|  |  |
| --- | --- |
| The LDN Research Trust is a UK registered Charity, founded in 2004, with the primary purpose of promoting research into the unlicensed use of Naltrexone at a low dose to treat conditions and diseases. Naltrexone at a low dose is referred to as LDN. **Formal Disclaimer** The information is designed to guide patients and enable them to make an informed choice about treatment. It does not replace the need for clinical involvement, and the LDN Research Trust will not support patients who obtain LDN without a prescriber’s prescription. **Naltrexone Background Information** Naltrexone has been commonly used at daily doses of 50-300mg since it was first licensed in 1984. Naltrexone has been used in lower doses to treat multiple diseases since 1988. Naltrexone is considered a “standard dose” when given in daily amounts of 25mg or more and low dose when the daily dose is less than or equal to 10mg. When prescribed in a standard dose, Naltrexone acts primarily to block opiate receptors and as such is used mainly in addictions. Multiple Phase I and II trials have shown efficacy. **Mechanism of Action** When used in a lower dose has Immunomodulatory, opiate blocking and anti- tumor effects, and multiple phase, I and II trials have shown efficacy.• Improves the immune system response • Creates an increase in the production of endorphins, which should result in a reduction of painful symptoms and an increased sense of wellbeing • Increased levels of endorphins can be expected to stimulate the immune system, promoting an increase in the number of T lymphocytes. This effect was observed in Dr Bihari’s research. This increase in T-cell numbers restores a more normal balance of the T-cells such that the effects of the disease process are significantly reduced. • It may also act directly on these immune cells to stimulate or restore normal function • Opiate Blockade for a short period (4-6 hours) • Levo Naltrexone molecule binds to opiate receptors • Causes rebound increased endorphin release. • Increases sensitivity of existing opiate/ endorphin receptors. • More Opiate receptors are formed to capture endorphins. **Cancer** * Intermittent Dosing with LDN causes increased cell death and increases cell sensitivity to chemotherapy agents.
* Cells treated with LDN upregulate genes that are responsible for cell death. (BAD and
 |  |

**LDN 2022 Patient Guide**

|  |  |
| --- | --- |
|  | BIK1) * Tumor cells pre-treated with intermittent

LDN dosing are far more likely to be killed by chemotherapy drugs. * LDN seems to have a direct cytotoxic effect

on cancer cells via a P13 kinase, cyclin P21 and downstream G-Protein coupled receptor routes. **Which Diseases Are Being Treated With LDN?** This list is not exhaustive and patients are directed to the LDN Research Trust website for more information www.ldnresearchtrust.org/ conditions Autoimmune HepatitisInflammatory Bowel Disease (Crohn’s/Ulcerative Colitis)Multiple SclerosisCFS/MELyme DiseaseChronic Viral InfectionsMast Cell Activation Syndrome (MCAS) Hashimoto’s ThyroiditisGrave’s DiseaseChronic Regional Pain SyndromeParkinson’s DiseaseDiabetes Type IVitiligoSclerodermaPsoriasisAnxiety and DepressionPCOSMelanomaNerve Pain (Neuropathic conditions) GlioblastomaEsophageal and Oral CancersNon-Small Cell CancerBreast CancerMultiple MyelomaLymphomaOvarian CancerRenal Cell CancerColorectal CancerDuodenal and Stomach CancerUterine CancerHepatic CancerPTSD PMDD Infertility (based on the research by Dr Phil Boyle, who is the Director of the NaProFertility Clinic in Dublin, Ireland and the Presidentof the International Institute for Restorative Reproductive Medicine) **How To Obtain LDN** Not all medical professionals are aware ofLDN, and its potential benefits and not all are prepared to prescribe LDN. It does help to have a knowledgeable LDN prescriber working with you. The LDN Research Trust has a list of LDN Prescribers which can be found here: (https:// www.ldnresearchtrust.org/LDN\_Prescribers). The LDN Research Trust works hard to maintain a support network for prescribers through regular conferences and media events. LDN is not generally covered by insurance plans but is an affordable prescription through your local compounding pharmacy (https://www. ldnresearchtrust.org/ldn-pharmacists). **How To Use** Read this guide before you use this medicine. It includes information that might be especially important for you. * ·  Keep this guide you may need it again
* ·  Ask your pharmacist or doctor for more advice if you need it. LDN comes in several forms: tablets, capsules, liquid, sublingual drops, troches, lozenges, and a cream.

Consult your doctor before using this medication if you are currently taking long- acting opiate medicines like codeine, tramadol, morphine, fentanyl or oxycodone. Do notuse this medicine if you are pregnant or breastfeeding without informing your doctor. • Dosing Options for LDN – For many conditions, your prescriber will usually start treatment at a low dose and increase gradually over a period of weeks untilyou are stable at your goal dose. Starting dose can vary from 0.5 mg to 1.5 mg and  |

**LDN 2022 Patient Guide**

|  |  |
| --- | --- |
| is often increased up to 4.5 mg. You may have a lower OR higher dose goal withyour prescribing clinician. You may be instructed to take multiple smaller doses on a daily basis for certain medical conditions, such as for mental health conditions. Higher, standard doses of 50mg or more may be required for TBI (Traumatic Brain Injury) patients until they are stabilized before transitioning to daily low doses of naltrexone. * LDN dosing for patients with chronic pain conditions will start at an Ultra-Low Dose, and you will take the medication twice daily, separating it by 4-6 hours from short acting opioid medications.
* For cancer patients, the dose should getto 4.5mg, or the goal dose, although your provider may adjust as necessary. In cancer patients, combining a cannabinoid (CBD) or Sativex (THC/CBD), seems to enhance the anti-tumor effect. No chemotherapy agents are currently contraindicated assuming standard tests are done, however, LDN should not be taken during treatment with immune checkpoint inhibtors (e.g. Opdivo or Keytruda -- PD1 inhibitors)

Storing the Medicine - LDN Liquid should be stored in the fridge once opened and can last 30 days or 12 months if unopened. Capsules should be stored at room temperature in their original container for up to 6 months. All forms of LDN will be labeled with a specific expiration date by your compounding pharmacy. Only obtain LDN via a doctor’s prescription and a reputable pharmacy - LDN is extensively counterfeited all over the world so it is not safe to purchase it from websites willing to sell itto you without a prescription—it is likely to be fake, or even dangerous, and it is illegal. **Possible Side Effects** LDN is well tolerated in most patients. However, care should be taken to titrate the dose up slowly to avoid side effects. Common: • Sleep disturbances • Mild headache• Mild agitation• Nausea/GI effects - consider switching to liquid sublingual LDN to bypass GI tract• Hyperthyroidism in Hashimoto’s patients Uncommon: * Flu-like symptoms (CFS/ME)
* Rash
* Herxheimer reactions (elevated

temperature) * Dizziness
* Increased fatigue or spasticity (Parkinson’s)

These side effects are usually only present in the initial phase and can be stopped by halving the dose for 2-3 days and then continuing with titration again. The half-life of LDN is about4-6 hours. Report any side effects to your prescriber. For Up-to-Date Clinical Trials and References visit - https://www.ldnresearchtrust.org/ldn-clinical-trials * 1. Brown N, Panksepp J. Low-dose naltrexone for

disease prevention and quality of life. Med Hypotheses. 2009;72:333-337. doi:10.1016/j. mehy.2008.06.048. * 1. Zagon IS, McLaughlin PJ. Naltrexone modulates tumor response in mice with neuroblastoma. Science. 1983;221:671-673. doi:10.1126/ science.6867737.
	2. Zagon IS, McLaughlin PJ. Naltrexone modulates body and brain development in rats: a role for endogenous opioid systems in growth. Life Sci. 1984;35:2057-2064. http://www.ncbi.nlm.nih. gov/entrez/query.fcgi?md=Retrieve&db=PubM ed&dopt=Citation&list\_uids=6092812.
	3. Bihari B, Ottomanelli GA, Drury F, Ragone VP. T-cell subsets and treatment response in AIDS. AIDS Res. 1986;2(4):263-266.
	4. Bihari B, Finvola DM, Ragone VP, Ottomanelli GA, Buimovici-klein E. Low Dose Naltrexone in the Treatment of Acquired Immune Deficiency Syndrome. 1988; (June).
	5. ClinicalTrials.gov. https:// clinicaltrials.gov/ct2/results? term=low+dose+naltrexone&Search=Search. Accessed January 1, 2015.
	6. Donahue MJ. Low-Dose Naltrexone (LDN). 1995;(4).
	7. Sajben N. LDN World Database. 2011. http:// painsandiego.com/2011/01/19/ldnworld- database/. Accessed February 23, 2015.
 |  |

**LDN 2022 Patient Guide**

1. LDNScience - How Does LDN Work? http://www. ldnscience.org/low-dosenaltrexone/how-does- ldn-work. Accessed February 23, 2015.
2. Grossman T. Low Dose Naltrexone (LDN) Lecture. 2014:1-10.

Psychiatry. 1987 Jun;144(6):813-4.
21. Vink R, McIntosh TK, Rhomhanyi R, Faden

AI. Opiate antagonist nalmefene improves intracellular free Mg2+, bioenergetic state, and neurologic outcome following traumatic brain injury in rats. J Neurosci. 1990 Nov;10(11):3524-

22. Yang L, Li F, Ge W, Mi C, Wang R, Sun R. Protective effects of naloxone in two-hit seizure model. Epilepsia. 2010 Mar;51(3):344-53. doi: 10.1111/j.1528-1167.2009.02250.x. Epub 2009 Aug 8.

23. Zhang H, Wang X, Li Y, Du R, Xu E, Dong L, Wang X, Yan Z, Pang L, Wei M, She L. Naloxone for severe traumatic brain injury: a meta-analysis. PLoS One. 2014 Dec 19;9(12):e113093.

doi: 10.1371/journal.pone.0113093.

eCollection 2014.
24. Toljan K, Vrooman B. Low-

Dose Naltrexone (LDN)-Review of Therapeutic Utilization. Med Sci (Basel). 2018 Sep 21; 6(4). Epub 2018 Sep 21.

25. Liptan, G. The FibroManual: A Complete Fibromyalgia Treatment Guide for You and Your Doctor. New York, Ballantine Books, 2016.

26. Leavitt SB. Opioid Antagonists in Pain Management. Practical Pain Management. 9 Articles in Vol 9, Issue #3.

11. The Low Dose Naltrexone Homepage. http:// www.lowdosenaltrexone.org/ #Are\_there\_any\_ 30.

side\_effects. Accessed February 25, 2015.

1. Trust LR. Low-dose Naltrexone ( LDN ) Fact Sheet 2015. 2015:1-17. doi:10.1111/ j.1526-

4637.2009.00613.x/abstract.

1. Naltrexone at low doses upregulates a unique

gene expression not seen with normal doses: Implications for its use in cancer therapy. Wai M. Liu et al Int Journ Onc 070616 793-802.

1. Lanius, U. F., Paulsen, S. L., & Corrigan, F.
M. (2014). Neurobiology and Treatment of Traumatic Dissociation: Towards an Embodied Self. Springer Publishing Company.
2. Pape, W., Wöller, W. (2015). Niedrig dosiertes Naltrexon in der Behandlung dissoziativer Symptome (Low dose naltrexone and the treatment of dissociative symptoms - Abstract in English). Nervenarzt. 2015 Mar;86(3):346-51. doi: 10.1007/s00115-014-4015-9.
3. Elsegood L., (2020) The LDN Book Volume: The Latest Research on How Low Dose Naltrexone Could Revolutionize Treatment for PTSD, Pain, IBD, Lyme Disease, Dermatologic Conditions, and More, Chelsea Green. Chapters Nine and Ten.
4. Calvanio R, Burke DT, Kim HJ, Cheng J, Lepak
P, Leonard J, Dwyer MA, Gavande V. Naltrexone: effects on motor function, speech, and activities of daily living in a patient with traumatic brain injury. Brain Inj. 2000 Oct;14(10):933-4.2
5. Faden AI, Jacobs TP, Holaday JW. Opiate antagonist improves neurologic recovery after spinal injury. Science. 1981 Jan 30;211(4481):493-4.
6. Persson AI, Thorlin T, Bull C, Zarnegar P, Ekman R, Terenius L, Eriksson PS. Mu- and delta-opioid receptor antagonists decrease proliferation and increase neurogenesis in cultures of

rat adult hippocampal progenitors. Eur J

Neurosci. 2003 Mar;17(6):1159-72.

1. Tennant FS Jr, Wild J. Naltrexone treatment

for postconcussional syndrome. Am J