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EXPERIENCE-INFORMED MENTAL HEALTH STRATEGY

Bupropion (Wellbutrin / Zyban SR) & Low-Dose Naltrexone (LDN)

Experience-Informed Reflections on Mental Health Use

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Bupropion (Wellbutrin / Zyban SR) & Low-Dose Naltrexone (LDN)

Experience-Informed Reflections on Mental Health Use

Context

This summary reflects my personal lived experience using low-dose bupropion (Wellbutrin) and low-dose naltrexone (LDN) for mental health, alongside independent research and under the supervision of my treating clinicians. It is not medical advice and is intended to support informed discussions with qualified healthcare professionals.

Bupropion (Wellbutrin/Zyban SR): Lived Experience

Before commencing bupropion (Wellbutrin/Zyban SR), I was experiencing persistent anxiety, intrusive negative thinking, depression, obsessive tendencies, and low mood that significantly affected my day-to-day functioning.

I commenced bupropion using a cautious, clinician-directed titration, starting at very low doses and increasing gradually. I noticed a clear and rapid reduction in anxiety and mental “noise” shortly after initiating treatment at low doses. As dosing increased, these benefits initially continued but diminished at higher doses.

At **300 mg/day**, I experienced a reversal of benefit, with increased anxiety and negative thinking compared to baseline. After discussion with my doctor, I reduced the dose and stabilised at approximately **75 mg/day**, which proved to be my optimal dose.

My experience with bupropion at this optimal dose included:

- Anxiety, depression and negative thinking reduced by approximately **30-50%**
- General calmness and emotional regulation improved
- Benefits became more consistent over **2-3 months**
- Side effects were minimal and manageable

For me, bupropion felt like *“turning down the volume”* on an overwhelming internal environment, making life more manageable and predictable.

Most side effects reduced over time with the most persistent issue being fatigue, which improved significantly when I switched dosing to nighttime (under clinician guidance).



Low-Dose Naltrexone (LDN): Lived Experience

After approximately **seven months** on low-dose bupropion, I commenced LDN following a discussion with my doctor regarding potential risks and benefits.

I initiated LDN at **1 mg nightly**, increasing gradually to **4 mg over four weeks**, using a dosing strategy consistent with commonly described clinical practice. I initially attempted tablet splitting but found this imprecise and difficult, and subsequently transitioned to **compounded capsules**, which significantly improved dosing accuracy and ease of use.

My experience with LDN at this optimal dose included:

- A noticeable increase in morning energy and positive mood within days of starting
- A further **20-30% reduction** in depression and anxiety beyond the improvement already achieved with bupropion
- Improved emotional steadiness and resilience
- Benefits that became more consistent over several months

I experienced mild gastrointestinal side effects (nausea and stomach discomfort), which reduced over time and remained intermittent. These effects were manageable and, for me, an acceptable trade-off.

Combined Impact

In my experience, the combination of bupropion and LDN was complementary rather than redundant.

- **Bupropion** reduced baseline anxiety, negative thinking, and mental overload.
- **LDN** added further lift, steadiness, and improvement in mood and energy.

Together, they provided broader symptom relief than either medication alone, without a significant increase in side-effect burden at the doses that worked best for me.

There is **no clinical research** examining this combination specifically for mental health. My experience reflects an individual response and should not be generalised.

Key Reflections

- Lower doses were more effective than higher doses for me.
- Benefits were noticeable early, but stability took time.
- Side effects were dose-dependent and manageable at lower doses.
- Careful titration, monitoring, and clinician involvement were essential.
- Consider the use of compounding pharmacists to prepare lower dose medication.
- More effective and less side effects than any previous medications used.



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Closing Note

These medications were presented to me as a carefully considered trial, not a guaranteed solution. In my experience, the benefits were meaningful and life-improving, while the risks were manageable under medical supervision.

If anything in this summary resonates, the appropriate next step is not self-experimentation, but a structured discussion with a qualified clinician, supported by credible information, clear goals, and careful monitoring.



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Patient-facing explainer

Key points

- This document is **not medical advice**. It is a combination of **lived experience** and **independent research** intended to support **informed discussions with qualified healthcare professionals**.
- In my experience, low-dose bupropion and low-dose naltrexone (LDN) had a positive and sustained impact on my mental health, with benefits noticed relatively quickly and with manageable side effects at lower doses. Bupropion was commenced first; LDN was added approximately seven months later.
- I believe that the combination was complementary rather than redundant: bupropion reduced mental “noise” and improved baseline mood/energy; LDN added further energy lift and steadiness.
- Conceptually, bupropion and LDN may support mental health through complementary pathways. Bupropion is commonly associated with effects on dopamine and norepinephrine signalling relevant to mood and motivation, while LDN is discussed in relation to endorphin regulation and potential modulation of neuroinflammatory processes.
- There are **real risks**, particularly with bupropion (e.g., seizure risk). Taking these medications should only occur under **medical supervision**.
- Evidence strength differs; there is robust research for bupropion in depression and some related conditions; for LDN and mental health, evidence is more limited and emerging. There are no research studies of their use in combination for mental health treatment.

Naming conventions

In this document I prioritise generic names. Bupropion refers to the active ingredient (marketed as Wellbutrin in the US and Zyban SR in Australia). Naltrexone refers to standard-dose naltrexone; low-dose naltrexone is abbreviated as LDN.

Quick glossary (plain language)

- Dopamine / norepinephrine: brain chemicals involved in mood, motivation, attention, and energy.
- Endorphins (endogenous opioids): the body’s own opioid-like chemicals linked to pain relief and wellbeing.
- Half-life: how long it takes the body to reduce a drug level by half.
- Neuroinflammation: inflammation-related processes in the brain and nervous system (a developing research area).
- Off-label: a medicine is used for a purpose not listed in the official product approval, based on clinician judgement and evidence.
- Modified-release / sustained-release: tablets designed to release medicine slowly and typically should not be altered unless your prescriber and pharmacist advise it is safe for your exact product.



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Purpose and scope

This document has been developed through a combination of **lived experience** and **independent research** undertaken for my own education. The information shared reflects material I gathered to support informed discussions and decision-making **in collaboration with my medical practitioners**. I also share my personal experience using the medications discussed.

My purpose in sharing this material is to provide information and lived-experience insights for consideration across each topic that may assist you in your own mental health journey, **always in consultation with qualified healthcare professionals**.

How this information was developed

To reduce bias and avoid reliance on any single narrative, I intentionally drew on a wide range of sources, including:

- Peer-reviewed research papers
- Pharmaceutical and medical journals
- Clinical publications and pharmacist resources
- Regulatory and industry materials

I also reviewed anecdotal sources such as blogs, interviews, and first-hand accounts from others with lived experience. While these sources do not carry the evidentiary weight of controlled clinical studies, they can provide practical context and real-world observations that are sometimes absent from academic literature.

This approach was used to ensure my understanding was informed by **multiple viewpoints**, rather than constrained by a single institutional, commercial, or regulatory lens. I encourage you to independently review and verify any information referenced here, particularly if you wish to explore or challenge the material presented.

Patrick O'Connor - Lived Experience

In 2012, shortly after my 40th birthday, my life took a profound turn when I experienced debilitating depression and anxiety. Over time, these symptoms were formally diagnosed as **complex post-traumatic stress disorder (C-PTSD), major depressive disorder, and severe anxiety**.

Medication became a central component of my mental health treatment. Over many years, I was prescribed a wide range of medications, often taking between two and seven medications concurrently.

Across this period, I trialled more than 250 different medication combinations and dosage variations, including **antidepressants, antipsychotics, benzodiazepines, mood stabilisers, and pain medications**. This includes a long-term use of SSRIs in high doses.

Despite the scale and duration of these trials, I experienced little in the way of sustained positive benefit from most of these medications. My treating clinicians ultimately described my condition as **treatment-resistant**, and over time it became apparent that the cumulative side-effect burden of many medications was contributing to, rather than improving, my overall health and functioning.



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Over the course of my treatment, some medication side effects persisted beyond active use and had lasting effects on my wellbeing. In addition, I experienced significant difficulty withdrawing from several medications, even with gradual, medically supervised tapering, with withdrawal effects at times more severe than the original symptoms being treated.

These experiences had a material impact on my relationship with medication. Over time, they left me with substantial reservations about trialling new medications, particularly those with known **withdrawal syndromes, serious side effects** or complex tapering requirements.

My caution was not ideological, but experiential. It was informed by repeated episodes in which medication changes resulted in meaningful distress and functional impairment.

This history strongly influenced my later approach to treatment. I became far more focused on:

- Tolerability as well as effectiveness
- Serious risks
- Lowest effective dosing
- Slow, carefully monitored changes
- A heightened awareness of potential withdrawal effects

Under the care of **new physicians**, I began exploring alternative medications and treatment approaches. Treatments perceived as lower risk or more tolerable are of particular interest to me.

This process was informed by overseas clinical experience, emerging research, and documented practitioner and patient experience, with an openness to new ideas where conventional options had been ineffective or poorly tolerated.

I share this background to provide context for the information that follows and to clarify the perspective from which my subsequent experiences, observations, and reflections are presented.





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Lived. Learned. Shared.

I founded **Lived. Learned. Shared.** to address a gap, I experienced firsthand within the mental health system: the gap between clinical strength and lived reality.

For more than 15 years, I navigated complex mental health treatment systems in Australia and the United States. During that time, I encountered both the strengths and limitations of conventional models of care. When traditional pathways did not deliver sustained improvement, I pursued recovery through medically supervised, research-informed exploration of emerging and innovative treatment strategies.

These included pharmacogenetic testing, supervised off-label medication approaches, ketamine IV treatment, psychedelic-assisted treatments, hormone optimisation, medical cannabis, and structured somatic interventions. Each decision was grounded in medical oversight and careful evaluation. The outcome was not incremental change, but a breakthrough in my recovery and restoration of quality of life.

Alongside treatment exploration, I undertook extensive independent research into health system design, emerging diagnostics, international treatment frameworks, and evolving therapeutic models. I engaged with clinicians, researchers, pharmaceutical developments, plant-based medicine experts, and cross-disciplinary innovation. This work allowed me to understand not only what helped me recover, but why certain models succeed where others stall.

Lived. Learned. Shared. is the result of that journey. A lived-experience consultancy like no other. I do not present lived experience as narrative inspiration or symbolic inclusion. I translate it into structured, experience-informed strategy that strengthens clinical expertise and improves system performance.

My advisory work is not focused on criticising what is not working. It is focused on identifying why certain gaps persist and how they can be addressed in structured, practical ways.

Through **Lived. Learned. Shared.**, I translate lived experience into implementable strategy. I help organisations:

- Understand where policy and lived reality diverge
- Identify systemic blind spots and how they affect outcomes
- Responsibly evaluate emerging and innovative treatment approaches
- Strengthen training and governance through real-world insight
- Improve patient engagement and system performance

Lived experience does not replace clinical expertise. It strengthens it.

Lived. Learned. Shared. exists to help mental health systems evolve thoughtfully, responsibly, and with measurable impact — grounded in both evidence and real-world experience.

More information can be found at www.lived.learned.shared.com.au



Part 1: Bupropion (Wellbutrin; Zyban SR in Australia)

Official information sources (US and Australia)

Bupropion hydrochloride is distributed under the brand names of Wellbutrin (US) and Zyban SR (Australia).

US: The Wellbutrin XL website includes substantial consumer information and safety warnings

<https://www.wellbutrinxl.com/>

Australia: Wellbutrin is supplied as **Zyban SR** and the Consumer Medicine Information (CMI) has the latest consumer information and safety warnings.

SR stands for 'slow release' which means that the tablets dissolve slowly and release the drug into your body over an extended period.

In Australia it is most widely used for **smoking cessation**, while in the US it is **also** widely prescribed for **depression** (and other indications).

In Australia, mental health use is often **off-label**. Off-label does not mean unsafe or unusual; it means the use is not listed as an approved indication, even though a clinician may prescribe it based on evidence and clinical judgement.

Note: The CMI for Zyban SR does not contain information on its use for mental health conditions. The US Wellbutrin XL website does contain information on its use for mental health conditions.

What is bupropion?

Bupropion is used for:

1. Smoking cessation support
2. Treatment of depression (and sometimes other mental health conditions)

Bupropion is commonly described as supporting mood, motivation, and energy by influencing dopamine and norepinephrine signalling. For some people, this translates into reduced depressive symptoms, less mental fatigue, and improved ability to function.

Treatment for depression and anxiety

Evidence strength snapshot (bupropion)

- Depression: robust evidence base (systematic reviews/meta-analyses and clinical trials).
- Anxiety symptoms/anxiety disorders: mixed evidence (smaller studies and subgroup analyses).
- Low-dose approaches: limited formal trial data; decisions rely on clinician judgement, safety, and individual response.
- Combination with LDN for mental health: no direct clinical studies.
- Bupropion was originally classified as an "atypical" antidepressant because it does not exert the same effects as the classical antidepressants such as Monoamine Oxidase Inhibitors (MAOIs), Tricyclic Antidepressants (TCAs), or Selective Serotonin Reuptake Inhibitors (SSRIs).



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- It has **comparable effectiveness** to typical first-line options for the treatment of depression such as **SSRIs**.^{1 2} Bupropion and SSRIs have **similar effectiveness**; however, bupropion was associated with **less weight gain, nausea, diarrhoea, drowsiness, and sexual dysfunction**.³
- A 2008 randomized controlled trial compared the action of bupropion in patients with generalized anxiety disorder to another medication called escitalopram, which has established efficacy for treating anxiety. The study found **comparable results** for each treatment in reducing anxiety symptoms⁴.
- A 2008 meta-analysis of 10 clinical trials found evidence for **comparable action of bupropion** in relation to anxiety symptoms in comparison to some other antidepressants commonly used to treat anxiety, such as sertraline⁵.

A real alternative treatment

In the United States bupropion is the **third most common antidepressant**, with more than 30 million prescriptions a year.^{6 7}

Reading multiple sources and summaries, I saw a similar theme: **bupropion can be comparable in antidepressant effectiveness** to first-line options for many people, with a side effect profile that may be more tolerable for some (especially regarding **sedation, sexual dysfunction and weight gain**).

That raised a question for me to discuss with a clinician: how often is bupropion considered for mental health use in Australia, and what factors guide that choice (particularly if SSRIs/SNRIs have not been effective or tolerable)?

What is “low-dose” bupropion?

There is no universal definition. In this document, “**low-dose**” refers to doses meaningfully below common starting, or target doses used in standard prescribing guidelines, particularly when using divided tablets or compounded preparations.

In Australia, commercially available tablet strengths are 150 mg and 300 mg sustained-release forms. However, in the US, additional strengths and immediate-release options exist, including smaller dose tablets of 75 mg.

I commenced bupropion after discussing the medication with my doctor as a treatment for the symptoms of depression, anxiety and complex PTSD. My optimal dose of bupropion is 75 mg, which is half of the prescribed tablet size.

That is supported by some US sources, which suggests using immediate release **bupropion of 75mg to 150mg for mental health conditions**. Some websites suggest **even lower doses** than 75mg, and I did experience benefits at those lower levels⁸.



Lived experience: dose exploration and what I noticed

Detailed step-by-step titration history and tablet-splitting notes are provided in Appendix A.

What I felt

- I noticed a **significant reduction** in my anxiety, negative thinking and an improvement in general calmness, **8 hours after taking the first ¼ tablet**.
- These benefits continued as I increased the dosage over the first two weeks. The benefits began to **diminish after commencing the 150 mg tablet** and further decreased on **300 mg**. I remained on 300 mg for 4 weeks.
- **In my experience, higher doses felt less effective**, and I felt worse at 300 mg/day than before starting. All benefits had ceased and I felt greater levels of anxiety and negative thinking than I did before I took the medication.
- I then discussed the results with my doctor, and we made the decision to titrate back down 75 mg and remain at this level to observe the response. It took 2 weeks to reduce to this level.
- When I reduced to an estimated **75 mg/day**, I found this to be my “sweet spot.” The benefits I had initially experienced at the lower doses returned within 3 days. I remained at this dose as I wanted to evaluate my response over an extended period, before considering any further changes with my doctor.
- After 4 weeks at this dose, the benefits had continued to improve, with some minor daily fluctuations.
- These fluctuations reduced over the next 2-3 months, and I have remained at this dose since then.
- I am aware of other lived-experience accounts of benefits at even lower doses (e.g., quarter tablet), but individual responses vary widely.

I do not chase target doses. I chase **benefit with tolerability**.

Practical principle: lowest effective dose that delivers benefit with tolerable side effects, determined collaboratively with your clinician.

Lived experience - benefits

Before starting bupropion, I was experiencing:

- significant anxiety and depression
- negative thinking
- obsessive tendencies
- low mood

After approximately three months, I **self-reported improvement** across these areas of **30-50%**, often closer to the higher end. The best way I can describe it is:

In my experience, it felt like someone turned the “deafening noise” down.

My world became more manageable.



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I recognise that other factors (e.g., **therapy**, sleep, stressors, and natural symptom fluctuation) may also have contributed, so I cannot attribute all change solely to medication. However the immediate benefits began after adding the medication, no other factors were changed.

Lived experience - how long does it take to work?

The US manufacturer outlines that it will take several weeks before the medication improves the underlying condition.

I include the following with caution, as individual response and timing vary considerably, in my experience:

- I noticed mood changes within **hours** of a very small first dose.
- Consistency took longer. At ~75 mg/day, the improvement stabilised over **2-3 months**, with fluctuations along the way.

Practical takeaway

If you and your doctor choose to trial it, it may be worth allowing enough time to evaluate it properly, while also monitoring side effects closely, especially during dose changes.

I would suggest that if you experience a **reduction in the benefits as the dosing increases**, that you discuss this with your doctor immediately.

Potential side effects

Established side effects

Please review the information provided by your doctor and pharmacist on the risks associated with any medication, including interactions with others you are taking.

Generic information on the risks associated with bupropion can be found on the NPS MedicineWise [website](#) (Aust) or the Wellbutrin [website](#) (US).

Seizure risk is a known concern with bupropion and should be discussed with your doctor, particularly if you have risk factors or if considering higher doses or altered release forms. Risk is dose-related and should be assessed individually. I do not experience any seizure symptoms at my current ~75 mg dose.

Lived experience

What I experienced (mostly mild, mostly early in commencing each dose):

- Fatigue
- Nausea
- Headache
- Dizziness
- Sweating
- Dry mouth
- Tremor
- GI symptoms (diarrhoea, abdominal pain, constipation)



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For me, the most persistent issue was **fatigue**, which improved significantly when I switched dosing to nighttime (under clinician guidance).

Alcohol: In my experience, alcohol was poorly tolerated on this medication, with noticeable changes in mood response and more severe hangover effects.

I noticed a clear pattern:

1. Higher dose = more side effects
2. Many side effects reduced over weeks
3. At lower doses, side effects became minimal

Recommended dosage for mental health conditions

There is no universal best dose. The most effective dose is highly individualised. As the medication is predominantly used in Australia for smoking cessation, there is a lack of dosing information in relation to mental health conditions.

The Wellbutrin website and others in the US indicates that 150mg slow release is the starting dose and then to increase to 300 mg if it is not improving your condition.

My lived experience: lower doses were more beneficial than higher doses. My 'sweet spot' was around 75 mg/day.

When should it be taken?

The timing is highly individual. I take it at night due to fatigue associated with the medication for me. Some people prefer mornings, especially if insomnia occurs.

My suggestion is to keep dosing time consistent for several weeks before changing, unless side effects require a change under clinician advice.

Withdrawal and stopping

I am still taking bupropion. When I have tapered up and down, I found changes noticeable within days. I did not experience significant side effects when making dosing changes.

Practical safety principle: do not stop abruptly. Even if a medication is not considered "addictive," abrupt cessation can be uncomfortable and destabilising. Tapering is generally the safer approach and should be clinician-guided.

Prescription and practical options (tablet splitting vs compounding)

Commercial products in Australia do not offer doses smaller than 150 mg. If a clinician supports a lower dose approach, two practical pathways are:

1. **Compounding pharmacy**
A compounding pharmacist can prepare specified capsule strengths. This is often the cleanest way to achieve precise low doses but may be more expensive.



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2. **Tablet splitting** (riskier and less precise)

Using a pill cutter (and sometimes a scale) to approximate smaller doses.

Summary

For further detail and safety cautions about tablet manipulation, see Appendix A.

The patent for bupropion has expired, and the medication is now available in multiple generic forms, **making it relatively inexpensive.**

Consequently, there is little commercial incentive for pharmaceutical companies to invest the substantial funding required to conduct new clinical trials specifically examining low-dose bupropion use for mental health conditions.

For this reason, it is reasonable to expect that many healthcare practitioners in Australia may have limited exposure to, or familiarity with, the emerging discussion around bupropion for mental health treatment.

There are no research studies or manufacturer information specifically on low-dose bupropion use for mental health conditions. Most available information is for prescribed doses.

If this is an option you wish to explore, it may be helpful to approach the **conversation with your doctor well prepared**, supported by credible sources and a clear understanding of both potential benefits and risks.

Within a mental health system that continues to explore treatments that are both effective and well tolerated, **bupropion may be a rational option to consider for some individuals**, under appropriate medical supervision.

In my experience, the potential benefits were meaningful and the risks manageable. If this perspective resonates with you, the appropriate next step is a considered discussion with your treating clinician.



Part 2: Low-Dose Naltrexone (LDN) for Mental Health

Official information sources (US and Australia)⁹

Naltrexone GH tablets contain the active ingredient, naltrexone hydrochloride. It is an opiate antagonist. This means it fights the effects of opiate drugs like heroin on the body, and blocks euphoria (or “high”) due to these opiates.

Naltrexone Hydrochloride is distributed under several generic brands in the US. It is sold under the brand REVIA in Australia.

US: The [U.S. FOOD & DRUG ADMINISTRATION](#) (FDA) has the latest consumer information and safety warnings for ‘Naltrexone Hydrochloride’.

Australia: The [REVIA](#) Consumer Medicine Information (CMI) has the latest consumer information and safety warnings.

What is naltrexone?

Naltrexone is used for:

1. The treatment of opioid use disorder (OUD)
2. The treatment of alcohol use disorder (AUD)
3. The treatment of other conditions including **depression**, fibromyalgia, Crohn’s disease, multiple sclerosis, and complex regional pain syndrome

In Australia and the US, mental health use is **off-label**. Off-label does not mean unsafe or unusual; it means the use is not listed as an approved indication, even though a clinician may prescribe it based on evidence and clinical judgement.

Naltrexone works by blocking the effects of alcohol and opioid medications, preventing the euphoria and intoxication (the “buzz”) these substances cause, and it also helps reduce the urge or cravings to use alcohol or opioids. It reduces the physiological dependence on these drugs to help people avoid relapses and remain opioid-free.

For depression, it is thought that by taking a very small amount of naltrexone, it **boosts endorphin levels, reduces neuroinflammation, and enhances dopamine**, leading to potential improvements in mood, anxiety, and depression^{10 11}.

What is low-dose naltrexone (LDN)?¹²

Naltrexone is commonly prescribed at a standard dose of **50 mg** per day for the treatment of opioid or alcohol use disorder.

LDN refers to doses commonly in the range of approximately **1.5 to 4.5 mg** per day or around 10% of the standard dose, with some variances in definitions.¹³



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I commenced low-dose naltrexone (LDN) after discussing the medication with my doctor as a treatment for the symptoms of depression, anxiety and complex PTSD.

Evidence note: *Clinical research into low-dose naltrexone (LDN) remains at an early stage. There is currently no large or definitive body of high-quality, accredited evidence supporting its use across mental health conditions.*

The information presented here draws on a range of sources, including published research, clinical commentary, and practitioner experience; however, the strength and certainty of evidence vary considerably by condition and study design.

Much of the available information originates from compounding pharmacists, and clinicians in the United States with specific experience prescribing LDN, and organisations established to support discussion, education, and ongoing research into LDN.

Evidence strength snapshot (LDN and mental health)

- Depression/anxiety: preliminary and emerging evidence; not a large or definitive body of high-quality clinical trials.
- Mechanisms (endorphins, immune/neuroinflammation hypotheses): developing science; many claims are theoretical or based on limited studies.
- Dosing approaches vary; individual response is highly variable and should be clinician-guided.
- Combination with bupropion for mental health: no direct clinical studies.

What does LDN do?¹⁴

LDN is often described as having different effects at low doses than at standard (higher) doses (sometimes called a paradoxical effect). One hypothesis is that very low doses transiently block opioid receptors.

A commonly discussed hypothesis is that this brief blockade may be followed by a compensatory increase in endogenous opioids/endorphins over time. The certainty and magnitude of these effects vary across sources, and the evidence base is still developing.

LDN has a very short half-life - around 4 to 6 hours - which means its binding effects wear off quickly, but this is long enough to boost levels of naturally occurring opioids for 18 to 24 hours. **Endogenous opioids** are natural pain relievers and having more of these around in the body is one of the ways LDN is thought to work.

LDN also appears to have **anti-inflammatory effects** by regulating microglial cells which have a key role in general and nerve inflammation. When microglial cells are activated, they produce pro-inflammatory cytokines, free radicals (reactive oxygen species), and nitric oxide - all of these substances have been associated with pain, inflammation, fatigue, feeling rundown or like you have come down with something.

LDN is thought to relieve symptoms such as pain, fatigue, stress, and inflammation by increasing the production of endogenous opioids and dampening down the effect of microglial cells.



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Dr Bernard Bihari MD, (1931-2010)

Dr Bihari was an early pioneer of the clinical effects of LDN in humans. Based in New York, he was a nationally recognized expert in the field of addiction medicine. He first noticed the impact of LDN when treating patients in the 1980's. During treatment of opioid dependence with naltrexone, he observed that as patients were gradually weaned off the medication, **some experienced positive effects on other conditions and symptoms**¹⁵.

In his groundbreaking clinical trial of patients with HIV/AIDS at Downstate Medical Center in 1985-86, Dr Bihari discovered the significant effectiveness of LDN in protecting the immune systems of those who were infected. The benefits of LDN were documented in a clinical trial in 1985 by Dr Bernard Bihari, *Low-dose Naltrexone for Normalizing Immune System Function*¹⁶.

Through his clinical observations and research, Dr Bernard Bihari proposed that endogenous endorphin production follows a circadian pattern, with peak activity occurring during the night, particularly in the early morning hours (approximately 2:00 am to 4:00 am).

Based on this hypothesis, he explored the administration of very low doses of naltrexone (**approximately 1 mg to 4.5 mg**) taken at night, with the aim of transiently blocking opioid receptors and triggering a compensatory increase in endorphin production during sleep. He theorised that this mechanism could support immune function and broader physiological regulation.

Dr Bihari suggested that, at doses far below those used in addiction treatment, low-dose naltrexone may significantly increase **endorphin levels, with estimates in the range of 200-300%**.

This proposed mechanism remains hypothetical, supported by limited clinical observations and emerging evidence, rather than large-scale controlled trials^{17 18}

Lived experience: dose exploration and what I noticed

Detailed step-by-step titration history and tablet-splitting notes are provided in Appendix A.

What I felt

- The morning after the first **1 mg** dose, I woke up feeling highly energised, in an almost euphoric mood. I describe it as being like I had taken a stimulant in the night and woke up feeling 'buzzed'.
- Over that first week I was waking up feeling positive, happy and energetic about the day. The 'buzzed' feeling diminished by around 30% over that time. That is not to say that it disappeared, rather the initial levels stabilised at notably positive level.
- I was grateful about that as I was noticing some insomnia around 3 am, as I woke feeling wide awake. Over the following 3 weeks that positive feeling remained.
- I increased the dose by **1 mg** a week for next three weeks to my current dose of **4 mg per day**.
- This approach is consistent with findings reported in published studies and with dosing

Critical point: Doses higher than 4.5 mg may lose the "LDN" effect and behave more like standard naltrexone. Strategies commonly described in clinical practice.



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Lived experience - benefits

Prior to commencing LDN, I had been on low-dose bupropion for 7 months.

- My levels of depression and anxiety had decreased by between **30-50% over this period**.
- At the end of week 4 taking LDN, I **self-reported** that my overall levels of depression and anxiety decreased **by a further 20-30%**.

As with bupropion, I recognise that other factors may also have contributed, so I do not assume medication was the only driver of change. However the immediate benefits began after adding the medication, no other factors were changed.

- There were fluctuations in these results, but the consistent benefits were noticeable 6 months after commencing LDN.
- In addition, LDN has improved my energy and mood significantly.

How long does LDN take to work?

It may take up to **8 to 10 weeks for LDN to work**¹⁹. It is important to keep taking it until at least then to know if it works for you. I found benefits after a few days, and it kept improving for several months.

Potential side effects

Established side effects

Please review the information provided by your doctor and pharmacist on the risks associated with any medication, including interactions with others you are taking.

Side effects with LDN are uncommon because the dose is low and have been reported by less than 8% of people. LDN is unlikely to cause the same side effects as standard dose naltrexone. Side effects of LDN may include:

- Difficulty sleeping (insomnia)
- Nausea
- Diarrhoea
- Nightmares or wild dreams
- Rarely, prolonged erections (priapism)
- Rarely, weight loss.

Difficulty sleeping initially was reported by approximately 8% of people receiving LDN but this resolved within two weeks in most people. Other side effects (such as nausea and wild dreams) were reported by less than 1% of people. LDN is usually well tolerated with few side effects.

The **long-term side effects of LDN** are unknown because research has not investigated what happens to people who take the medication long term.

However, naltrexone has a long history of safe use when used to treat opioid addiction.²⁰



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Naltrexone is designed to block opioid receptors and can precipitate opioid withdrawal, so if you take any **opioid (narcotic) pain** relieving drugs at the same time as LDN, they are unlikely to work. There are other warnings in the CMI, including other medication warnings.

My lived experience

I experienced gastrointestinal side effects including **nausea, stomach discomfort, and cramping**. These symptoms reduced in severity after the first few weeks of treatment. While they have not resolved completely, they occur intermittently and remain manageable.

For me, these side effects have been an **acceptable trade-off** given the perceived benefits. My review of patient reports and clinical commentary suggests that this pattern is not uncommon.

I also found that alcohol did not interact well with this medication. Although I drink infrequently, when I do consume alcohol, I do not feel the normal uplift in mood, and the subsequent hangover effects are more pronounced. This is in line with the use of naltrexone for AUD. Based on this experience, caution with alcohol consumption is warranted

What dose works best?

A common approach described in practice is:

- start very low (e.g., ~1 mg to 1.5 mg/day)
- increase gradually (e.g., by ~1 mg weekly)
- target often cited ~4.5 mg/day (varies)

I did not increase to the **4.5 mg per day dose** as I was titrating by 1 mg doses and felt comfortable that 4 mg was achieving sufficient benefits.

- Critical point: Some clinicians report that higher doses may be less likely to produce “LDN-style” effects and may resemble standard naltrexone effects; evidence is limited.

Prescription practicalities (splitting vs compounding) are provided in Appendix A.

When should it be taken?

The effects of low-dose naltrexone are highly individual. Although there are commonly cited benefits to taking LDN at night, this timing does not suit everyone. I take LDN at night, it has been effective for me, and I have not seen a reason to change.

When I first commenced the medication, I noticed that I woke in the morning feeling unusually energised, similar to having already had a coffee. This effect diminished over time but served as an early indication, for me, that the medication was having an effect.

Some individuals may experience sleep-related side effects when taking LDN at night, including insomnia or vivid dreams, which may be uncomfortable. For this reason, some people prefer daytime dosing.²¹



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When initiating a new medication, I believe patience and consistency are important. Maintaining the same dosing time each day for several weeks before making changes may help in assessing both effectiveness and tolerability. As always, do not change your prescribed dosing advice without consulting your doctor.

Withdrawal and stopping

I am still taking LDN and have not tapered off. I did not find strong warnings suggesting dependence. As a cautious principle, tapering down the same way you tapered up is often the safer approach, guided by your prescriber.

I found changes noticeable within days of increasing the medication. I did not experience significant side effects when making dosing changes.

Practical safety principle: do not stop abruptly. Even if a medication is not considered “addictive,” abrupt cessation can be uncomfortable and destabilising. Tapering is generally the safer approach and should be clinician-guided.

More Information

In my experience, there is relatively limited readily accessible information on LDN within Australia. I found that many of the most practical and detailed resources were available through **U.S.-based compounding pharmacy websites**, where clinicians and pharmacists have been actively prescribing, compounding, and managing patients using LDN for several decades.

I also found educational material produced by compounding pharmacies to be informative, including a video from [The Healthy Choice Compounding Pharmacy](#), which provided a clear overview of LDN use in clinical practice.

The LDN Research Trust in the United Kingdom is a registered non-profit organisation that works closely with prescribers, pharmacists, and patients to support education and research into LDN.

Its website (www.ldnresearchtrust.org) includes information on clinical trials and studies involving LDN, conditions for which LDN has been explored, directories of prescribers and pharmacists worldwide, and practical guides for both clinicians and patients.

What other medical conditions has it been used for?

Studies have shown that LDN may provide benefits in the treatment of chronic pain and inflammation²², fibromyalgia²³, and chronic fatigue syndrome²⁴. Using LDN for these conditions is “off-label”. [The use of low-dose naltrexone \(LDN\) as a novel anti-inflammatory treatment for chronic pain](#) may be useful when discussing this matter with your health care professional.

Contrave (Bupropion + Naltrexone combination product)

Contrave is a medication that contains bupropion 90 mg and naltrexone 8 mg and is used for weight management in some adults alongside diet and exercise.

Contrave **may appear to be an alternative** instead of dosing bupropion and naltrexone separately.



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- **90 mg bupropion** may be in a potentially useful range for mood for some people.
- **8 mg naltrexone** is significantly above commonly described “LDN” ranges (often **1.5-4.5 mg/day**) and may reduce the likelihood of the hypothesised paradoxical LDN effect.

This is not a recommendation either way, but a prompt for careful clinician discussion.



Appendix A: Detailed case notes and dosing logistics (personal history only - not instructions)

Important: The material in this appendix describes my personal history and is not instructions. Do not split, crush, or otherwise alter any modified-release tablet unless your prescriber and pharmacist explicitly confirm it is safe for your exact product.

Bupropion: personal titration history (as conducted under clinician guidance)

My titrating experience

- I was prescribed bupropion 150 mg tablets, with my doctor recommending a **cautious, stepwise dosing approach**.
- Under this guidance, I was advised to begin at a very low dose by **dividing the tablet into quarters**.
- The initial dose was approximately **¼ tablet daily (≈37.5 mg)** for three days, to assess early benefit and tolerability.
- Subject to tolerability and ongoing clinical review, I was advised to **increase the dose gradually over approximately two weeks**, progressing through:
 - **½ tablet daily (≈75 mg)**
 - **⅔ tablet daily (≈100 mg)**
 - **1 full tablet daily (150 mg)**
- After a further two weeks at 150 mg daily, and following continued assessment of response and side effects, the dose was increased to **2 tablets daily (300 mg total)** in accordance with my doctor's guidance. One 150 mg tablet was taken in whole morning and night.
- The total titration period was approx. 4-6 weeks.
- Practically, the tablets were difficult to divide accurately without a pill splitting tool. **150 mg is the lowest manufactured dose in Australia**. The tablet does not break evenly when using a pill splitter. As such the amounts of bupropion detailed are estimates, other than the 150 mg and 300 mg doses.



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Bupropion: tablet-splitting and pill-cutter notes (personal history only)

What is a pill cutter?

A pill-splitter is a simple and inexpensive device to split medicinal pills or tablets, comprising some means of holding the tablet in place, a blade, and usually a compartment in which to store the unused part. They can be purchased from most pharmacies or online and are relatively inexpensive.

I have found more robust and accurate cutters from online stores. I prefer the ones that enable you to hold the pill in place (with a wheel you turn on the outside of the case) and have the option to cut it into quarters (see image).



Important caution:

In Australia bupropion is sold as a 'Sustained Release Formulation'. Following oral administration of bupropion hydrochloride sustained-release tablets (SR), peak plasma concentration (C_{max}) of bupropion is usually achieved within 3 hours. SR formulations provide a 12-hour extended release of medication and are therefore generally dosed twice per day.

Modified-release tablets are **generally intended to be swallowed whole**. The medication comes with a warning that the tablets should be swallowed whole and not crushed, chewed, or divided. **Dividing them can change release characteristics and may increase risk**. Any approach involving tablet splitting or compounding should be done **with medical and pharmacist advice and supervision**.

Low-dose naltrexone (LDN): personal titration history (as conducted under clinician guidance)

My titrating experience

- I was prescribed Naltrexone GH **50 mg** tablets, with my doctor recommending a **cautious, stepwise dosing approach**.
- Under this guidance, I was advised to begin at a very low dose of **1 mg** a day for one week, to assess early benefit and tolerability. Taken at night.
- I increased the dose by **1 mg** a week for next three weeks to my current dose of **4 mg** per day.

This approach is consistent with findings reported in published studies and with dosing strategies commonly described in clinical practice.

- **start very low (e.g., ~1 mg to 1.5 mg/day)**
- **increase gradually (e.g., by ~1 mg weekly)**
- **target often cited ~4.5 mg/day (varies)**

Critical point: Some clinicians report that doses above ~4.5 mg may be less likely to produce "LDN-style" effects and may resemble standard naltrexone effects; evidence is limited.



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Practically, the tablets were difficult to divide accurately **even with a pill splitting tool. 50 mg is the lowest commercially manufactured** dose in Australia.

The tablet does not break easily when using a pill splitter. I used a small scale to approximate 1 mg of the tablet. I used this process for the first 4 weeks of titrating LDN to 4 mg per day.

I highly advise against this approach. It is open to dosing errors and inconsistent results. From a practical perspective, initiating LDN via a prescription prepared by a compounding pharmacist at the required low dose was, in my experience, the safest and most manageable approach.

Low-dose naltrexone (LDN): prescription practicalities (splitting vs compounding)

Prescription tips (splitting vs compounding)

Commercial naltrexone is typically 50 mg tablets, which makes accurate low dosing difficult by splitting alone, especially when dosing **1 mg**.

Practical options:

1. **Tablet splitting + scale** (imprecise and difficult)

Based on my personal experience with this approach, I would advise caution. I found the process to be imprecise and difficult to execute consistently, with an increased risk of inaccurate dosing that may compromise both tolerability and potential benefit.

2. **Compounding pharmacy** (commonly used for LDN)

An alternative approach is to obtain LDN from a compounding pharmacist. This requires a prescription from a medical practitioner specifying the exact amount of naltrexone to be included in each capsule.

In practice, an initial prescription for **1 mg capsules** allows for gradual titration up or down while assessing tolerability and response. Once an effective dose is established, the prescription can be adjusted to reflect that dose (for example, **4 mg capsules**), in accordance with ongoing clinical guidance.

Based on my experience, I strongly preferred this approach. While it requires additional logistical planning prior to commencing treatment, the precision and ease of dosing during initiation and ongoing use at the effective dose made the additional effort worthwhile.

I titrated up to a dose of **4 mg**, and once this dose was established as effective, my prescription was updated to reflect this amount as a single capsule for ongoing use.

Moving to this method was supported by my treating doctor, and I did not experience any difficulty locating a compounding pharmacist to dispense the prescription.



References

Sources are provided as endnotes below.

-
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 - ³ <https://journals.sagepub.com/doi/10.1345/aph.1A099>
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 - ¹⁹ Same as Endnote 12.
 - ²⁰ Same as Endnote 12.
 - ²¹ <https://www1.racgp.org.au/ajgp/2023/april/low-dose-naltrexone-in-the-treatment-of-fibromyalg#>
 - ²² <https://pubmed.ncbi.nlm.nih.gov/38532991/>



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²³ <https://pubmed.ncbi.nlm.nih.gov/38226027/>

²⁴ <https://casereports.bmj.com/content/13/1/e232502>

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