

## Introduction to Long-Acting Injectables

The term long-acting ARV injectable refers to an antiretroviral drug that is delivered via an injection and persists in the body for an extended period of time. These drugs are being developed as treatment for people living with HIV and as pre-exposure prophylaxis (PrEP) for HIV-negative people. The goal is to develop an injectable-only regimen that would minimize adherence requirements. For both treatment and prevention, daily dosing can be a challenge. Some people might prefer a product that is discreet and requires less frequent dosing. The candidates that are furthest along are rilpivirine (also known as TMC278, brandname Edurant) and cabotegravir-LA (also known as GSK744-LA—and is an analog of the drug dolutegravir). Injectable antibodies are also being considered for PrEP.

The physical and chemical properties of ARVs like cabotegravir and rilpivirine make them good candidates for long-acting injectables. Specifically, they are potent, poorly water-soluble and have relatively small oral doses, meaning that the volume of an injected dose will not be too high.

A drug only works if it is present in sufficient quantities in the body. Each medication is processed, or metabolized, by the body in a specific way. Some drugs are processed rapidly, others more slowly. Long-acting injectables have a long half-life, which means the drug remains in the system for a long time. This is good because it allows less frequent dosing. But it can be challenging if someone wants or needs to stop using the medication, since it takes some time for it to leave the body. For long-acting injectables, it is essential to understand how the drug is processed—the pharmacokinetics and pharmacodynamics of the drugs in the body—to be sure that a given dose leads to blood levels that are safe and effective.

## What does it take to develop a long-acting injectable for HIV treatment and prevention?

