

# Modeling the Future Need for Adult Protease Inhibitors (PIs) in Generic Accessible (GA) Low- and Middle-Income Countries (LMICs) in the Context of Dolutegravir (DTG) Roll-Out

Vineet Prabhu<sup>1</sup>, Shaun McGovern<sup>1</sup>, Zachary Panos<sup>1</sup>

<sup>1</sup>Clinton Health Access Initiative (CHAI), Boston, MA, USA



## Background

PIs have long been the vanguard of second-line (2L) antiretroviral treatment (ART) in GA LMICs. However, DTG-based therapy is set to transform first-line (1L) treatment, with the WHO in 2018 recommending DTG for nearly all populations. In particular, DTG's durability in terms of a high genetic barrier to resistance could lead to lower second-line (2L) migration relative to what has been seen with non-nucleoside reverse transcriptase inhibitors (NNRTIs).

Further, positive early results from the DAWNING study, WHO guidance, donor interest, and significantly lower costs may lead to DTG quickly replacing protease inhibitors (PIs) in 2L. With these dynamics, it is important to understand what role PIs (especially optimal ones like darunavir (DRV)) will have in the coming years.

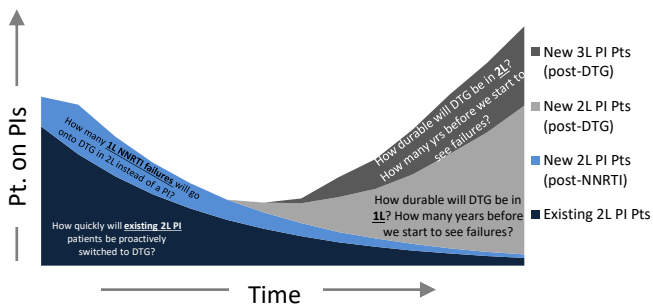
## Methods

Starting in 2018, four patient segments who may eventually need PIs were modeled, those:

- Already on PIs in 2L in 2017
- Newly failing NNRTI in 1L
- Newly failing DTG in 1L
- Newly failing DTG in 2L (after 1L NNRTI failure)

Some of the key questions on the evolution of the PI market pertaining to these segments are illustrated in Graph 1.

**Graph 1: Illustrative representation of potential need for PIs over time**



CHAI's forecast for GA LMICs was used to establish the 1L NNRTI and DTG patient pools between 2018 and 2025, as well as the baseline 2L patient pools on PIs. NNRTI patients were assumed to fail their therapy at historical rates. Assumptions were used for the timing and rate of adoption of DTG as the preferred 2L therapy after 1L NNRTI-failure, and proactive switching of stable 2L patients from PIs to DTG. Varied assumptions were made on median time to failure on DTG, with an even distribution on either side of the median.

## Results

In the short term, the number of individuals on PI-based therapies is expected to decrease. The rate and extent of the decline will be dependent on how quickly existing 2L PI patients are proactively switched to DTG and the extent to which 1L NNRTI failures will go onto DTG for 2L treatment rather than using a PI.

In the long term, the need for PIs will increase as those individuals failing DTG-based 1L and 2L regimens will ultimately likely need a PI. The durability of DTG will be fundamental in determining when that eventual rise in PI need will occur (Table 1).

**Table 1: Potential scenarios based on 2L DTG adoption and DTG durability**

Patients needing PIs ('000s)	2018	2019	2020	2021	2022	2023	2024	2025
<b>Scenario 1:</b> • 2L DTG adoption in 2020 • 6 yr median DTG durability	990	1,150	990	580	460	970	2,390	4,300
<b>Scenario 2:</b> • 2L DTG adoption in 2019 • 6 yr median DTG durability	990	920	520	250	410	980	2,460	4,460
<b>Scenario 3:</b> • 2L DTG adoption in 2020 • 7 yr median DTG durability	990	1,150	990	530	240	360	890	2,260
<b>Scenario 4:</b> • 2L DTG adoption in 2019 • 7 yr median DTG durability	990	920	520	200	180	360	910	2,330
<b>Scenario 5:</b> • 2L DTG adoption in 2020 • 8 yr median DTG durability	990	1,150	990	530	190	160	310	840
<b>Scenario 6:</b> • 2L DTG adoption in 2019 • 8 yr median DTG durability	990	920	520	200	130	140	310	860

## Conclusions

It is important to note that PIs are likely to always be needed as long as patients fail other classes of therapy. These findings on the likely market dynamics around the demand for PIs, and timing of demand growth in particular, can help inform appropriate strategies for efforts to provide access in LMICs to optimal PI options (such as DRV) in suitable formulations and at affordable prices.

## Acknowledgements

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