



Since its introduction into South Africa's HIV treatment program in 2019, the antiretroviral dolutegravir has been widely rolled out in public healthcare sector.

Over 4.7m people in SA placed on new HIV med in four years

News & Features

17th July 2023 | Elri Voigt

In what is likely one of the largest treatment rollouts in South African history, well over four million people living with HIV have started taking the antiretroviral dolutegravir since its introduction around four years ago. Now, according to a recent study published in the *Lancet* medical journal, use of dolutegravir in South Africa is associated with more people staying on treatment and higher rates of viral suppression.

The use of a three-in-one combination of the antiretroviral drugs tenofovir, lamivudine and dolutegravir (TLD for short) for the treatment of HIV was first recommended by the World Health Organization (WHO) in 2018. A year later it was **recommended** in the South African treatment guidelines as first line treatment for HIV and a three-year tender was awarded. Since then, dolutegravir has largely replaced another antiretroviral called efavirenz.

Today, TLD is the recommended treatment option for most people living with HIV in the country. The 2023 [National antiretroviral \(ARV\) guidelines](#) also include recommendations for the use of child-friendly formulations of dolutegravir and dolutegravir containing regimens in kids. Spotlight reported on these [here](#).

Around 4.7m people in SA taking dolutegravir

According to Foster Mohale, spokesperson for the National Department of Health, in 2019 the HIV clinical guidelines were revised to include a fixed combination dose of TLD “for all eligible people for use as the first line regimen.”

Based on this, the department set a goal that 90% of those eligible for it should receive TLD as a first line regimen. In terms of meeting this goal, Mohale says that by March 2023, just over four million (4 127 427) people were on TLD. Additionally, about 650 000 (653 884) people were on other dolutegravir based regimens. Altogether, there are thus now over 4.7 million people in the country on treatment combinations that include dolutegravir.

“Based on the March 2023 data, 90% of clients on first line regimen were on TLD. However, performance varies by province,” he says.

Of the total number of people on ART in the public health sector, 75.8% are on TLD, according to Mohale.

Trends in the roll out

While on paper the country’s transition from efavirenz to dolutegravir-based regimens seems to have been smooth, the reality on the ground has been more complex.

A [study](#) published in the Lancet earlier this year looked at real-world rollout data from 2019 to 2022. The study was conducted in 59 clinics across the country and collected data from two cohorts-one cohort were first time initiators of ART and the other were transitioning from regimens that did not include dolutegravir to ones that did.

In the initiator cohort, just over 45 000 people were initiated on ART between December 2019 and February 2022. Of those, 68.9% were initiated on dolutegravir-based regimens, 31.1% on efavirenz-based regimens, and 0.1% on nevirapine-based regimens.

Those initiated on dolutegravir-based regimens were more likely to still be on treatment a year later and were also more likely to be virally suppressed than those who were initiated on the other regimens.

In December 2019, in the transition cohort, just over 180 000 people were on a non-dolutegravir first line regimen. By February 2022, 67% of them had transitioned to a dolutegravir-based regimen. These people were also more likely to be retained in care

at 12 months and be virologically suppressed than those who had not switched to a dolutegravir-based regimen.

“That’s good for a number of reasons. It means that the treatment’s working, people are less likely to get unwell and also, they can’t transmit the virus onto other people,” explains Dr Jienchi Dorward, one of the study authors and an academic clinical lecturer at the University of Oxford and honorary associate scientist at the Centre for the AIDS Programme of Research in South Africa (CAPRISA).

‘Bumpy transition’

Dr Yuktेशwar Sookrajh, a Senior Medical Practitioner at the eThekweni Municipality Health Unit who was also involved in the study, tells Spotlight that the rollout quickly gathered momentum.

“But initially there were some issues to navigate around drug interactions; concurrent TB infection and the use of dolutegravir in women of childbearing potential,” he says. “Once those concerns were addressed, the comfort of switching to dolutegravir was increased and we find that the majority of our patients have now safely transitioned across to dolutegravir-based regimens.”



A study recently published in the Lancet found that the use of dolutegravir in South Africa is associated with more people staying on treatment and higher rates of viral suppression. PHOTO: Spotlight

In many ways South Africa was slow in rolling out dolutegravir compared to other African countries, according to Professor Francois Venter, the head of Ezintsha at Wits University. Reasons for this, he says, include an initial concern around the safety of dolutegravir use among pregnant women, and disruption in training due to the COVID-19 pandemic.

He says that the South African Clinicians society was alerted during the COVID-19 pandemic that many patients in the public health sector had still not been transitioned to dolutegravir. An education campaign was then launched to encourage clinicians to start or switch patients to dolutegravir.

However, as it stands now the rollout of the drug in the public sector has been a huge success, despite what Venter calls a “bumpy transition”.

“All the data we have on it [dolutegravir] suggests that the patients have done much better, their viral load suppression levels are better, the side effect profiles so far are better,” he says.

Initial safety concerns

One important reason to conduct the study reported in the Lancet, according to Dorward, was a safety concern regarding the use of dolutegravir by pregnant women. An earlier study conducted in Botswana called Tsepamo found a higher prevalence of neural-tube defects (a type of birth defect) associated with dolutegravir exposure at conception than with other types of antiretroviral exposure. As more data has been gathered since, it has however become clear that dolutegravir does not in fact increase the risk of neural-tube defects.

But the Tsepamo scare did impact who was initiated and transitioned onto dolutegravir in first two years of the rollout.

“The initial concerns around neural-tube defects and the use of dolutegravir in women of childbearing potential clearly hampered rollout of dolutegravir in women – and this has been clearly demonstrated in this study,” says Sookrajh.

The Lancet study found that pregnant women and non-pregnant women were less likely to be initiated on dolutegravir than men early in the rollout, with the biggest difference between women and men aged 15 to 24 years old. This difference decreased with age and by age 55 there was no difference between men and women receiving dolutegravir.

But this changed over time and by September 2021 women were as likely to get initiated on dolutegravir as men. Spotlight previously **reported** that the rollout was done in two stages. In the first stage men, adolescent boys, women on reliable contraception, and older women were prioritised.

Of those who started treatment during the study period, 46.9% of the pregnant women in the cohort were initiated on dolutegravir-based regimens, while 63.9% of the non-pregnant women and 82.3% of the men in the cohort were initiated on dolutegravir-based regimens.

“In both those groups [cohorts] we found that women were less likely than men to get dolutegravir, but interestingly, this was particularly in younger women,” Dorward

explains. "As time went on, the difference between men and women became much less...around June to September 2021 was a time period where we found that women and men pretty much began to equally get dolutegravir."

Dorward says the data showed an uptick in women in the study being given dolutegravir once the South African guidelines changed to reflect that there was no longer a concern around neural-tube defects. It is thus likely that the safety concern was responsible for the lower initial uptake among young women.

According to Sookrajh based on his experience "working at the coal face, the concerns around neural tube defects were a significant concern amongst all healthcare workers at the time."

He adds that the messaging around this potential risk was based on the evidence available at the time and was clearly outlined in the guideline document and training for dolutegravir use, but these did not appear to adequately allay these concerns among healthcare workers.

"The risks versus benefits needed to be messaged in a more effective way such that healthcare workers were more comfortable and confident in offering dolutegravir to women," he says. Based on this experience Sookrajh adds that in future there needs to be more engagement with "practitioners on the ground to determine what type of messaging and supportive materials are required to facilitate better understanding of guidelines at the coal face."



Of the total number of people on antiretroviral treatment (ART) in the public health sector, 75.8% are taking the three-in-one combination of the antiretroviral drugs tenofovir, lamivudine and dolutegravir (TLD for short).

Another concern for some healthcare workers has been that dolutegravir-based regimens have been associated with greater weight gain than efavirenz-based regimens. But, as argued in a recent editorial in [the Southern African Journal of HIV medicine](#), association is not the same as causation and it may well be that efavirenz inhibits weight gain rather than dolutegravir promoting it. People living with HIV who start taking antiretroviral medicines often gain weight as their health recovers.

New guidelines should further boost uptake

Sookrajh says that the National Department of Health's **antiretroviral** (ARV) 2023 guidelines will further improve the uptake of dolutegravir in the public healthcare system.

"With the April 2023 National Department of Health ARV Guidelines, we actually find that further barriers to switching to dolutegravir have been removed and dolutegravir is clearly placed as the preferred drug of choice in almost all scenarios for both first- and second-line antiretrovirals," he says.

"I think the new [ARV] guidelines hopefully will be a big improvement for people who are on treatment, and part of that is possible because we're using the drug that is better. You're less likely to get resistance with dolutegravir so we're less worried if people don't take treatment properly that they might get drug resistance, although we still need more research to be sure about that," Dorward says. "And it's still very important for people to take treatment consistently to suppress the virus and maintain their own health and prevent onward transmission."

According to Venter, there needs to be proper resistance surveillance to detect potential dolutegravir resistance.

"We can't take for granted we'll never have resistance [to dolutegravir]...eventually there will be the occasional patient that does have resistance, but we need proper surveillance there," he says. "And then we need to keep an eye on things. There are still patients getting HIV...there's still a lot of new infections...we need to make that stop...we've got amazing PrEP and way too few people getting it. So, we do need to start addressing that." (PrEP, or pre-exposure prophylaxis, refers to antiretrovirals taken to prevent HIV infection.)

Venter adds that while successful in the public health sector, the uptake of dolutegravir has been extremely slow in the private health sector for reasons unknown to him.