

Cabotegravir PrEP Implant Might Prevent HIV for a Year

The removable implant maintained adequate cabotegravir levels for several months in a mouse study without the injectable drug's "long tail."

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An experimental biodegradable implant for [pre-exposure prophylaxis \(PrEP\)](#) could potentially offer protection against HIV for up to a year, according to early study results published in the [Journal of Controlled Release](#). What's more, drug levels dropped rapidly when the implant was removed, avoiding the "long tail" problem seen with cabotegravir injections.

Based on these findings in mice, the researchers suggested that the ultra-long-acting implant could "potentially revolutionize current HIV PrEP and help curb the global HIV epidemic."

Daily PrEP pills and long-acting injectables—Apretude (cabotegravir) administered every other month or Yeztugo (lenacapavir) given twice a year—are highly effective for HIV prevention. ViiV Healthcare is working on [longer-acting cabotegravir injections](#) that could be administered every four to six months, while Gilead Sciences is working on a [once-yearly formulation of injectable lenacapavir](#). But [PrEP has still not reached its full potential](#), and more options would be welcome.

One such alternative could be PrEP implants inserted under the skin that release drugs over an extended period. This type of implant is already widely used for contraception.

Rahima Benhabbour, PhD, of the University of North Carolina at Chapel Hill, and colleagues evaluated a biodegradable ultra-long-acting subcutaneous cabotegravir/barium sulfate (CAB/BaSO₄) implant capable of maintaining therapeutic cabotegravir concentrations for up to 390 days.

An advantage of biodegradable implants is that recipients do not need to undergo repeated minor surgery to remove spent devices. A notable benefit of implants over injections is that they are fully removable. When using Apretude for PrEP, residual cabotegravir can remain in the body for a year or more after the last injection, known as a "[long tail](#)." If a person acquires HIV after stopping Apretude, the virus can develop resistance to cabotegravir.

In 2023, [Benhabbour's team reported](#) that a biodegradable subcutaneous cabotegravir implant was well-tolerated in female mice and macaque monkeys, with no signs of toxicity or chronic

inflammation. In macaques, cabotegravir concentrations exceeded established PrEP protection levels within three weeks and provided complete protection against repeated rectal exposures to an HIV-like hybrid virus.

In the new study, the researchers added the contrast agent barium sulfate to the implant, enabling them to use X-rays to see where it ends up in the body. The CAB/BaSO₄ implant was well-tolerated in mice and showed minimal to moderate signs of local inflammation and little to no systemic inflammation.

After removing the implant, cabotegravir plasma levels fell below the established inhibitory concentration within 24 hours and below the limit of quantification within 14 days in five out of six mice. A full biodistribution study showed that cabotegravir was mainly localized in subcutaneous tissue and plasma at the injection site with no detectable drug in other organs. Whole-body X-ray imaging showed that the implants remained visible for up to 268 days with no noticeable migration.

The development of ultra-long-acting removable implants “represents a significant advancement in the field of HIV PrEP,” the researchers concluded. “These technologies address key challenges associated with currently available preventative options, primarily related to patient adherence and potential drug resistance.”

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