Low-dose Naltrexone (LDN) Fact Sheet 2017

Naltrexone is a class of drug known as an opiate antagonist. Its normal use is in treating addiction to opiate drugs such as heroin or morphine. The dose used for this purpose is usually between 50 and 300mg daily.

Low-dose Naltrexone (LDN) has been used in the treatment of autoimmune diseases in the USA since 1985, but is relatively new in the United Kingdom and Europe. Despite the fact that the drug is used at a very low dose, the occurrence of significant introductory or long term side effects cannot be excluded.

This method was devised and subsequently developed by the late Dr. Bernard Bihari, a Neurophysician from New York, USA who passed away on May 16th 2010. Dr. Bihari was qualified in Internal Medicine, Psychiatry and Neurology, and we hope to honour him by continuing with his pioneering work.

Suggested Method of Therapy

LDN has been used for over a decade internationally, so internet searches will bring up conflicting information about dosing and optimal time of day to take LDN. The LDN Research Trust produces this factsheet to inform clinicians and patients of the most up to date and practical uses of LDN.

In order to avoid common side effects, such as GI disturbance, headache, increased malaise, flu-like symptoms, agitation or worsening tiredness/spasticity in MS – doses should be started at 0.5-1mg and increased gradually.

The most common form of LDN is Liquid 1mg/1ml, and this can be started at 0.5mg for 7 days, increasing by 0.5mg weekly until at 3mg or 4.5mg, whichever is tolerated best.

As of July 2016, LDN 1mg/1ml from Dickson’s Chemist in Glasgow is stable at room temperature for 12 months. Other suppliers do not follow this formula so liquid LDN from these sources may be stable for only 28 days. Many websites and internet resources state that LDN only works if taken at nighttime; however, clinical experience over the last decade clearly demonstrates that it is as effective in the morning – with far fewer side effects.

After starting LDN, some response is expected to be seen at 6 weeks, with maximal effects at 12 weeks.
How Naltrexone Works

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

This is a wide range of diseases and many clinicians will find it difficult to understand how one drug can have a positive effect on all these pathologies.

The first thing to understand is that Naltrexone – the drug in LDN – comes in a 50:50 mixture of 2 different shapes (called isomers). It has been recently discovered that one particular shape binds to immune cells, whilst the other shape binds to opioid receptors.

Although consisting of exactly the same components, the two isomers appear to have different biological activity.

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” which are heavily involved in immunity.

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

EU:  https://www.amazon.co.uk/Ldn-Book-Little-Known-Naltrexone-Revolutionize/dp/1603586644

Summary of mechanism of action

The summary of 10 years of research is that LDN works because:

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

- Antagonises “TLR,” suppressing cytokine modulated immune system
- Antagonises TLR-mediated production of NF-kB – reducing inflammation, potentially downregulating oncogenes

Taking Naltrexone in larger doses of 50-300mg seems to negate the immunomodulatory effect by overwhelming the receptors, so for the effect to work, the dose must be in the range of 0.5-10mg, usually maxing at 4.5mg in clinical experience.

The Use of Low-dose Naltrexone, and the Occurrence of Side Effects

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

As mentioned earlier, your symptoms may become worse – in MS, this can be characterised 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.

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.

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 two or three 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.

Some patients, very rarely, experience gastro-intestinal side effects, such as nausea and or constipation/diarrhea. The reason for this is currently unknown, but may be due to the presence of large numbers of delta-opiate receptors in the intestines.

Patients experiencing this side effect can request LDN Sublingual Drops, which transfer the LDN directly into the bloodstream – avoiding the GI tract.

Patients who do have these side effects should increase their dose by no more than 0.5mg per week, and should consult with their GP or pharmacist for appropriate treatment for the stomach upset, if necessary. (Omeprazole, Ranitidine, Gaviscon, Fybogel, Mucogel and Pepto Bismol are ok – but not Kaolin & Morphine or Loperamide/Imodium.)
Types of LDN

**Liquid**

Oral Liquid Formulation at 1mg/1ml is the most commonly used type of LDN. It is taken daily, and dosed using a baby oral syringe. It does not contain very high amounts of lactose or any other excipient known to cause hypersensitivity. The base is similar to children’s cough syrup, and so is quite palatable. Because there are so few preservatives, it should be stored in the fridge.

**Capsules**

For patients who find the liquid would be impractical, there are capsules available in 3mg and 4.5mg strengths in the UK. Other strengths are available from different manufacturers – but these are made on a case by case basis. These have up to 12 months stability data and can be stored anywhere. They contain no lactose filler and are instant release.

**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.

**Cream**

LDN Cream in 0.5mg/ml is available for application to the skin. This is helpful for children, or for patients allergic to colourants, flavourants or any excipients in all other forms of LDN.

The efficacy of this product in adults is extremely dubious, as absorption into the bloodstream is very low.

NB: Naltrexone has been investigated as a method of speeding up wound healing time – LDN Cream, unless specifically specified on the prescription, will not be sterile and cannot be used for this purpose. Check with your pharmacist first. Sterile cream will be significantly more expensive. Using non sterile cream on an open wound would be very dangerous.

**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 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:**

LDN is compatible with most other therapies. It 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.

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.

The LDN Research Trust retains medical and pharmaceutical advisors to assist with this process. If you are unsure whether you can take LDN with your current medications, please email us or our pharmaceutical advisor, Stephen Dickson MRPharmS. directly on: [www.askaboutldn.com](mailto:www.askaboutldn.com) [mailto:homedeliverypharmacy@yahoo.co.uk](mailto:homedeliverypharmacy@yahoo.co.uk)

**Low Dose Naltrexone - Key clinical studies**

Low Dose Naltrexone has been the subject of much debate but actually very few clinical trials. 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 Professor Jill Smith from Penn State. These 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.

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 randomised controlled trial. The pilot study showed significant improvement in symptoms of pain in these patients (5).

Multiple Sclerosis 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.

**Key references :**


The latest up-to-date references are always being added to the website, however, the current authority is the LDN BOOK available on Amazon.