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# GUIDELINES ON LONG-ACTING INJECTABLE CABOTEGRAVIR FOR HIV PREVENTION

**WEB ANNEX E. PREDICTED EFFECTS OF INTRODUCTION OF LONG-ACTING INJECTABLE CABOTEGRAVIR PRE-EXPOSURE PROPHYLAXIS IN SUB-SAHARAN AFRICA: A MODELLING STUDY**

Guidelines on long-acting injectable cabotegravir for HIV prevention. Web Annex E. Predicted effects of introduction of long-acting injectable cabotegravir pre-exposure prophylaxis in sub-Saharan Africa: a modelling study

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## HIV Modelling Consortium Working Group on Modelling Integrase Inhibitor Drug Resistance in Relation to Injectable Long-acting Cabotegravir Use in Sub-Saharan Africa

### Abstract

**Background:** Long-acting injectable cabotegravir (CAB-LA) is an HIV integrase inhibitor that has demonstrated high efficacy as HIV pre-exposure prophylaxis (PrEP) and is now under consideration as a new option for HIV prevention in sub-Saharan Africa. There is concern, however, that this could lead to increases in integrase inhibitor resistant virus undermining current treatment programmes that rely on dolutegravir. We used an individual-based model of HIV transmission and effects of ART to jointly model the positive and negative effects of CAB-LA introduction in settings in sub-Saharan Africa.

**Methods:** We simulated 1000 “setting-scenarios” reflecting both variability and uncertainty about HIV epidemics in sub-Saharan Africa. PrEP use is assumed to be risk-informed and to be used only in 3-month periods of having condomless sex. For people who initiate on CAB-LA after being infected with HIV or seroconvert while on CAB-LA, or for those with high cabotegravir concentrations due to being in the early tail period after stopping CAB-LA, we consider the risk of integrase inhibitor resistance emergence. We projected the outcomes of a policy of no CAB-LA introduction and CAB-LA introduction in 2022 over 50 years. We considered in 50% of setting-scenarios that RNA-based HIV testing, rather than regular antibody-based HIV testing, be used to allow higher sensitivity and to reduce resistance risk. For cost–effectiveness analysis we assumed the cost of CAB-LA to be the same as for oral PrEP (US\$ 116 per year), a cost–effectiveness threshold of US\$ 500 per DALY averted, and a discount rate of 3% per year.

**Results:** As modelled, CAB-LA PrEP introduction leads to a substantial increase in PrEP use with approximately 2.6% of the adult population (and 46% of those with a current indication for PrEP) on PrEP compared with 1.5% (28%) without CAB-LA introduction over 20 years, due to the relative preference for injectable PrEP. Given our assumption that PrEP use is risk-informed and there is high use of PrEP in those at risk, there is a predicted reduction in HIV incidence of 29% (90% range across setting-scenarios 6–52%) over the same period. In people initiating ART, the proportion with integrase inhibitor resistance (including to dolutegravir) is projected to be in 20 years’ time only 1.7% (0–7.2%) without CAB-LA introduction but 13.1% (1.9–29.7%) with CAB-LA introduction. CAB-LA PrEP introduction is predicted to lower the proportion of all people on ART with VL < 1000 copies/mL by 0.9% (–2.6 – +0.5%) at 20 years. For an adult population of 10 million, an overall decrease in numbers of deaths of approximately 4540 HIV-related deaths per year (–13 000 – –300) over 50 years is predicted, with little discernible benefit of using RNA-based testing. HIV-related deaths are averted with CAB-LA introduction in 97% of setting-scenarios. Over the 50-year time horizon, overall HIV programme costs are predicted to be lower if CAB-LA is introduced rather than not (total mean discounted annual HIV programme costs per year over 50 years US\$ 151.3 million vs. US\$ 150.7 million), assuming use of standard antibody testing. Introduction of CAB-LA is cost-effective under an assumed threshold of US\$ 500 per DALY averted in 82% of setting-scenarios at the fully-loaded PrEP cost of US\$ 116 per year and in 52% of setting-scenarios if the annual cost of CAB-LA is US\$ 224, and cost-effective in 87% of setting-scenarios if the annual cost of CAB-LA is US\$ 86.

**Interpretation:** Despite leading to increases in integrase inhibitor drug resistance, CAB-LA introduction is likely to have net benefits in terms of reduction in HIV-related deaths in addition to reductions in incidence. It is predicted to be cost-effective if delivered at the same cost as oral PrEP.

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