

Low Dose Naltrexone

Pharmacokinetic and Pharmacodynamic interactions, formulation, preparation, stability and considerations for practical prescribing of Low Dose Naltrexone.

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Apologies

- Due to an unexpected event, I am unable to attend the conference!
- Thanks to Dr Mark Mandel for presenting on my behalf.

Drug Interactions

- Pharmacodynamics = study of what a drug does to a body
- Pharmacokinetics = study of what a body does to a drug
- When considering potential drug interactions, standard reference sources are not suitable as Naltrexone in full dose has a different biological effect from LDN.
- Pharmacists must be experienced, and consider the overall holistic picture to make an informed decision.

Drug Interactions

- If LDN modifies the immune system, then what potential drug interactions can arise if other treatments have been prescribed when the immune system was faulty.
- Example: Hashimotos disease.
 - Drug interaction is Levothyroxine / LDN
 - Problem – rapid increase in thyroid function as immune system normalises.
 - Dose must be reduced of thyroid medicine

Drug Interactions

- Example: Resurgence of latent infections due to autoimmune state changing, can cause potential prostaglandin cascade in ME / CFS. Herxheimer reactions have been reported when initiating too fast.
- Elevated Liver Enzymes (transient) could cause other drugs to be broken down faster and not work as well.
- Decrease in Renal function (usually transient) could decrease clearance of other drugs from the system, leading to toxic levels.
- Patients with leaky gut may not absorb the LDN properly. Or LDN may stop loperamide working as well and lead to transient diarrhoea, delaying or reducing absorption.

Drug Interactions

- Example: Eating a fatty meal at the same time as taking an LDN capsule could delay the absorption of the drug.
- LDN in a recent trial by Dr Zagon was shown to make certain chemotherapy drugs less effective during treatment. (Do not take LDN during chemotherapy – but how long before and after will depend on the drug used!)
- Supplements – patients on LDN often take large numbers of supplements (Herbal/Chinese).
 - Pharmacist needs to understand the possible interactions, effects on kidney/liver function and advise appropriately.

Drug Interactions - myths

- LDN cannot be used with any sort of morphine product....?
 - TOTAL MYTH, we have patients taking oral:
 - Oxycontin SR
 - Tramadol SR
 - Co-codamol
 - Morphine SR
 - However, never use it in someone with a syringe driver or instant release morphine / analogues for pain – it is however possible to schedule dosing with multiple painkillers successfully.
 - **Only do this under medical supervision.**

Formulation

- Formulations current available in the UK
 - **Capsules 3mg** – Specialist Manufacture under GMP
 - **Capsules 4.5mg** – Specialist Manufacture under GMP
 - **Liquid 1mg/1ml** – Compounded in pharmacy
 - **Sublingual Drops 10mg/1ml** - Compounded in pharmacy
 - **Transdermal Cream 0.5mg/1ml** - Compounded in pharmacy

Capsules

- Only 3mg and 4.5mg Capsules are available due to difficulties getting affordable pricing under GMP
- Contents:
 - *Naltrexone HCL 99.99% powder*
 - *Magnesium Stearate*
 - *OR Avicel (Microcrystalline Cellulose)*
 - Compliant with MHRA, and GMP regulations, and each batch is assayed for accuracy and safety.
 - Expiry: 18months.
 - Indication: Maintenance therapy after initiation with liquid or cream.



Oral Liquid 1mg/1ml

- *Liquid formulation where one millilitre by volume equates to one milligram of drug.*
- Contents:
 - Naltrexone Tablets 50mg – sourced from GMP manufacturer.
 - SF Preserved Syrup BP
 - Natural colour
 - Sodium benzoate or Methyl/Ethyl Paraben in tiny amounts
 - Glycerol, simeticone, flavour and water.
 - Expiry: Legally 28days from opening (trial data show 90 days). Refrigerate.
 - Indication: Initiation and maintenance therapy. Cost effective solution.



Sublingual Drops 10mg/1ml

- 10mg/1ml = 0.5mg PER DROP
- Used under tongue.
- Contents:
 - Currently a closely guarded secret!
 - Excipients: Water, esters (lime/lemon /strawberry). Allergies: Parabens.
 - Expiry: 56 days. Refrigerate.
 - Indication:
 - Where capsules or liquid have been ineffective, caused stomach/bowel problems or where measurement with oral syringe is not possible.
 - Where low dose of 0.5mg is desired. Paed?
 - NB: Bypasses first pass metabolism, higher blood level peak and faster onset of action.



Transdermal Cream 0.5mg/1ml

- Measured using a syringe, doses as low as 0.1mg can be administered.
- Originally formulated for use in **autistic children**.
- Contents:
 - Vanishing cream – BP formulation
 - Preservative free LDN Liquid
 - No EMU oil used in this product.
- Indication: Paediatrics, Ileostomy/colostomy, Psoriasis, Arthritis.
- Bioavailability: ~40%
 - Cycle application sites
 - Do not use on broken skin, **non sterile**.
 - Expiry: Legally 28 days from opening. Long term studies unknown, likely to be >90days.



Preparation

- Paula Clarke and Sandra Roan are specialist pharmacy technicians who prepare and dispense our LDN.



- NVQ Level 2/3 with Local ACT approval.
- Compliance with Extemporaneous paperwork
- Medication manufacture to GPHC standards
- Each dose is *freshly prepared* according to prescriber instructions.
- Prescription fulfilment and stock replenishment
- Cash handling and website management
- Electronic recording of prescriptions
- First point of contact on telephone
- Good practical and clinically useful knowledge.

Preparation



- Making LDN takes about 1/3 of any working day, as it must be freshly prepared to make sure of maximum shelf life at patient level.
- Specialist homogenizing* equipment used which must be meticulously maintained.
- Dispensing, cross checking and shipping take the other 2/3.
- 80 hours a week to supply current demand.
- Pharmacist on hand, but largely autonomous.

*
Homogenizer - Its just a big blender!

Pharmacist

- As well as being on hand for queries, we have a new LDN Pharmacist Consultation – where 30 minutes or more can be dedicated to checking interactions and looking holistically at all medicine, supplements and treatments being used.
- Medicines information at UK wide level are useful for complex regimens but can only be accessed by an NHS pharmacist or doctor.
- Most useful for cancer patients, who usually want to know everything possible and the latest trial data specific to their illness. (NB: £25)

Doctor

- Most doctors prescribe LDN online, privately.
- We have e-Prescribing agreements with the top 5 in the UK for speed and data recording.
- Top 5 by volume are published on **www.idn-international.com**



Please note that the Consultation does NOT include the cost of the medication.

Clinic158

Consultation
£35.00

Repeat Prescriptions
£25.00 every 3 months

MORE INFO

ORDER

E-MED

Consultation
£15.00

£20.00 to register
(Annual)
£15.00 for a 3 month
prescription

MORE INFO

ORDER

LDNI

Consultation
£30.00

Repeat Prescriptions
£14.50
Repeats up to 3 months

MORE INFO

ORDER

Prescribe4me

Consultation
£30.00

Repeat Prescriptions
£14.50

MORE INFO

ORDER

EHC

Consultation
£60.00

Repeat Prescriptions
£14.50

MORE INFO

ORDER

Doctor: Considerations for prescribing LDN

- Does the patient have an autoimmune disease diagnosed?
- If patient undergoing treatment for cancer, take advice first.
- Have standard therapies failed?
- Is Vitamin D level normal?
- Is renal and liver function normal for disease state?
- Which formulation is suitable?

Doctor: Considerations for prescribing LDN

- GUIDE:

- If Opiate naive:

- Start CFS/ME/Hashimotos/Underactive Thyroid/ Type1 Diabetes patients on 0.5mg
- Other patients can start on 1mg
- BMI unimportant mostly
- Age unimportant mostly (<12 half adult dose <6 quarter adult dose)
- Start it in the MORNING to avoid vivid dreams
- Increase by their **starting dose** every 1-2 weeks, until they feel better. 3mg or 4.5mg is usually a good review point.
- Do not be concerned with Mild Tachycardia, Transient Hyperactivity, Mild headache, Mild Stomach Upset, Increase in spasticity (MS), vivid dreams. **Treat symptomatically** (beta blockers, benzos etc).
- DO be concerned with palpitations etc in thyroid disease – reduce dose of thyroxine symptomatically, remember half life!
- DO be concerned with 'flu like symptoms or rapid onset of diarrhoea – half the LDN dose for 7 days if this happens and treat symptomatically. If herxheimer suspected, 40mg Pred stat.

Doctor: Considerations for prescribing LDN

- Maximal dose:
 - When **opiate block** reached, or autoimmune symptoms improve.
 - Do regular LFT/Renal/ HBA1c in Type 1 Diabetes.
 - CHD/AF/Angina, review GTN/Nitrate dose (Reduce as required.)
 - Dose can be doubled to twice daily, with 12 hour gap
 - once at maximal dose. (Useful in Crohns)
 - Common doses:
 - *3/4.5mg daily in the morning or night.*
 - *3/4.5mg BD*

 - *Max ~25mg bd in CFS/ME patients*

Doctor: Considerations for prescribing LDN

- GUIDE:
 - If NOT Opiate naive:
 - Before initiating therapy with LDN:
 - Switch full opiates to **partial agonists** or lower affinity molecules if possible.
 - Tylenol Codeine 8/30 → Tramadol SR 100-400
 - Morphine Sulphate → Oxycodone SR
 - Fentanyl Patch → Oral SR Opiate
 - Consider Buprenorphine or removal of all opiates and replace with NSAID/Tylenol.
 - Consider Gabapentin, Pregabalin, Amitriptyline.
 - Give dose of LDN after the longest period between SR Opiate doses.
 - Most patients this is 1st thing in the morning WITH their 1st SR Opiate tablet of the day.
 - Most importantly, review pain relief requirements

Doctor: Considerations for prescribing LDN

