# Long-Acting Antiretroviral Injectables (LAARVI) Information Sheet

## Long-Acting Injectables

Long acting injectables (LAIs) allow for the long-term slow release of medication into the body. LAIs have the advantage of infrequent (less than daily) dosing and are intended to provide sustained medication levels. LAIs have been used as contraceptives and have been used to treat a variety of other conditions such as mental health disorders, and now they are being considered for HIV treatment and prevention. LAIs are administered as injections to deposit medication into the muscle (typically of the arm or buttocks).

## How might LAARVIs help with HIV treatment and prevention?

LAARVIs are not currently available outside of research studies for HIV treatment or prevention. However, they may be available in the near future, first for treatment. For individuals living with and managing HIV, having options other than taking daily HIV pills is important. Recent studies have shown that LAARVIs were just as effective for the study participants as taking daily pills for managing HIV, with the added benefit of less frequent dosing[i]. The research suggests that people living with HIV may be able to receive injectable treatment once every 1-2 months instead of taking daily oral medication. The US Food and Drug Administration is currently reviewing an application for the approval of two LAARVIs for HIV treatment: *cabotegravir* and *rilpivirine*.

For people who are HIV-negative but vulnerable to contracting HIV, it is also important to have options other than taking a daily pill for HIV prevention. Research is underway to determine if a LAARVIs could prevent HIV. When starting a LAARVIs for the first time for treatment or prevention, individuals have to take oral medication for a few weeks to make sure they don't experience any major side effects to the medication, as once the medication is injected into the muscle it will stay in the body for many months.

## Resistance Concerns with LAARVIs for treatment and prevention

If someone stops taking LAARVIs for treatment of HIV infection, they will need to switch to oral drugs, as the probability of developing resistance to the LAARVIs is very high as their levels in the body slowly decrease as HIV rebounds. Likewise, if LAARVIs are taken for prevention, over the course of many months after they are stopped the blood levels decline and HIV exposure and infection during that time can lead to HIV-resistant infection.

## LAARVI HIV Research (As of July 2019)

The **AIDS Clinical Trials Group** (ACTG) has developed two research studies to evaluate LAARVIs as an option for HIV treatment. The first study in development, ACTG 5357, will test an LAARVI medication called *cabotegravir,* in combination with an infusion of a broadly-neutralizing antibody. The second study which is already accruing participants, ACTG 5359, will test two LAARVI medications *(cabotegravir* and *rilpivirine),* specifically among people who have had difficulty managing their HIV with daily oral medication.

The **HIV Prevention Trials Network (HPTN)** is conducting two studies to evaluate the safety and efficacy the injectable *cabotegravir* compared to daily oral tenofovir disoproxil

fumarate/emtricitabine (TDF/FTC), for pre-exposure prophylaxis (PrEP) for the prevention of HIV infection. HPTN 083, a study among men who have sex with men and transgender women. HPTN 084 is a study being done among HIV-uninfected women.

The **International Maternal Pediatric Adolescent AIDS Clinical Trials Network** (IMPAACT) is conducting IMPAACT 2017. IMPAACT 2017 is studying the safety and efficacy of injectable *cabotegravir* and *rilpivirine* among children and adolescents living with HIV.

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[i] **Janssen Pharmaceutical** confirmed in March 2019 that the novel, investigational, LA two-drug injectable regimen of *rilpivirine* and *cabotegravir* met its primary endpoints in two major Phase 3 studies - the Antiretroviral Therapy as Long-Acting Suppression (ATLAS) trial and the First Long-Acting Injectable Regimen (FLAIR) trial. The positive 48-week results from both studies showed that **Janssen's** rilpivirine and **ViiV Healthcare**'s cabotegravir, injected every four weeks, had similar efficacy in maintaining viral suppression in adults living with HIV-1 when compared to a standard of care, daily, oral three-drug regimen. This data is the basis of the pending FDA and EMA applications for the approval of these agents for the treatment of chronic HIV infection.