

Client Guide to Opioid Agonist Maintenance Treatment and Long-Acting Depot Buprenorphine

**Developed as part of the Unitaid
LADB Values and Preferences Study**

Acknowledgments

This resource was developed as part of the Unitaid-funded HCV Portfolio long-acting depot buprenorphine study delivered through three cross-country consortiums / led by: the CUTTS HepC Consortium (Médecins du Monde; MdM); HEPC III Consortium (Frontline AIDS); and HepC3P Consortium (PATH/Population Services International - PSI). This resource drew on a series of resources developed by or in partnership with people who use drugs:

- New South Wales Users and AIDS Association (NUAA)'s Consumers' Guide to the Opioid Treatment Program: Depot Buprenorphine Starters' Guide
- L'Équipe de Soutien Clinique et Organisationnel en Dépendance et Itinérance Do you think you may have an opioid dependence? Make an Informed Choice.
- Central Coast Drug and Alcohol Services - NSW Health Central Coast Local Health District Microdosing Transfer from Methadone to Buprenorphine.

The LADB Client Guide was researched, drafted and designed by Coact Technical Support in consultation with medical experts, INPUD, PATH and the study's Community Advisory Board. A number of people on LADB informed this work.

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What this guide does

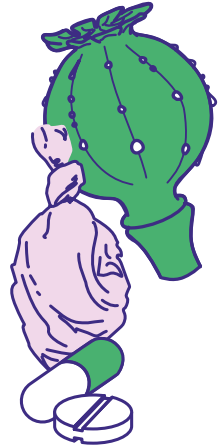
In this guide we will talk you through different options for treatment for opioid dependence. We start by describing what opioids are, what it means to be opioid dependent before going through different types of opioid agonist maintenance treatment (OAMT). We discuss their advantages and disadvantages. The aim is to help you decide if OAMT is right for you and if so which option best matches your needs.

Long acting depot buprenorphine (LADB) is a new drug treatment option available at your clinic. LADB is injected under the skin where it forms a deposit of buprenorphine which lasts for about a month between doses. There is a version that lasts for about a week that may be used while you are transferring onto LADB.

This leaflet is written by your peers who describe our community's experience with OAMT and LADB. This leaflet is designed to help you make an informed choice about which OAMT medication will work best for you and whether LADB can best help you achieve your goals.

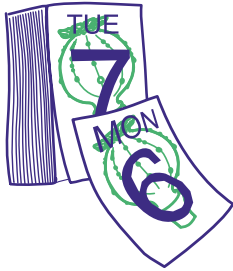
What are opioids?

Opioids are substances frequently prescribed for pain relief. They can also cause relaxation and euphoria. In high doses, opioids can cause an overdose through respiratory depression or arrest. They act to stimulate opioid receptors which provide relief from pain and distress.



What is opioid dependence?

A person is said to be dependent when their use of opioids, whether prescribed or illicit, has a significant impact on their ability to function and their quality of life, and they are having difficulties controlling their opioid use. Another aspect is that when people who have opioid dependence are not using opioids, they experience withdrawal symptoms.

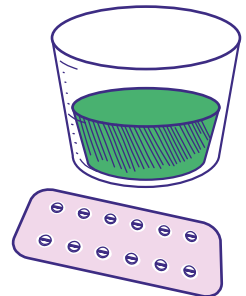


What is opioid agonist maintenance treatment (OAMT)?

Opioid agonist maintenance treatment (OAMT) are medications that are taken on a regular basis to eliminate withdrawal symptoms and cravings, reduce the risk of an overdose, and help people regain control over their opioid use.

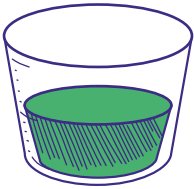
How long can I take OAMT?

The recommended length of OAMT use varies according to each person's circumstances and individual needs, but it is usually given over a long period of time. There may be ups and downs during treatment but, in general, OAMT can support people to make positive changes.



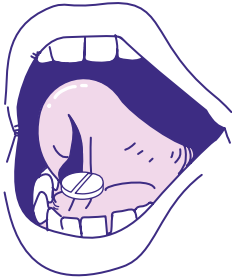
What types of OAMT are there?

There are different types of OAMT medication. The best known are oral methadone and sublingual buprenorphine, which are taken orally, once daily. Buprenorphine is a new version of buprenorphine that will be available in <name of country>.



What is methadone?

Methadone, a long-acting opioid agonist that reduces opioid craving and withdrawal symptoms and particularly at higher doses blunts the effects of opioids.



What is buprenorphine?

Buprenorphine has some of the same effects as other opioids (e.g. heroin, morphine), but tends not to make people as drowsy. Many people report they are more clear minded and energetic on buprenorphine compared to methadone.

What are take home doses?

In some countries people are provided with greater treatment flexibility as they demonstrate positive progress. This can include receiving your doses of methadone or buprenorphine for several days or weeks. This practice increased during the COVID-19 pandemic and led to positive outcomes for many people.

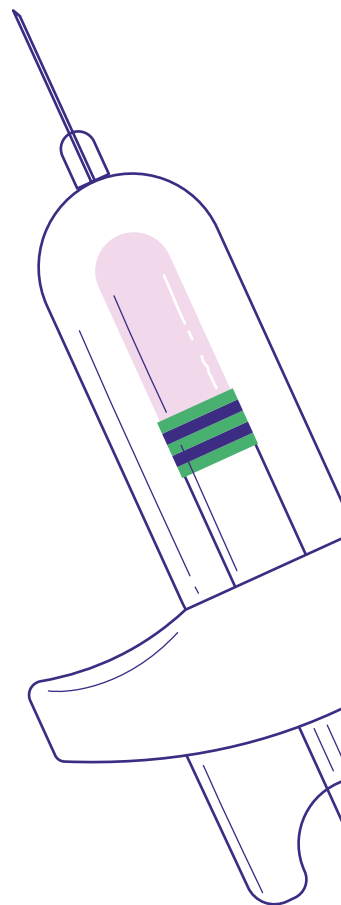


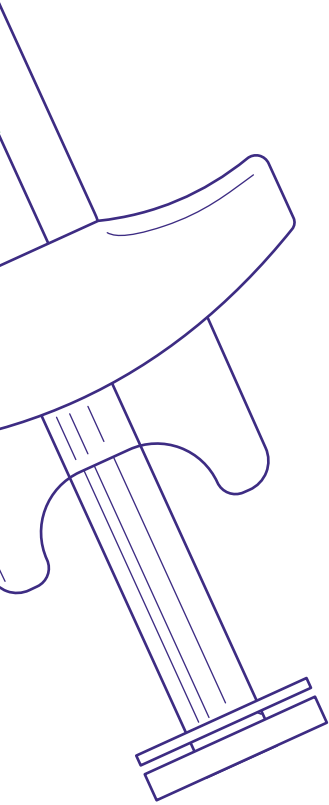
What is Long-Acting Depot Buprenorphine (LADB)?

LADB is injected under the skin where it forms a deposit or “depot”, of buprenorphine which lasts for a week or month between doses. The depot is slowly absorbed by the body, lasting for around a week or a month, depending on the formulation. Being on a depot medication just means the medication is stored under your skin and releases gradually, instead of having to be taken daily. It is dangerous to inject LADB into a vein as it hardens after injection. Depot products are not like implants. You do not have to get anything removed before you are re-dosed. With LADB, your system will have absorbed most of the medication by the end of the set period.

There are two LADB products on the market globally which are approved for use in several high-income countries. Both LADB products were approved after clinical trials demonstrated their effectiveness. The one described in this guide is known as Buvidal.

Buvidal® is an oily liquid that, when injected, forms a wax like deposit under the skin which is slowly absorbed by the body over several weeks. It cannot be easily removed once it is injected. Buvidal has two formulations – one that lasts approximately for a week and one that lasts approximately for a month. The monthly depot offers the great-





est treatment flexibility. The one-week depot is used as people start on Buprenorphine. Buprenorphine comes in different dose strengths.

LADB may be more attractive to people trying to stop using drugs completely and who want greater freedom and less engagement with their clinic so they can focus on other issues in their lives.

While LADB may help some people achieve positive changes, it's important to remember that LADB will not be the right option for everyone. There is no evidence that LADB is more successful than oral methadone or sublingual buprenorphine, but it does offer greater treatment flexibility as it allows for much greater freedom of movement between doses and an end to daily treatment dosing.

How do they work?

All OAMT medications work by attaching to opioid receptors present in the brain and other parts of the body and thus stopping withdrawals. Morphine and methadone are referred to as pure or full agonists. Buprenorphine however has slightly different properties some of which give greater safety in terms of the potential for overdose – thus it is called a partial agonist. This isn't important once you are stabilised as both medications have the same effects to stop withdrawals and ensure that you are feeling comfortable. Moving from methadone to buprenorphine needs to be done with care, particularly when your methadone dose is over 30mg daily. Doctors have become very skilled in managing this changeover (see section in appendix about microdosing).

Which OAMT is best for me?

Below is a table that lists the properties of oral methadone, sublingual buprenorphine and LADB. When you are reviewing this table, you might want to consider the following issues:

Have you tried methadone or buprenorphine in the past? What was your experience?

Your experience with OAMT can help you know what works for you. If you had a positive experience with buprenorphine, then this shows you can benefit from buprenorphine whether taken under the tongue or by depot. If methadone helped you achieve your treatment goals, then this may be a better match for you. You should be able to decide which is best for you based on your experience and the advice of your treatment provider.


Do you plan to continue using opioids during treatment?

If you plan to continue using opioids, methadone may be a better match or taking buprenorphine in lower doses, as higher doses of buprenorphine may block the effects of additional opioids.

How will taking the medication fit into your daily routine, given your work schedule, family responsibilities, distance from the pharmacy and ability to travel?

Take-home doses for methadone and buprenorphine are available in some but not all countries. <country situation>

LADB offers greater flexibility as the depot injection lasting for one month between doses reducing the need for regular clinic engagement. However, the depot injection must be administered by a nurse at a drug treatment clinic. There can be flexibility around the day of administering the depot.



**Factors to consider
when choosing
a treatment**

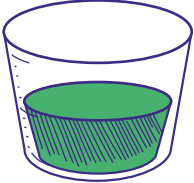
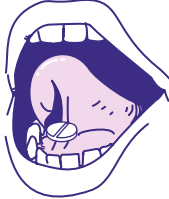

Medication form

**How often the
medication is taken**

**Use of opioids during
treatment**

**Frequency of clinic or
pharmacy visits**

**Frequency and intensity
of the most commonly
observed side effects,
in addition to those
present for all opioids**

<p>Methadone</p> 	<p>Buprenorphine Sub-lingual</p> 	<p>Long-acting Depot Buprenorphine (Buvidal)</p> 
<p>Liquid / syrup</p>	<p>Tablet taken under tongue</p>	<p>Depot injection in clinic under the skin</p>
<p>Daily unless take home arrangements</p>	<p>Daily unless take home arrangements</p>	<p>Monthly or weekly during induction</p>
<p>Option to consider to continue opioid use</p>	<p>Option to consider to stop opioid use</p>	<p>Option to consider to stop opioid use</p>
<p>At start of treatment, methadone is taken at the clinic or pharmacist under supervision on a daily basis. Different clinics may offer take home doses on a case-by-case basis</p>	<p>Take home doses may be offered depending on clinic or country policies</p>	<p>The injection is given normally on a monthly basis in the clinic</p>
<p>Possible sexual problems (erectile difficulties, low testosterone, disruption of menstruation etc), weight gain, itching.</p>	<p>Headaches in the first few weeks of treatment</p>	<p>Headaches in the first few weeks of treatment Monitor the injection sites for side effects (redness, swelling, infection, etc)</p>

Is LADB the right option for me?

Pros	Score
More convenience and greater flexibility with work and education	
Only having to go to the clinic once a month	
Not having to wait at the pharmacy or dispensing service	
Reduced transportation costs due to less frequent visits to clinic compared to daily treatment	
Greater mental clarity and energy	
Less likely to use while on it (particularly when on higher doses of LADB) – less exposure to risk of using while receiving medication or attending drug treatment service	
Less incentive or possibility of diversion (selling your meds)	
Level treatment – less of the ups and downs of daily dosing	
It's much easier to travel when on LADB	

To help you decide, we've put together a list of some of the pros and cons of being on LADB. Depending on your situation and priorities, some of these will be more important for you than others.

You can use the columns below to score which factors are most important for you

Cons	Score
Monthly injections that can be painful - some describe it as like a bee sting, which passes in a few minutes. Some find it itchy	
Some people reported being restless and having too much energy the first 48 hours after their injection	
Constipation (also a common side effect with other OAMT medications)	
Potential increased waiting time to get injected at some clinics	
Less spontaneous access to social or psychosocial support of attending drug treatment service	

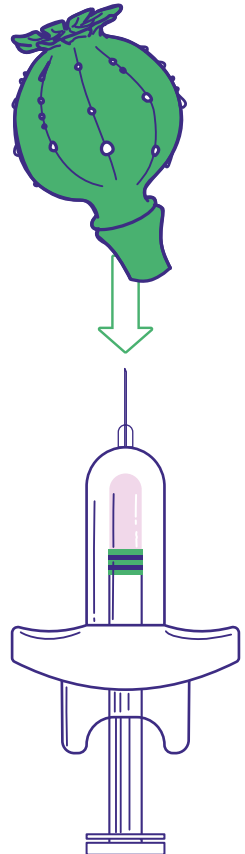
Starting on LADB

There are three pathways to start on LADB: 1) going from street heroin and opioids; 2) swapping from methadone; and 3) swapping from sublingual buprenorphine. Below we outline what to expect from each of these pathways.

1. Going from street heroin and opioids to LADB

If you think the Opioid Agonist Maintenance Treatment (OAMT) might be for you, your prescriber will assess you and discuss the available medications (including LADB). Even if you think LADB is for you, your prescriber is unlikely to start you on a monthly product straight away so they can assess how you react to buprenorphine itself.

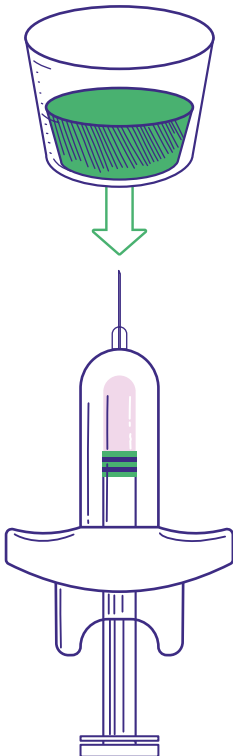
You may be offered a sublingual dose of buprenorphine to make sure you can tolerate buprenorphine. If you have already successfully used buprenorphine before, you may be offered the chance to start on a weekly depot injection without needing to start daily sub-lingual buprenorphine first. After one or more weekly Buvidal doses you will then be offered to move to the monthly depot. (More detail on transition will be added to reflect the country context).



Your prescribing doctor is more likely to agree to you starting quickly on LADB if you have tried buprenorphine before without any problems, and if there are practical reasons that make LADB a better option for you (e.g. living in a regional area, being unable to afford travel costs, work or family commitments).

2. Swapping from methadone to LADB

If you're swapping from methadone to LADB, then you will normally reduce your dose of methadone to 30MG before being asked to stop taking all opioids for 24 hours. The reason for this is that some people can have what is called a precipitated withdrawal. This can occur when a person who has been taking pure "agonist" opioids like methadone or heroin takes a dose of buprenorphine.



Once you are in mild to moderate withdrawals you will be offered buprenorphine which you should experience as comforting and reducing any feelings of withdrawal. Your first dose may be a tester dose of sublingual buprenorphine to make sure you won't get withdrawal symptoms from the buprenorphine. You may choose to take sublingual buprenorphine to try out this medication before committing to a weekly/ monthly depot injection or you may proceed to the depot injection. You should be able to give input as to how you wish to proceed.

However, the good news is that there is a newer dosing option to avoid some of these challenges when moving from traditional opioids like heroin and methadone. It is called

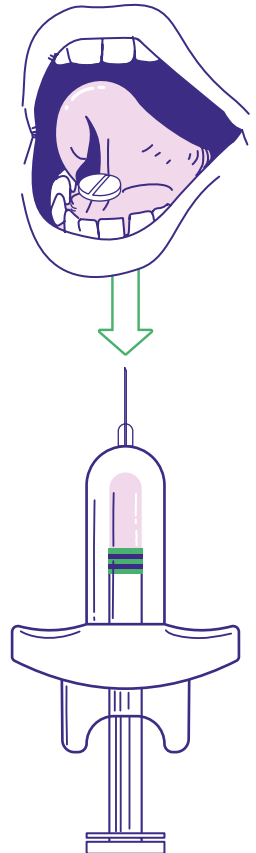
“microdosing” or “low dose” induction, and there is now literature and guidance for doctors on how to do this, as it results in a much more comfortable changeover.

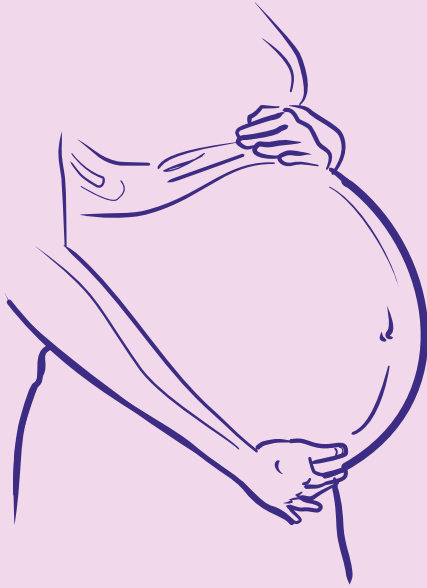
In this “microdosing” or “low dose” induction, you stay on the same dose of oral methadone while gradually introducing low doses of buprenorphine which get bigger every day. This avoids the need for a period of mild to moderate withdrawals. You can talk with your prescribing doctor about the different options and then work out which would be best for you. Some people are confident about managing mild to moderate withdrawal symptoms whereas for others this could be a barrier to swapping to LADB. Doing a changeover using microdosing has greatly increased the ability of people to manage the transition with only minimal discomfort or withdrawals.

If you want to explore the microdosing option in more detail, you’ll find a detailed guide to microdosing at the end of this leaflet.

3. Swapping from sublingual buprenorphine to LADB

Swapping over from sublingual to depot buprenorphine is very straightforward. With Buvidal, most people will take the weekly depot first to make sure Buvidal is going to be useful and effective. This allows you to also secure your other support needs before moving to a monthly depot injection. If you prefer, you can also start straight on the monthly depot.





4. Pregnancy and breastfeeding

There is a lack of certainty about the impact of Buprenorphine in pregnancy and breastfeeding. For this reason, it is not possible to start the medication if you are currently pregnant or breastfeeding. If you are planning to get pregnant it may be better to stay with methadone or sub-lingual buprenorphine, as we are still learning about LADB. For this reason, it is not advisable to start on LADB if you are currently pregnant or breastfeeding. This will include having a discussion about the options, providing information about the risks and benefits of different options, and supporting you to come to the decision that is right for you.

There is, however, now considerable experience with buprenorphine (the main ingredient in Buprenex) in pregnancy and breastfeeding, and it is regarded as safe, and more importantly, much safer than the alternative of attempting to stop opioid use completely. Buprenex contains very small

doses of other substances to create the matrix which enables the medication to be long-acting. Both Buvidal Weekly and Buvidal Monthly contain very small doses of alcohol, although in doses which are unlikely to cause any adverse effects. If you become pregnant while on LADB then you should discuss options with your clinician who will support you to make the best decision for your health and the health of your fetus / breastfeeding child.

If you have not benefited all that much from Buvidal compared to your previous treatments with methadone or sublingual buprenorphine, it might be prudent to switch back to methadone or sublingual buprenorphine.

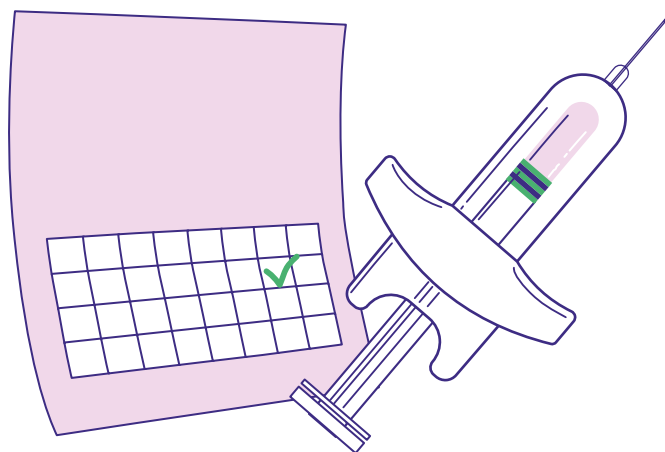
If you decide to continue with Buvidal and are deciding whether or not to breastfeed, the benefits of breastfeeding to infant health should be balanced against the known effects of buprenorphine (see WHO document Guidelines for the Identification and Management of Substance

Use and Substance Use Disorders in Pregnancy for more details on this). In most situations, the benefits of breastfeeding outweigh the risks of small amounts of buprenorphine in breastmilk to breastfed babies.



LADB – getting the dose right

According to information from the clinical trials, you will feel the effects of Buvidal 1-2 hours after dosing.



Finding out the right dose for you is part of the 'stabilisation' stage of OAMT. There is normally a bit of trial and error at the start of your treatment. You may be worried that your depot won't hold you the full week or month. Generally, there will be no problem because LADB builds up and stays in your body for a long time. However, if you start feeling withdrawal symptoms or opioid cravings before the end of your week or month, you can get your next dose early or else take a 'booster dose'. A 'booster dose' is a top-up of sublingual-buprenorphine to hold you until your next injection. If you get a booster dose, it's a sign your medication needs to be adjusted, and your prescriber may want to increase your dose.

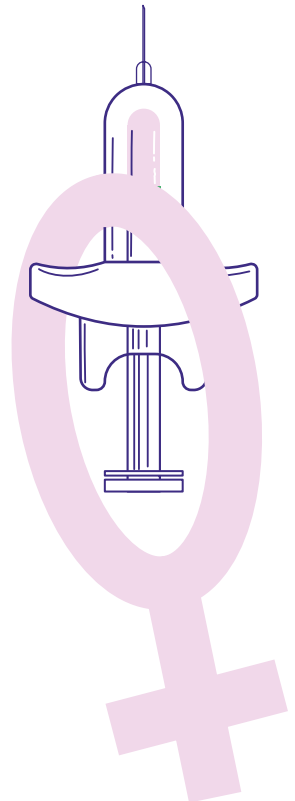
You may find that you need to come in earlier than planned for your next depot. There is no euphoric experience with LADB so working out the right dose is about making sure you are well covered and not experiencing withdrawals. You may find that you can comfortably go for longer periods between depot injections.

People reporting withdrawal symptoms or opioid cravings at the end of the month are likely to top up and receive relief from street heroin or other opioids if they don't have access to a booster dose or early redosing. There is no euphoric effect from dosing early but experiencing withdrawal symptoms or cravings in the last few days of the dose can undermine treatment goals.

LADB is always administered in a clinic setting so there are no take aways. Travelling must be managed to accommodate redosing.

LADB and women

Women and parents on LADB describe the benefit of greater treatment flexibility in supporting them to work, care for the children and manage wider family responsibilities. They welcomed not having to take their children to dispensing services. Some women found that issues of historic trauma bubbled up when switching to buprenorphine including LADB. For many this passed as they settled onto the medication. Some found that a full agonist like methadone better met their needs.

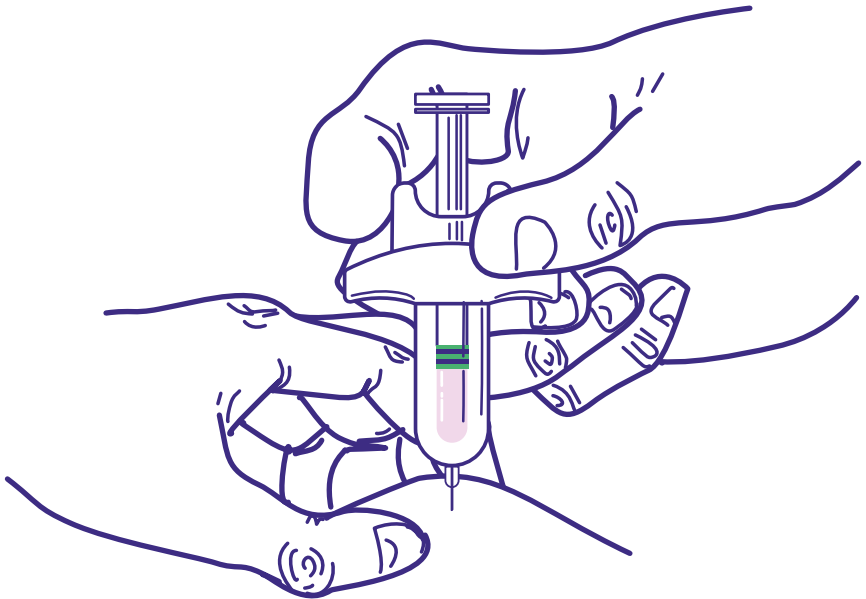


Administration of depot

Buvidal is injected under the skin above various muscle groups - generally the upper arm, stomach, buttock, or thigh by a health care worker.

When you get a LADB injection, they should change (or rotate) the place they inject you each time. Rotating between injection sites is done to avoid continually irritating the same place on your body.

You have the right to tell your doctor or nurse where you want to be injected. Some people experience pain or side effects when they are injected into a particular place or may not want to be injected in certain areas because of their religious or cultural backgrounds. If you do have an issue around being injected in a particular place, you should discuss it with your prescribing team and find a work-around.

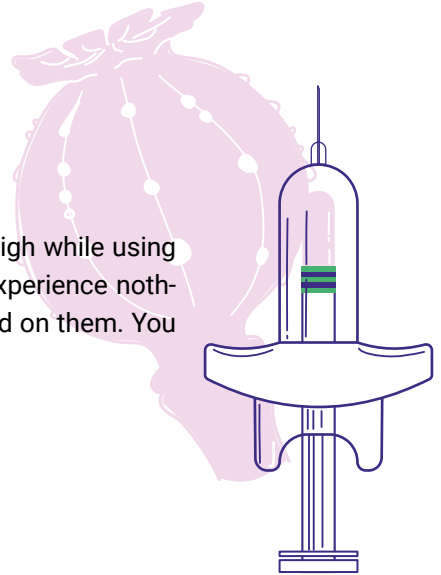


Using other drugs and alcohol on LADB

Heroin and other opioids:

Some people report feeling some type of high while using opioids on top of LADB. Others say they experience nothing at all and the heroin was entirely wasted on them. You are less likely to feel high if you:

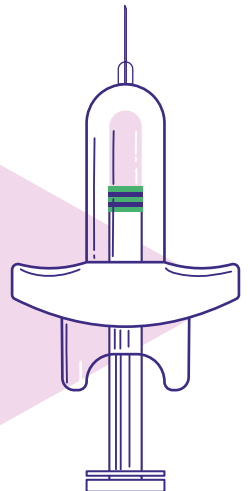
- have recently taken your depot injection
- are new to the LADB programme
- are on a higher dose of LADB

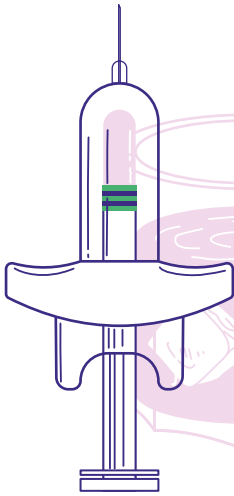


Stimulants

Some people who use stimulants use heroin or other short acting opioids to help regulate and manage the come down after taking stimulants like crack cocaine or methamphetamine or Alpha PVP / flakka (cathinone). Some report experiencing greater problems regulating stimulant use without short acting opioids to help come down, which makes the urge to keep using hard to control. This problem can be most challenging with buprenorphine.

Some people turn to stimulants when they don't have access to the euphoric effects of short-term opioids, and this could undermine positive change.





Alcohol

Drinking alongside OAMT in moderation is manageable. Sometimes people drink more alcohol when they can't get relief from opioids, and this could undermine positive change.

If you are using other drugs and alcohol regularly and in a harmful way, your prescribing team may want to see you in between your dosing days. Having extra appointments isn't a punishment – they just want to check in with you and continue offering support to match your needs.

Opioid Overdose and Naloxone

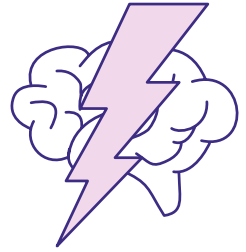
People who are already dependent on opioids are at a very low risk of overdose from buprenorphine alone. However, the risk of overdose increases if you are using alcohol or other drugs, or if you have detoxed after exiting treatment for other opioid use. Research has shown that using 'sedative' drugs while on buprenorphine will increase your risk of overdose, breathing difficulties and death. Sedatives are 'depressant' drugs, including alcohol, benzodiazepines, barbiturates, GHB, and some antipsychotic medications. It's unclear whether these risks are the same on LADB as for sublingual buprenorphine. If you do use sedatives, you should always carry naloxone when you're using and keep some at home. Make sure that your family and friends know how to use it.



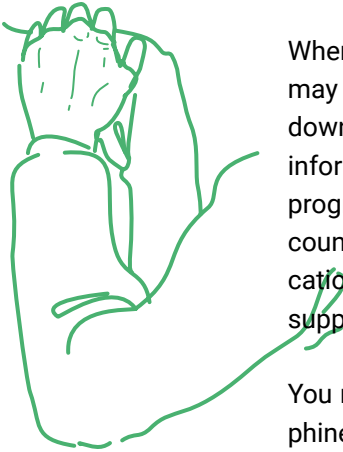
Pain Control

LADB has been shown to be effective in managing moderate to severe pain. LADB can free up time so you can focus on other health issues that you may have previously neglected. If you experience chronic pain, you should talk to your doctor about your options.

If you have an accident or surgery, you should still receive pain relief while on the programme. Your medical team need to know that you are on LADB so that you get enough analgesic (pain relief) cover.



Psychosocial support needs

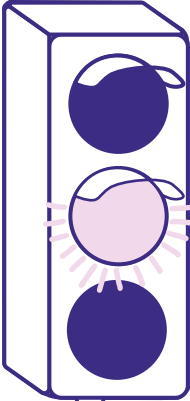


When you start on Buprenorphine including LADB you may find emotional issues bubble up. This often calms down in time. If emotional issues start bubbling up then inform your medical team know so they can monitor your progress and offer advice. Psychosocial support includes counselling, groupwork, practical help with housing, education and employment, mindfulness activities, and peer support groups.

You may find that when you start on OAMT and buprenorphine that psychological issues come up. You may find it helpful to have space and support to explore such issues. Drug workers can also help you plan how to use the extra treatment flexibility available with LADB and to change thinking and behaviour patterns. Your support needs are likely to change over time.

What if LADB doesn't work for me?

If LADB is not the right OAMT for you then you will be swapped over to oral methadone / sublingual buprenorphine. You should always have access to a daily oral alternative to LADB.



Stopping OAMT from LADB

Some people find that LADB makes them feel so 'even' that they think they don't need their next dose. However, even if you do not feel you need your next dose, you should re-dose as scheduled. Taking your medication when you are supposed to means you shouldn't start going into withdrawals and you are protected from overdose if you do use opiates.

If you are really ready to stop taking OAMT, you will have weighed up the good and bad things about being on the program and have come to the decision that your life would be better if you came off LADB. Once you have made the decision, exiting off LADB is just like exiting off other OAMT medications. It is best to take it nice and easy when detoxing. Most people who exit the OAMT successfully do it by gradually reducing their dose. However, because it is new, there is very little research around withdrawing from LADB. We do know that monthly doses stay in your system much longer than daily doses, and buprenorphine will stay in your system much longer than street drugs. It is likely that LADB will naturally decrease the amount of buprenorphine in your system, so it won't be a hard stop.

Appendix on Microdosing

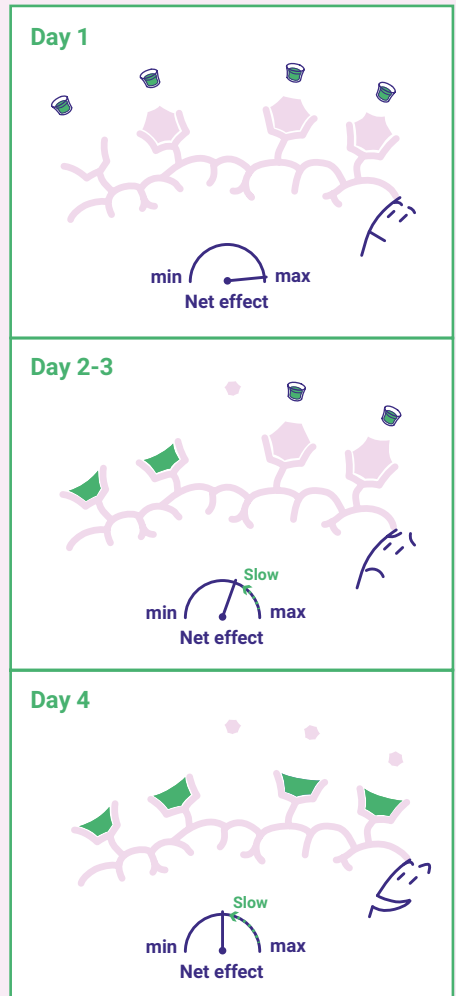
What is Microdosing

What is Microdosing Microdosing is a means of transferring from high doses of methadone to buprenorphine where the buprenorphine is initiated slowly while continuing your current prescribed methadone therapy. The 'micro'-dose of buprenorphine will slowly replace the methadone on the opioid receptors. Each day the buprenorphine dose prescribed will increase and because buprenorphine binds more strongly to the opioid receptors than methadone, it will move additional methadone off the opioid receptors until buprenorphine has fully saturated the receptors. At this point the methadone is ceased.

This is an image to explain how microdosing of buprenorphine will move the methadone (full mu-agonist) off the opioid receptors.

Who is eligible?

Those who are prescribed methadone up to and including 150mg and are wanting to change to buprenorphine products. Transfer from high doses may be undertaken in a more supportive setting such as an inpatient unit ('detox' ward).



Is it withdrawal free?

Short answer: 'NO, but manageable'

You may experience some withdrawal symptoms however these will be less severe than a more rapid transfer approach, and the process will be much quicker than reducing your methadone down to 30mg to swap over (as in the traditional method). Withdrawal symptoms can be managed with additional short-term medications to relieve symptoms.

Do I have to daily dose at the clinic?

This will depend on your clinic. Being in daily contact with the clinic during the transfer can be useful so that any withdrawal symptoms can be picked up quickly and managed; if this is a barrier to transitioning, discuss this with your prescriber. If you require your normal takeaways, discuss with your prescriber to align the 'micro'-doses with your takeaway regime.

Will this impact my work and driving?

You may still be able to drive and work, but if undertaking dangerous work, you may consider having time off or lighter duties. You should not experience increased sedation, but if in any doubt, clinic staff are always available to advise.

When and how do I start?

You can start when you feel ready to start transitioning. Speak to a staff member

about your intentions to transfer via microdosing, they will help you get an appointment with a doctor.

What to expect after the transition?

You may be offered sublingual buprenorphine or Buvidal (weekly or monthly injectables). The dose of buprenorphine may need to be adjusted a few times to suit your individual requirements.

What if I change my mind?

This is your program. You can change your mind; even if it is half-way through the process. The transition can easily be suspended or a consultation arranged quickly to sort it out.

Any further questions?

Please speak to a staff member to assist with any further inquiries or if you want external information, contact the Opioid Treatment Line or do your own research online.

How is the transition done?

The script will generally start at 0.4mg buprenorphine and will increase gradually over a fortnight to 16-32 mg per day. See below for an example of dosing program, sometimes it can be done in a shorter time. A final review will be required after day 14 (when the transition is complete) where the doctor will cease the methadone and review your current buprenorphine dose.

Information about local services