

Low Dose Naltrexone (LDN) for pain and fatigue in ME/CFS

Prepared by MECFS Canterbury (v28.02.2024)

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Disclaimer:

The information in this leaflet is for informational purposes only. It does not substitute the need for professional medical advice or consultations with medical professionals. Always seek the advice of your doctor before starting a new medication or changing dosage.

Summary

- Low Dose Naltrexone (LDN) is used 'off-label' in ME/CFS, Fibromyalgia and now Long COVID. Naltrexone was originally used to manage opiate addictions (50mg+), but in this context it is used at much lower doses (0.2 mg to 5mg).
 - For people with ME/CFS, initial dosage starts at 0.5mg (or lower if sensitive) and is slowly titrated upward over several weeks and months.
 - It has a good safety profile, with minimal side effects at a low dose.
 - Case studies, and limited published research, report improvements particularly in pain, but also in fatigue, sleep, and brain fog. It may take months to work and will not help everyone.
 - Possible Mechanism:
A 2021 study¹ suggested that LDN's ability to tamp down the activity of microglial cells in the brain could reduce the levels of the pro-inflammatory cytokines that may be producing pain, fatigue, and other symptoms in ME/CFS and Fibromyalgia. LDN may also increase levels of the natural "feel-good" substances such as endogenous opioids and endorphin that have become depleted in these diseases.
 - In New Zealand, LDN is prescribed by a medical professional. It is not funded by Pharmac and is paid for by the patient.
 - Naltrexone is usually sold in 50mg capsules, so low-dose naltrexone must be ordered from a compounding pharmacy.
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Prescription Guidelines

Dose guidelines

- To limit side effects, start at 0.5 or 1mg/day – or lower if the patient is sensitive to medications. After 2 weeks increase by 0.5 or 1mg depending on any side effects.

¹ Helene Cabanas et al. (2021). Potential Therapeutic Benefit of Low Dose Naltrexone in ME/CFS: Role of Transient Receptor Potential Melastatin 3 Ion Channels in Pathophysiology and Treatment. *Frontiers in Immunology*, 12. <https://www.frontiersin.org/articles/10.3389/fimmu.2021.687806/full>

- LDN is often taken at bedtime but may cause vivid dreams and insomnia. For this reason, some medical practitioners advise taking it in the morning.
- If side effects are troublesome, then reducing the dose by 50% for 7 days, before increasing it again is a good idea².
- Some people who can't tolerate taking LDN daily are able to take it every two days.

Form

Liquid form is easiest to adjust the dose and can reduce gastrointestinal side effects. Liquid form has a 30-day refrigerator life, so will need monthly repeats.

Once an appropriate dose is found, this can be compounded in capsule form by a specialist pharmacy.

Possible Side Effects

The LDN Research Trust states² “Many patients who start LDN do not experience any severe side effects” and “... symptoms may become worse initially - In CFS/ME, this can be the onset of apparent flulike symptoms.” (p.3).

Side effects are usually reported to be minimal at the low dose but some patients (with chemical sensitivities) can have a great deal of difficulty with this drug. By starting the dosage off low and going slow many patients can tolerate dosages that would otherwise be intolerable.

Side effects can include sleep dysfunction (insomnia, wild dreams) and more rarely things like priapism (prolonged erections) and weight loss. In general side effects are described as ‘mild’ with few issues occurring so long as the dose begins low and is slowly titrated upwards.

The LDN Research Trust states “Clinical experience shows that in less than ten percent of cases treated, increased introductory symptoms may be more severe or more prolonged than usual, sometimes lasting for several weeks. Rarely, symptoms may persist for two or three months before the appropriate beneficial response is achieved.”

Contraindications

The LDN Research Trust states² that “LDN is compatible with most other therapies. It does not directly interact with steroids. However, it can negate the effect of opiate-based* painkillers.” and “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.” (p.4).

*Some opioid drugs are codeine, tramadol, oxycodone, vicodin, hydrocodone, fentanyl and morphine.

The Trust also states² that “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.” (p.4).

Compounding guidelines

Pharmaceutical compounding is the process used to combine individual ingredients in the exact strength and dosage form required by an individual patient.

² LDN Research Trust, (2022). LDN 2022 Prescriber Information, Pdf. Retrieved from <https://ldnresearchtrust.org/sites/default/files/2022-01/Prescriber-Info-2022.pdf>

The LDN Research Trust advises³ that: "Pharmacies should be instructed NOT to provide LDN in a "SR" or slow-release or timed-release form. Unless the low dose of naltrexone is in an unaltered form, which permits it to reach a prompt "spike" in the blood stream, its therapeutic effects may be inhibited.". It also states that calcium carbonate filler should NOT be used because they reduce absorption, instead Avicel, lactose, or sucrose fillers as alternative fast-release fillers." (p.5.).

Compounding Pharmacies in New Zealand

LDN can be sourced and couriered nationwide from Compounding Labs www.compoundlabs.co.nz and Optimus Healthcare www.optimushealth.co.nz in liquid and capsule form. Cost is about \$30 month including courier.

Local pharmacies can also be approached e.g. In Christchurch, StayWell Pharmacy in Hornby stock 0.5, 1, 1.5 up to 4.5mg. Union Pharmacy in New Brighton will prepare the liquid form.

If the pharmacist is unsure of process, they can contact their local hospital lab to ask how to prepare it.

Research and clinical guidelines

- **Potential Therapeutic Benefit of Low Dose Naltrexone in ME/CFS: Role of Transient Receptor Potential Melastatin 3 Ion Channels in Pathophysiology and Treatment**

Helene Cabanas et al, 2021, Frontiers in Immunology

<https://www.frontiersin.org/articles/10.3389/fimmu.2021.687806/full>

"In conclusion, this study for the first time assessed and identified the effect of LDN on TRPM3 ion channel function in NK cells in ME/CFS patients. This novel study reports the underlying restoration of TRPM3-opioid receptor channel interaction in NK cells from ME/CFS patients taking LDN. Moreover, the wide distribution of TRPM3 ion channels in the body suggests that their compromised function may contribute to signs and symptoms of ME/CFS and therefore treatment with LDN may have a therapeutic role. Finally, this study serves to support the planning and approval of prospective randomized clinical studies on the role and dose of NTX in treating ME/CFS patients."

- **Low-dose naltrexone in the treatment of ME/CFS**

Olli Polo et al, 2019, in Fatigue: Biomedicine, Health & Behavior

<https://www.tandfonline.com/doi/full/10.1080/21641846.2019.1692770>

Conclusions: "high frequency of treatment response and good safety profile observed in this retrospective open label study" (n=~200)

Results: "A positive treatment response to LDN was reported by 73.9% of the patients. Most patients experienced improved vigilance/alertness and improved physical and cognitive performance. Some patients reported less pain and fever, while 18.3% of patients did not report any treatment response to LDN. Mild adverse effects (insomnia, nausea) were common at the beginning of the treatment. Neither severe adverse effects nor long-term adverse symptoms were reported."

- **Consensus Recommendations for ME/CFS: Essentials of Diagnosis and Management**, Lucinda Bateman et al, 2021, Mayo Clinical Proceedings

[https://www.mayoclinicproceedings.org/article/S0025-6196\(21\)00513-9/fulltext](https://www.mayoclinicproceedings.org/article/S0025-6196(21)00513-9/fulltext)

Table 4 includes a recommendation for LDN for pain.

³ LDN Research Trust, (2014). Low-dose Naltrexone (LDN) Fact Sheet 2014. Pdf. Retrieved from <https://ldnresearchtrust.org/sites/default/files/Doctors-info-pack-US.pdf>

- Low-dose naltrexone as a treatment for chronic fatigue syndrome**
 Monica Jane Bolton et al, 2020 BMJ Case Report
<https://casereports.bmj.com/content/13/1/e232502>

Summary: This series of three case reports shows the range of responses they observed when taking LDN, from life changing to a reduction in some symptoms only.

Patient 1: Experienced improvement in cognitive abilities.
Patient 2: Experienced reduction in pain and sleep issues.
Patient 3: Experienced improved sleep and functional level.
 - Safety and efficacy of low dose naltrexone in a long covid cohort; an interventional pre-post study**
 Brendan O’Kelly et al, in Brain, Behavior, & Immunity - Health, 2022
<https://pubmed.ncbi.nlm.nih.gov/35814187>

Conclusions: “LDN is safe in patients with PCS and may improve well-being and reduce symptomatology in this cohort. Randomised control trials are needed to further explore this.”
 - The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain.** Younger J et al. (2014) Clinical Rheumatology 33 (4): 451 – 459. Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3962576/>
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Other Information

- The LDN Trust website**
<https://ldnresearchtrust.org>, including in-depth guides
https://ldnresearchtrust.org/2022_LDN_Guides
- Facebook group: LDN FOR ME/CFS & FIBROMYALGIA**
<https://www.facebook.com/groups/200010163370187>

A peer support group for patients only to share information and experiences.
- Article: Low Dose Naltrexone Explored as Option for Chronic Pain**
 Miriam E. Tucker, 2018, Medscape News.
<https://www.medscape.com/viewarticle/894020>
 Text of article available: <http://www.drvallings.co.nz/articles/low-dose-naltrexone-for-chronic-pain>

In this article, ME/CFS specialists discuss their experience prescribing LDN to people with ME/CFS to manage chronic pain and sleep.
- Article: Addiction drug shows promise lifting long COVID brain fog, fatigue** Julie Steenhuisen, 2022, Reuters. [Link](#)

Following promising off-label use for pain, fatigue and brain fog, there are now several clinical trials to test LDN in patients with Long COVID.
- Article: Low Dose Naltrexone (LDN) Fibromyalgia and CFS Resource Center**
 Cort Johnson, Health Rising blog.
<https://www.healthrising.org/treating-chronic-fatigue-syndrome/drugs/low-dose-naltrexone-ldn-fibromyalgia-chronic-fatigue-syndrom/>

A comprehensive summary article, with links to Resources and Health Rising LDN blogs.
- ME-pedia Webpage:**
 Curated information from the ME/CFS community.
https://me-pedia.org/wiki/Low_dose_naltrexone