pharmacy at the University of British Columbia. He worked at Northmount Pharmacy in North Vancouver for 11 years, specializing in HRT, veterinary, pain and sports compounding. He also was the manager of Pharmacy Operations with the 2010 Vancouver Winter Olympic/Paralympic Games, and then the manager of the Whistler Olympic Village Polyclinic Pharmacy. In addition to his role as a PCCA clinical compounding pharmacist, Sebastian works with both the U.S. and Canadian CORE compounding training education teams and the pharmacy student education team.

Sebastian also speaks at physician, pharmacist and other health care professional education symposiums and events. He has recently lectured for the American Academy of Anti-Aging Medicine on *Nutrition and Pain*, *Pharmacy Compounding and Collaborative Practice, and Alternative Uses for Naltrexone.* Sebastian is currently completing the Metabolic Medical Institute's Fellowship in Metabolic & Nutritional Medicine Fellowship.

REGISTER ONLINE BY MARCH 16

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Questions?

Contact Drew Gray at 207-899-0886 or agray@CoastalPharmacyAndWellness.com

LDN Prescriber Information

LDN Prescriber Information

Naltrexone is often classified as an opiate antagonist. However, at low-doses, Naltrexone acts to inhibit certain inflammatory pathways, which involve Toll-Like Receptors (TLRs). Naltrexone's traditional use is in treating addiction to opiate drugs, such as heroin or morphine, or to treat acute overdose of these opioids. The daily dose of Naltrexone used for this purpose is usually between 50 mg (moderate dose naltrexone) to 300mg (high dose Naltrexone). Similar levels of Naltrexone are used for acute dosing.

In the USA, Low-dose Naltrexone (LDN) has been used for the treatment of autoimmune diseases since 1985. Although LDN has used at low-dosages for many years by patients with autoimmune disorders, the occurrence of significant introductory-effects of LDN, as well as long-term side-effects of LDN, have not been extensively studied.

A widely-used LDN dosage protocol was first developed in the 1980s by the late Dr. Bernard Bihari, who was qualified in Neurology, Internal Medicine, and Psychiatry.

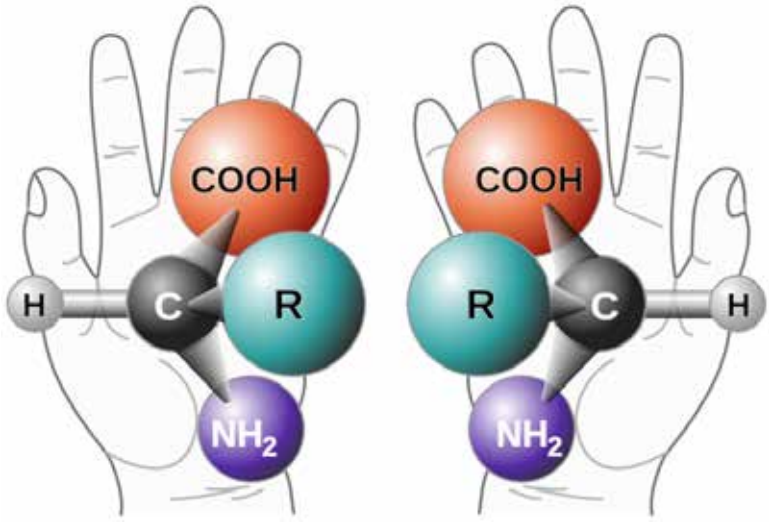
How Naltrexone Works

As of 2016, LDN is most commonly being used for Chronic Fatigue, Multiple Sclerosis, CFS/ME, autoimmune thyroid diseases, and various cancers. Many autoimmune diseases seem to respond to LDN.

This is a wide range of diseases. Some Clinicians may find it difficult to accept that a single drug can have a positive effect on a wide range of pathologies. However, LDN is a known to be a potent antagonist to (a) certain opioid receptors, as well as (b) a wide range of inflammation-mediating Toll-Like Receptors (e.g. TLR4, TLR7/8/, TLR9).

It is important to emphasize that Naltrexone (the drug in LDN prescriptions) is produced in a 50:50 mixture of two different chemical-shapes (called isomers). It has been recently discovered that one chemical-isomer binds to immune cells, while the other chemical-isomer binds to opioid receptors.

Although having the same atomic-composition, the two chemical-isomers of Naltrexone have very different therapeutic activities.



The LEVO (left-handed) version of Naltrexone blocks opiate receptors.

The DEXTRO (right-handed) version blocks receptors on immune cells. These include "Toll-Like Receptors" (TLRs), which are heavily involved in immunity. LDN is a potent antagonist of TLR-4, as well as an antagonist of TLR7/8 and TLR-9 (ref 10).

For clinicians interested in reading more about the pharmacology behind this, there is a published resource available here:

https://www.ldnresearchtrust.org/ldn-book

Summary of Mechanism of Action

Levo-Naltrexone is an antagonist for the Opiate/Endorphin receptors

- This causes increased Endorphin release
- Increased Endorphins modulate the immune response
- This reduces the speed of unwanted cells growing

Dextro-Naltrexone is an antagonist for at least one, if not more immune cells

- Antagonizes "TLR," thereby suppressing cytokine modulated immune system
- Antagonizes TLR-mediated production of NF-kB – thereby reducing inflammation, potentially down-regulating oncogenes

Taking Naltrexone in larger doses of 50-300mg seems to negate the immunomodulatory effect by overwhelming the opioid receptors. The Naltrexone dose must be in the range of 0.5mg, usually maxing out its benefit at 4.5mg in clinical experience. However, some individuals experience positive clinical effects at lower doses, others at higher doses than 4.5mg.

Side Effects

a. Many patients who start LDN do not experience any severe side effects.

As mentioned earlier, your symptoms may become worse. In Multiple Sclerosis (MS), this can be characterized by increased fatigue, or increased spasticity. In CFS/ME, this can be the onset of apparent flu-like symptoms.

LDN can cause sleep disturbances if taken at nighttime – this is most likely because of the increase in endorphin release. These disturbances can take the form of vivid dreams, or insomnia.

b. In various studies (and anecdotal accounts), the number of T-Lymphocytes has been shown to dramatically increase when a patient starts on LDN. This may account for some of the benefits patients feel when they are being treated for an autoimmune disease, or cancer. This has not been directly evidenced in Multiple Sclerosis.

c. Clinical experience shows that in less than ten percent of cases treated, increased

introductory symptoms may be more severe or more prolonged than usual, lasting sometimes for several weeks. Rarely, symptoms may persist for 2-3 months before the appropriate beneficial response is achieved.

If side effects are troublesome, then reducing your dose by 50% for 7 days, before increasing it again, is a good idea.

Very rarely, some patients experience gastro-intestinal (GI) side effects, such as nausea and or constipation/diarrhea. The reason for this is currently unknown. The side effects may be due to the presence of large numbers of delta-opiate receptors in the intestines. Patients experiencing GI side-effects can request LDN Sublingual Drops, which transfer the LDN directly into the blood-stream – avoiding the GI tract.

Types of LDN:

a. Capsules

Capsules are the most common dosage form of low dose naltrexone. Compounding pharmacies can compound any, and all custom strengths - even as low as 1 microgram per capsule. The most common capsule strengths are 1.5mg and 4.5mg. These have up to 6 months stability data and can be stored in a wide range of temp-eratures. Capsules are typically compounded with only microcrystalline cellulose as a filler, con-taining no lactose or other needless excipients.

b. Liquid

Oral Liquid Formulation can be compounded for patients who have difficulty swallowing capsules. A common strength for oral liquid is 1mg/1ml. It is taken daily and dosed using a 1ml oral syringe. It can be compounded to exclude excipients like lactose, or others known to cause hyper-sensitivity. The liquid can also be flavored by the com-pounding pharmacy – so is quite palatable. Because there are so few preservatives, it should be stored in the refrigerator.

c. Sublingual Drops

Sublingual drops are designed for patients who are having problems taking the medication orally, or for people who want to guarantee the fastest delivery of the drug into their bloodstream. A number of drops are placed under the tongue from a dropper bottle and dose is increased and decreased by the number of drops taken. There are very few excipients in this product as well.

d. Cream

LDN Cream can be compounded for topical application to the skin. It can be custom made into any strength, however the most common strength is 0.5mg/gm. Topical LDN is especially helpful for dosing in children, or for direct treatment to skin conditions. It is also helpful for veterinary use, avoiding the difficulty of oral dosing.

Intrinsic Toxicity of the Drug:

Naltrexone, in full doses of 50-300mg, has been shown to transiently increase liver enzymes. Patients being prescribed Naltrexone for addictions must have liver function tests performed before initiating therapy.

This is not necessary with LDN – as the dose is much smaller. However, patients with advanced liver failure should consult their General Practitioner (GP) before considering treatment.

Patients with renal or liver failure should only start treatment after a consultation with their own GP or specialist, and should be monitored during the treatment initiation period. It is normal for people with poor renal or liver function to experience a transient elevation – but this usually resolves after a few weeks.

Contraindications and Special Precautions:

a. LDN is compatible with most other therapies. LDN does not directly interact with steroids. However, LDN can negate the effect of opiate based painkillers. Patients should give their doctor a full drug history before starting therapy.

b. Patients who are taking multiple medications and/or herbal medicines – especially those with cancer or advanced disease, should take careful advice from a qualified doctor or pharmacist before initiating LDN.

LDN Prescriber Information

Key Clinical Studies

a. Low Dose Naltrexone (LDN) has been the subject of much debate but actually very few clinical trials. Dr. Ian Zagon from Penn State University has been studying LDN for over 20 years and conducted many pre-clinical studies investigating LDN in cancer and in the animal model of MS (1,2). He has also been involved in two clinical studies into Crohn's disease with his colleague, Dr. Jill Smith, from Penn State. These two researchers have demonstrated a significant improvement in symptoms and in bowel mucosal appearance with LDN treatment (3,4). In the RCT, LDN patients were twice as likely to have a 70-point decline in the Crohn's Disease Activity Index. 78% of the LDN group achieved an endoscopic response compared to 28% with placebo.

b. Dr. Jarred Younger from Stanford University has studied LDN in Fibromyalgia, firstly in a small pilot study, and more recently in a yet to be published randomized controlled trial. The pilot study showed significant improvement in symptoms of pain in these patients (5).

c. Multiple Sclerosis (MS) is one of the areas where LDN has been used the most frequently. There are three published studies, one in primary progressive MS (6) and two on quality of life (7,8). The results of two studies was positive with improved quality of life in one and reduced spasm in the PPMS study. The third showed no significant difference between the treatment and placebo groups but found the treatment to be safe. A review of the available studies into LDN and MS was published in 2009 (9). All studies have confirmed the safety of the drug and there is enough positive evidence to merit greater investigation.

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