Low Dose Naltrexone – Information For Doctors

LDN is short for Low Dose Naltrexone.

Naltrexone is a drug that was approved by the FDA in 1985 to treat opiate dependence. It is marketed under the trade names, ‘Revia®’ and ‘Depade®’, and in some countries (including the United States), an extended-release formulation is available as ‘Vivitrol®’. Naltrexone is commonly used at a dose of 50mg–100mg daily for treating opiate dependence.

The term ‘LDN’ refers to the use of naltrexone at low doses; specifically between 3mg and 10mg per day. Naltrexone exhibits novel and paradox effects when administered as these low doses, as discovered by Dr. Ian S. Zagon and his team at Hershey Medical Center, Penn State University in 1980.

Low Dose Naltrexone (LDN) & Autoimmune Disorders

LDN is being used as a regulator of the immune system, providing relief to patients with autoimmune diseases, and central nervous system disorders. Physicians are permitted to prescribe LDN ‘off-label’ for any use they think is appropriate.

The apparently diverse conditions in which LDN appears to have a therapeutic effect are united by their ability to benefit from increased levels of endorphins (naturally occurring opioids – specifically OGF). The theory is that LDN may stimulate the pituitary to increase the production and release of endorphins,

The therapeutic dosage range for LDN is from 1.5mg to 4.5mg every night. Dosages below this range are likely to have no effect at all, and dosages above this range are likely to block endorphins for too long a period of time and interfere with its effectiveness.

Warning! Those patients who are taking thyroid hormone replacement for a diagnosis of Hashimoto’s thyroiditis with hypothyroidism ought to begin LDN at the lowest range (1.5mg for an adult).

Be aware that LDN may lead to a prompt decrease in the autoimmune disorder, which then may require a rapid reduction in the dose of thyroid hormone replacement in order to avoid symptoms of hyperthyroidism.

Are there any side effects?

All sources indicate that LDN has virtually no side effects. Occasionally, during the first week of use, patients may complain of difficulty sleeping. (Reports indicate that sleep disturbance is rare, occurring in less than 2% of users.)

LDN, in the low doses, is virtually non-toxic, simple to administer, and, compared with other drug therapy, very inexpensive.

How does Low Dose Naltrexone work?

LDN is a member of a group of agents collectively known as ‘Modulators of Opioid and Receptor Activity’ (‘MORAs’). Another related ‘MORA’ drug discussed on this website is OGF. It works by briefly obstructing the effects of brain endorphins (the
brain's natural painkillers). This has an effect of stimulating the increased production of these same endorphins, which re-balances the immune system, thus reducing the activity of the Hashimoto’s. This effect lasts around 18 hours.

In order to understand how LDN works, it is crucial to briefly introduce the workings of the ‘natural opioid’ (endorphin) system.

Endorphins are opiate-like molecules produced naturally in the body. The term ‘endorphin’ comes from ‘endogenous morphine’, meaning that it is created within the body, and differentiating it from opioids that are administered from external sources.

Endorphins are produced in most cells in the body, and are important regulators of cell growth and therefore the immune system. Disorders of the immune system can occur with unusually low levels of these endorphins. The particular endorphin that has been found to influence cell growth as well as immunity is called Opioid Growth Factor (OGF) or Met-Enkephalin.

For an endorphin such as OGF to exert its beneficial effects, it must interact with the body’s cells. It does this by binding to a receptor on the surface of the cells. The receptor to which OGF binds is the ‘Opioid Growth Factor Receptor’ (OGFr) – previously known as the Zeta (ζ) receptor.

Thus, for the endorphin system to be fully functional, two elements are required: opioid production and cell interaction.

Naltrexone is an externally administered drug that binds to opioid receptors. In doing so, it displaces the endorphins which were previously bound to the receptors. Specifically, by binding to the OGF receptor, it displaces the body’s naturally produced OGF.

As a consequence of this displacement, the affected cells become deficient in OGF and three things happen:

- Receptor production is increased, in order to try to capture more OGF.
- Receptor sensitivity is increased, also to try to capture more OGF.
- Production of OGF is increased, in order to compensate for the perceived shortage of OGF.

Since LDN blocks the OGF receptors only for a few hours before it is naturally excreted, what results is a rebound effect; in which both the production and utilization of OGF is greatly increased. Once the LDN has been metabolized, the elevated endorphins produced as a result of the rebound effect can now interact with the more-sensitive and more-plentiful receptors and assist in regulating cell growth and immunity.

The duration of the rebound effect varies from individual to individual, but generally persists for about one day.
The benefits of the rebound effect can only be utilized by taking a low dose of regular naltrexone. Taking a high dose of naltrexone or using a timed-release formulation will result in continuous blockade of OGF receptors, and the rebound effect will not serve any useful purpose.

In scientific terminology, the use of regular-dose naltrexone results in ‘continuous opioid receptor blockade’ whilst the use of LDN results in ‘intermittent opioid receptor blockade’. In order to benefit from the rebound effect and achieve the therapeutic benefit of LDN, it is essential to avoid timed-release versions of naltrexone.

How is LDN prepared?
LDN is prepared by a compounding pharmacy, who will make capsules by either grinding up 50mg tablets of Naltrexone, or using Naltrexone powder purchased from a primary manufacturer. The most popular source of Naltrexone is the 50mg "ReVia" Naltrexone tablet (DuPont), usually prescribed for treatment of drug and alcohol addictions.

Naltrexone may also be taken as a solution (in distilled water) with 1mg per ml dispensed with a 5ml medicine dropper. If LDN is used in a liquid form, it is important to keep it refrigerated.

**IMPORTANT: Make sure to specify that you do NOT want LDN in a slow-release form.**

Full-dose Naltrexone (50mg 3x day) carries a cautionary warning for patients with liver disease. (This warning was placed because adverse liver effects were noted in early experiments involving 300mg daily.) The 50mg dose does not apparently produce impairment of liver function nor, of course, does the much smaller 1.5mg - 4.5mg dose.

What about cautionary warnings?
Because LDN blocks opioid receptors throughout the body for three or four hours, people using narcotic medication such as Ultram, morphine, Percocet, Duragesic patch or codeine should not take LDN until such medicine is completely out of the system. Steroids would counteract the effects of LDN, and so should not be combined except for small amounts of natural HC that the body would normally produce.

LDN cannot be used by people already receiving beta interferon. Because LDN stimulates the immune system and beta interferon suppresses it, the two therapies are incompatible.

What does it feel like to be on LDN?
At both high and low dosages, patients taking Naltrexone usually say they are largely unaware of being on medication. Naltrexone usually has no psychological effects and patients (at both high and low dosages) don't feel either "high" or "down" while
they are on naltrexone. It is not addicting. However, there is the benefit from the Endorphins, the 'feel good' one! Like eating chocolate or having sex!

Other ways LDN can benefit autoimmune disorders:
Here is still a list of other possible ways that low dose naltrexone can benefit autoimmune disorders:

- Reduced inflammation
- Reduced oxidative stress
- Reduced apoptosis of oligodendrocytes in MS
- Decreased inflammatory cytokines
- Increased tissue repair and wound healing
- Increased CD4+ levels
- Increased levels of NK lymphocytes.

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