Long-acting depot buprenorphine: an opportunity to expand choices for opioid agonist maintenance therapy and increase coverage of HIV and HCV prevention

Background

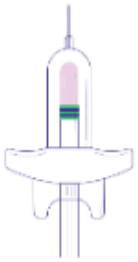
People who inject drugs are disproportionately affected by HIV and hepatitis C virus (HCV). HIV prevalence among people who inject drugs remains significantly higher than in the general population, and insufficient access to harm reduction tools continue to drive transmission of both HIV and HCV. Opioid agonist maintenance therapy (OAMT) is a critical intervention for the treatment of opioid dependence and is part of the recommended package of HIV and HCV prevention interventions recommended by the World Health Organization (WHO). OAMT can reduce the use of other opioids via injection, therefore reducing the risk of exposure to HIV and HCV. It can also promote sustained engagement with harm reduction services and links to other health and social services.

Despite the strong evidence for and demonstrated impact of OAMT reducing HIV and HCV transmission, poor health outcomes, and improving quality of life, access to treatment remains limited in many settings.[i,ii] Stigma and discrimination experienced while seeking services, alongside criminalization of drug use or possession of drugs can hinder access to harm reduction services as people are concerned about arrest or how they will be treated by families, friends, and the wider community should their drug use become known. In addition, limited choice in types of OAMT available at services or policies that require daily attendance for supervised consumption can undermine treatment access and retention.[i] OAMT coverage is higher in high-income countries with more treatment options (e.g. methadone, sublingual buprenorphine, long-acting depot buprenorphine [LADB], naloxone) and more drug services available.

More recently LADB, a new extended-release injectable formulation of buprenorphine administered weekly or monthly has been trialed. LADB reduces the need for frequent clinic visits while maintaining effective treatment for opioid dependence. Many people report strong preference for LADB because of increased flexibility, ability to work and travel, and reduced clinic attendance, while others continue to prefer methadone or sublingual buprenorphine depending on treatment goals, side effects, and preference.

WHO recommendation: In 2026, WHO updated the global guidelines on opioid dependence treatment and overdose prevention to include, for the first time, **LADB** as an additional treatment option for opioid dependence. Read the full updated guidance statement here.

What is LADB?



LADB is one option that can be added to existing OAMT treatment programs. LADB is an extended-release injectable formulation of buprenorphine administered subcutaneously using prefilled syringes. The product is administered weekly or monthly, maintaining therapeutic levels while reducing the need for frequent clinic visits. The slow-release nature of the treatment in contrast to other forms of sublingual buprenorphine or methadone, reduces the needs for such frequent attendance at harm reduction services.

Expanding client choice

A diversified range of OAMT options allows health systems to better respond to different patient needs. [iii] LADB, a formulation of OAMT, is administered weekly or monthly, and offers a more discreet and convenient treatment option that may reduce stigma and improve retention in care, with potential benefits for social and economic stability.[ii,iii,iv] Evidence from OAMT programs globally suggests that offering choice in treatment options can support greater treatment uptake, improve retention,[v] and enable more client-centered care for people who inject drugs, contributing to lower HIV/HCV transmission.[vi,vii]

Benefits of LADB

- **Benefits of LADB for clients may include:** lower risk of HIV/HCV transmission, fewer clinic visits, leading to more time for family life, employment and educational opportunities; and cost savings that come with reduced clinic visits (e.g., transportation fees, time away from work.[iv] Less frequent attendance can also minimize unintended disclosure of drug use and reduce associated stigma and discrimination. Evidence from Scotland suggests that less frequent attendance at drug services can support reduction in use of other drugs by limiting contact with peers and getting drawn into unplanned using. However, some participants reported missing the social and service engagement opportunities of attending harm reduction services, particularly when weekly or ten-day take-home doses were available.
- **Benefits for harm reduction programs may include:** reduced HIV and HCV incidence, improved treatment adherence and retention, reduced treatment disruption due to missed daily doses, increased flexibility for service delivery programs, and reduced risk of medication diversion and simplified service delivery models.

Community leadership

It is vital for people with lived/living experience of drug use to be involved in OAMT product selection, values and preferences assessments (see the WHO Needle and Syringe Program [NSP] Operational Tool Annex 3 for additional details), design of rollout messaging and user education materials, implementation monitoring, identification of access barriers after introduction—and monitoring implementation challenges, treatment transitions, unintended harms, and barriers to continued access after introduction. Community involvement can create demand for services, increasing uptake, strengthen counseling services, and ongoing feedback to quickly respond to gaps and community needs.

LADB at a glance

LADB is an extended-release injectable formulation of buprenorphine administered subcutaneously using prefilled syringes and provides sustained therapeutic levels of buprenorphine over extended periods.

Administration: The LADB product available through The Global Fund, Buvidal,® can be injected in several areas of the body, including upper arm, thigh, abdomen, and buttocks. The product is delivered using a prefilled 23-gauge needle and a controlled-release formulation designed to maintain stable buprenorphine levels over time.

Available dosing formulations: LADB is available in both weekly and monthly formulations. Weekly dosing is often used during treatment initiation and stabilization, after which many clients may transition to monthly dosing. The product available through The Global Fund comes in the following doses:

LADB Formulations (Buvidal®)	
Weekly	**Monthly**
8 mg	**64 mg**
16 mg	**96 mg**
24 mg	**128 mg**
32 mg	**160 mg**

Storage and handling: The product should be stored at room temperature (<25°C) and must not be refrigerated or frozen. Each shipment includes a temperature monitoring device to support appropriate storage conditions. The product has a three-year shelf life. These storage conditions allow LADB to be integrated into standard pharmaceutical supply chains used for other injectable medicines, which may simplify logistics compared with products requiring cold chain storage.

Clinical protocol considerations: Treatment protocols for LADB may vary by country and clinical program. In some settings, treatment initiation may involve induction with sublingual buprenorphine prior to administration of LADB. Countries developing national treatment protocols should review clinical guidance and regulatory requirements when introducing LADB into OAMT programs.

Procurement and quantification: LADB will be available to countries through The Global Fund's wambo.org platform, enabling countries to procure the product using financing from The Global Fund as part of HIV prevention and harm reduction programs. The Global Fund's HIV Technical Guidance identifies LADB as a priority harm reduction intervention within comprehensive HIV prevention programs for people who inject drugs, encouraging countries to consider incorporating it into their funding requests for The Global Fund Grant Cycle 8 (GC8) where appropriate.

Careful introduction: Introducing LADB requires careful planning, provider training, and informed client choice. Particular care is needed when transitioning people from methadone, especially at higher doses, as some people may experience withdrawal, destabilization, or prefer to remain on existing treatment. In settings with limited prior experience of buprenorphine, phased introduction, peer support, and strong clinical guidance are particularly important.

Early evidence from studies in LMICs

Evidence on the feasibility, acceptability, effectiveness, and cost-effectiveness of LADB in low- and middle-income countries (LMICs) is currently being generated through a multi-country implementation study funded by Unitaid. The study is being implemented by PATH, Population Services International, Médecins du Monde, and Frontline AIDS in eight countries: Egypt, India, Kyrgyzstan, Nigeria, South Africa, Tanzania, Ukraine, and Vietnam.

- Preliminary findings from early implementation sites in Kyrgyzstan, Nigeria, South Africa, and Ukraine indicate that LADB can be introduced within existing OAMT programs and delivered safely in routine program settings.
- Early observations suggest that LADB is acceptable to both clients and providers**,** although findings are based on early enrollment and limited follow-up. Reported adverse events have been mostly mild to moderate, with injection site reactions such as redness or tenderness occurring in a small proportion of participants. People with opioid dependence who participated in focus group discussions expressed great interest in LADB and its potential to improve autonomy, health, and quality of life. There were, at the same time, concerns regarding potential withdrawal, injection site pain, and continued access to LADB.
- Many participants who initiated treatment have expressed interest in continuing LADB, suggesting potential for sustained engagement in OAMT services.
- LADB medication costs are currently more expensive than standard of care OAMT, but costs for LADB are much lower than standard of care due to requiring less frequent visits to the provider. **Preliminary estimates for South Africa based on early LADB implementation compared to the current standard of care suggest that under model assumptions reducing the cost of LADB medication to below 180 USD could make LADB implementation cost-saving compared to methadone** at a willingness to pay threshold of 3,535 USD/disability-adjusted life years (DALYs).[viii] †,‡

Alignment with The Global Fund's GC8 priorities

Harm reduction remains a core priority for The Global Fund under GC8 (Program Essential 3), including support for OAMT, needle and syringe programs (NSPs), overdose prevention, and community-led service delivery. GC8 guidance emphasizes prioritization of high-impact, evidence-based interventions that improve effectiveness, efficiency, accessibility, and alignment with community needs.

Within this context, LADB represents an opportunity to expand treatment choice within OAMT programs through a more client-centered and flexible service delivery model. The Global Fund's GC8 HIV prioritization guidance specifically encourages countries to assess the potential role of LADB as part of comprehensive harm reduction programming, recognizing its potential to simplify service delivery, prevent HIV/HCV transmission, improving acceptability for users, and—depending on pricing and implementation context—potentially reduce program costs.

Countries may therefore consider including LADB within GC8 funding requests, budgeting exercises, and broader national harm reduction planning processes, particularly where expansion of OAMT access and retention are identified priorities.

Access through The Global Fund GC8

Indicative price (for GC8 planning and budgeting): 120 EUR (~140 USD) per monthly dose.[i; xi ; 1]

This indicative planning price is intended to support GC8 budgeting and costing exercises and may continue to evolve as access pathways, procurement volumes, and implementation experience expand.

Cost-saving and value

The indicative planning price represents a substantial reduction compared to prices currently observed in many high-income markets for LADB. Based on publicly reported pricing in selected European markets, The Global Fund indicative price is approximately 50–60 percent lower than current monthly treatment costs, with even larger differences observed in some other markets.

This indicative planning price may represent one of the first opportunities for many LMIC programs to realistically consider large-scale introduction of LADB within publicly financed harm reduction programs.

It may also offer compelling value for money. Although LADB's drug costs remain higher than the standard of care, its substantially lower delivery costs can offset that difference. Preliminary modeling from South Africa suggest that, under the model assumptions, reducing LADB drug costs to below approximately 180 USD per month could make LADB implementation cost-saving compared to the country's standard of care—and the indicative GC8 planning price falls below that threshold. If these assumptions hold in practice, GC8 financing could enable countries to expand treatment choice without increasing costs, and while potentially reducing them.[Error! Bookmark not defined.]

[1] Indicative price for budgeting purposes; subject to programmatic assumptions and implementation conditions. EUR–USD conversion based on approximate exchange rate (~1.17 EUR–USD).

In addition to potential economic value, LADB may also offer:

- Clinical benefits, including improved treatment continuity for some clients.
- Programmatic efficiencies through reduced dosing frequency and service delivery burden.
- Greater flexibility and client choice within OAMT programs.

As access expands and implementation experience grows across LMIC settings, pricing and delivery models may continue to evolve with increased demand and scale.

Regulatory and introduction considerations

LADB already meets key international regulatory standards that support procurement through programs financed by The Global Fund. Products procured through The Global Fund generally require a WHO Prequalification Program or a stringent regulatory authority (SRA). LADB has received approval from multiple SRAs, including the European Medicines Agency, United States Food and Drug Administration, United Kingdom Medicines and Healthcare products Regulatory Agency, and Australia's Therapeutic Goods Administration, among others.

Under The Global Fund's Quality Assurance Policy for pharmaceutical products, medicines that are not antiretrovirals, tuberculosis, or malaria treatments must additionally meet the national regulatory authority requirements in the country where the product will be used. As LADB is not yet registered in many LMICs, countries may need to pursue national authorization through standard registration procedures and/or other nationally recognized pathways, such as import waivers or special authorizations, to support early introduction while full registration processes are underway.

To help accelerate national authorization, countries and manufacturers may also leverage the WHO Collaborative Registration Procedure (CRP). The WHO CRP allows national regulators to rely on existing regulatory assessments conducted by trusted authorities to facilitate faster national approvals. The manufacturer of the LADB product expected to be available through The Global Fund's Pooled Procurement Mechanism plans to utilize the WHO CRP to support national registration processes. Countries participating in the WHO CRP are therefore encouraged to consider using this reliance pathway to facilitate timely authorization of LADB. A list of countries currently participating in the WHO CRP is available here.

Given these existing regulatory approvals and available acceleration pathways, many countries may be able to pursue accelerated authorization pathways for LADB introduction. Countries planning to introduce LADB should work with manufacturers, national regulatory authorities, and technical partners to develop country-specific regulatory strategies that support timely authorization, procurement, and program implementation. Countries should also plan for continuity of supply, transition pathways between OAMT products, and management of treatment interruption to avoid destabilization.

What can countries do now?

1. **Include LADB in The Global Fund GC8 funding requests:** Countries are encouraged to assess the potential role of LADB where appropriate and aligned with community needs, existing OAMT systems, provider capacity, and informed client choice. LADB can be included as an option within existing harm reduction services as part of a comprehensive HIV/HCV prevention package.
2. **Engage community organizations and harm reduction partners** to support treatment uptake, and design and delivery of services, monitoring and demand generation.
3. **Update national OAMT policies and treatment guidelines to include LADB.**
4. **Assess regulatory pathways for national authorization to determine the most appropriate pathway for authorizing LADB for use:** Where applicable, countries participating in the WHO CRP may consider using this reliance mechanism to facilitate the regulatory approval process.
5. **Estimate demand and budget implications:** Countries can use available quantification tools to estimate the number of clients who may initiate LADB treatment and the corresponding procurement and program costs. These estimates can support development of realistic budgets within GC8 funding requests.
6. **Consider service delivery models for LADB introduction within existing OAMT programs,** assessing facilities that could pilot introduction and training needs for health care providers.

Tools available to support LADB introduction and scale-up: All tools were developed by the community, clinicians, and researchers as part of the Unitaid HCV Portfolio and reviewed by a global Community Advisory Board. These tools can be adapted to your country context to support the introduction and scale-up of LADB (linked here: https://inpud.net/global-hepc-community-advisory-board-cab/).

Resource name	Purpose
LADB Client Guide	A guide that explains LADB, the transition process, benefits and other key considerations.
LADB Brief Guide	A three-page brief guide that explains LADB, the transition process, benefits and other key considerations.
LADB Peer Educational Tool (flipbook)	Educational resource to be used by peers to explain what LADB is and guide client choice.
LADB Training for Peers on Client Choice	Training for peer workers to support informed client choice, treatment adherence and positive change.
LADB Explainer Video	A brief film explaining LADB, including clinician guidance and client testimony: https://www.youtube.com/watch?v=BLxjih0c9JE
LADB Quantification Tool	A tool for policymakers, implementers and clinicians to help estimate the quantity and budget for LADB within OAMT services.

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† *Note on modelling methods:* A dynamic deterministic mathematical model of HIV and HCV transmission among people who inject drugs was developed to project the likely impact and cost-effectiveness of LADB. The model of people who inject drugs assumes initiation and cessation of injecting over time, HIV transmission through sexual contact and needle sharing, HCV transmission through needle sharing, and the progression of disease through clinical stages. Transmission rates, mortality rates, and risk of fatal overdose vary depending on the status of individuals with respect to use of OAMT, NSP, antiretroviral treatment, stage of disease progression, race, sex and duration of injecting. The model is calibrated using Bayesian methods to four biobehavioral surveys over 2013–2023 and OAMT and NSP programmatic data. DALYs associated with opioid dependence, liver disease, and HIV are calculated over a 24-year time horizon with three percent annual discounting. Based on data from high-income settings, we assume that compared to methadone, the standard of care in South Africa, LADB reduces overdose risk, halves injecting-related transmission of HIV and HCV and increases quality of life by six percent. Incremental costs and benefits are obtained by comparing the modelled standard of care scenario to a scenario in which all enrollments to OAMT after 2026 receive LADB.

‡ *Note on costing methods:* The 2025 cost of LADB implementation (one month of treatment initiation, followed by ongoing maintenance) at a community-based harm reduction site in South Africa was estimated from the provider perspective using a rapid micro-costing approach. The cost per person treated is comprised of staff, equipment, supplies, other recurrent overhead, and medication costs. The monthly assumed unit cost for LADB medication was based on production costs and profits in European and Australian markets. The standard of care OAMT unit costs utilized for the counterfactual were derived for country level budgeting of services for people who inject drugs in South Africa, which was external to this LADB study. Broader societal costs, including any economic gains due to increased productivity, or reductions in crime and incarceration, have not been included.