Imagine a child in the Sahel protected from malaria for an entire season after just one injection of chemoprophylaxis. Or a woman at risk of HIV in Zambia taking a single capsule every 2 weeks that slowly releases an antiretroviral drug to protect her from infection. Could the risk of resistance to medications for infectious diseases be reduced through the use of long-acting (LA) patches, implants, or injectable drugs?

Thanks to scientific and technological advances, these scenarios might be feasible over the next decade. In high-income countries, the shift from daily oral medication to weekly, monthly, and less frequent LA formulations has been reported to have better adherence and health outcomes across many areas such as antipsychotic treatment for schizophrenia, the management of severe, chronic asthma, and opioid substitution therapy. In sub-Saharan Africa, LA hormonal contraception, as an injection or implant, has become the method of choice for most women of reproductive age.

LA formulations are not approved for prevention or treatment of HIV, tuberculosis, malaria, or hepatitis C, but active research is being undertaken in these areas, some with non-traditional delivery methods. The pipeline for LA injectable drugs for HIV prevention and treatment is the most advanced. Cabotegravir, a new antiretroviral in the integrase inhibitor class, is being studied in phase 3 trials as a single intramuscular injection every 8 weeks for pre-exposure prophylaxis, with support from public and private sources, including the Bill & Melinda Gates Foundation. Several other LA formulations of new and existing antiretrovirals are in earlier stages of development. In addition, the broadly neutralising antibody VRC01, delivered every 8 weeks by intravenous infusion, is being studied in a phase 3 trial for HIV prevention, and other broadly neutralising antibodies are at earlier stages of development. In malaria, LA formulations are being explored for chemoprophylaxis and vector control. Nanotechnology might even have the potential for development of a one-shot cure for hepatitis C virus or a one-shot treatment for latent tuberculosis infection.

Injectables are just part of this emerging landscape. Once-weekly gastric resident capsules, various types of patches, implants, and vaginal rings are all being developed to deliver LA medicines. Some of these might also serve as multipurpose technologies that could deliver more than one drug, such as pre-exposure prophylaxis and hormonal contraception to prevent both HIV and unwanted pregnancy.

Despite their promise, LA technologies are likely to pose substantial challenges in low-income and middle-income countries (LMICs). With regard to service delivery, intramuscular injections and implants would need to be given by a health-care provider, potentially increasing the frequency of clinic visits, but at a time when treatment and care for HIV and other diseases are fairly straightforward, and often provided in community settings. New models of care and adherence support would be needed to mitigate the consequences of missing a monthly or less frequent dose of medicine. Strengthening health systems would also be required in areas such as management of supply chains and medical waste.

Developing a healthy market for LA products in LMICs will be more challenging than for conventional, oral medications. Currently, more than 90% of the antiretroviral drugs supplied by major funders such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and the US President’s Emergency Plan for AIDS Relief (PEPFAR) are sourced from generic suppliers. If a similar approach is to be applied to LA products, complex intellectual property and generic manufacturing issues—for the drugs themselves, the processes used for LA formulation, and the delivery devices—will have to be addressed before the completion of clinical trials, and...
those trials will need to include all potential beneficiary populations in LMICs. Overall, the costs of manufacture, delivery, and demand creation must be comparable to those for currently available products. Above all, LA approaches in addition to being safe must be designed upfront for simplicity to minimise burden and increase convenience for patients, providers, and health services.

To avoid the pitfalls of the past, when new medicines were introduced first in high-income countries and only much later in LMICs, we need to be thinking ahead about LA technologies for infectious diseases. That is why Unitaid is working with a wide range of partners and stakeholders to explore these issues, including through a global technical consultation in Geneva, Switzerland, on Nov 1–2, 2018, that will consider the science and market landscapes for LA technologies. Our shared goal should be to accelerate the development and implementation of these new approaches so that they have the greatest possible impact against global epidemics.

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