MODERN ART FOR SOUTH AFRICA

March 2018

A guide for HIV treatment activists and communities

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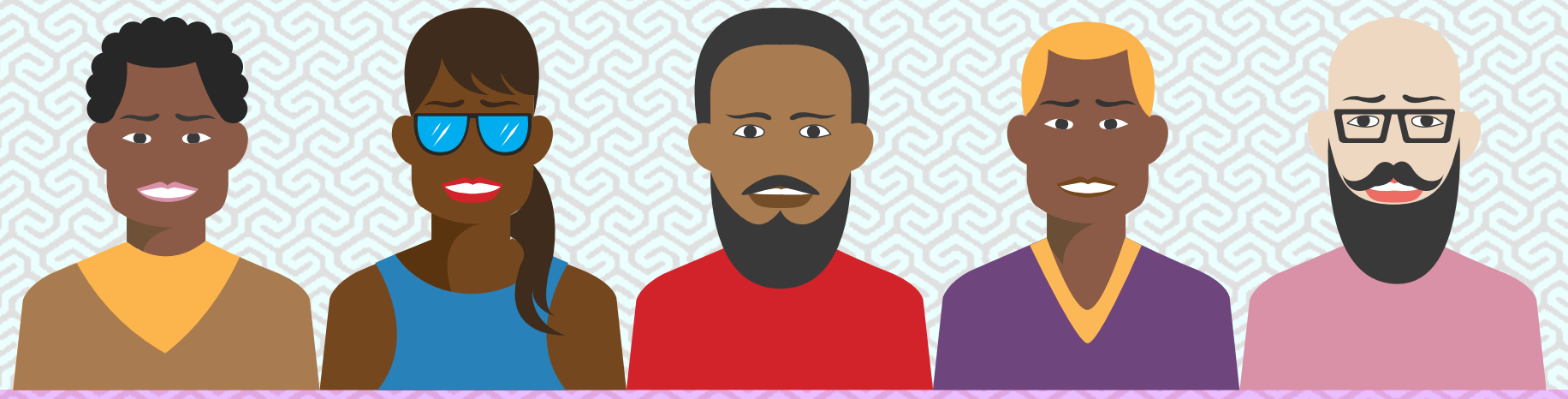


ART today

A pricing agreement was announced in 2017 that will speed up access to generic, dolutegravir-based fixed dose combinations.

This means an HIV positive person in a low- and middle-income country – including South Africa – can be treated for around US $75 (about 900 rand) a year.

This is the first time that a newer and better fixed-dose combination (FDC) will be made available at a lower price than the previously recommended first-line HIV treatment.

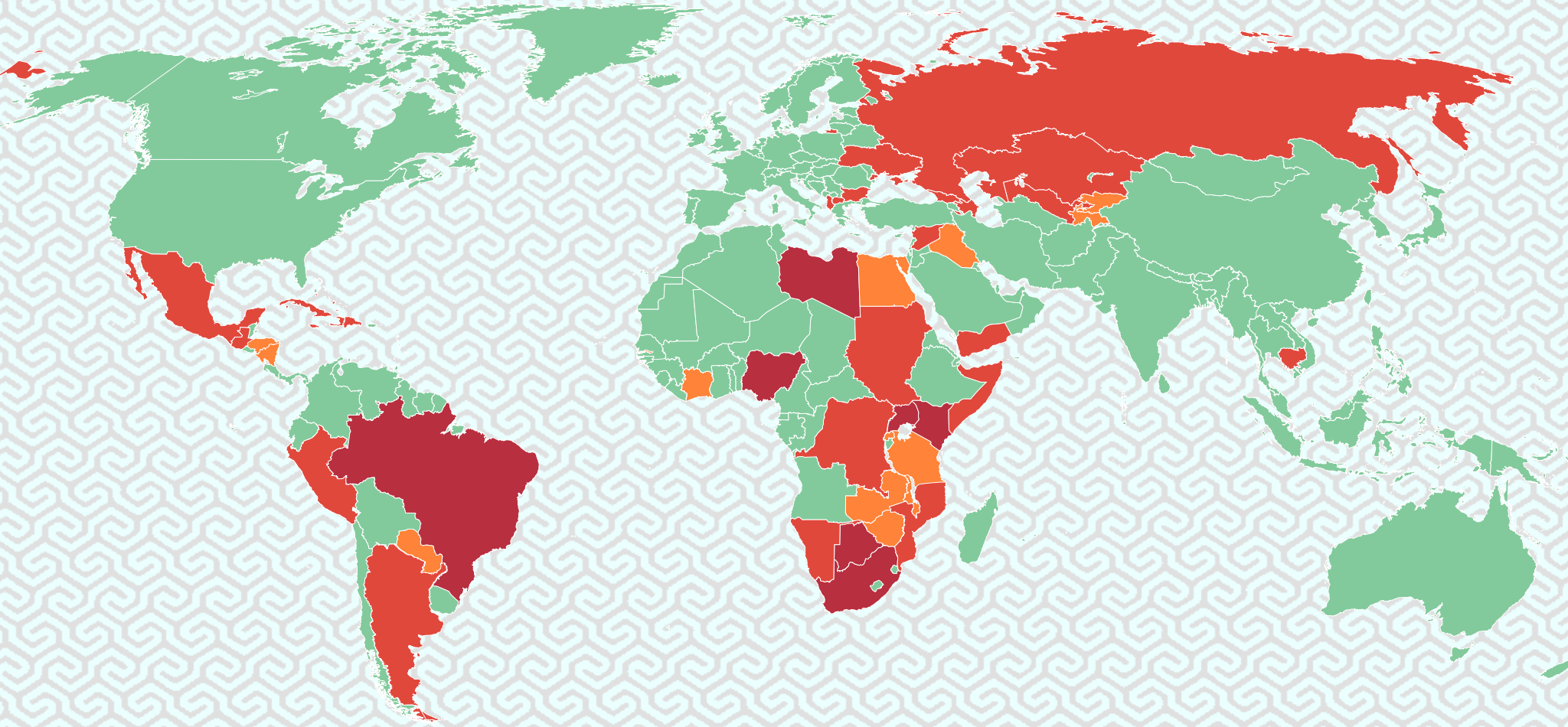
The World Health Organisation (WHO) and South African National Department of Health current preferred (and most widely used) first-line regimen is tenofovir disoproxil fumarate (TDF), emtricitabine (FTC) and efavirenz (EFV).

The new FDC combines the three ARVs: TDF, lamivudine (3TC) and dolutegravir (DTG). Its name is shortened to TLD. It will also be a smaller tablet than the EFV-based FDC.

WHO currently recommends a DTG-based combination as an alternative first-line regimen.

WHO FIRST-LINE RECOMMENDATIONS

First line ART	Preferred regimen	Alternative regimens
Adults	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + DTG TDF + 3TC (or FTC) + EFV400 TDF + 3TC (or FTC) + NVP AZT + 3TC + EFV (or NVP)
Pregnant / breastfeeding women	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + NVP



ART in low- and middle-income countries

Almost 60 low- and middle-income countries have already included or are planning to include DTG in their national guidelines.

Botswana and Brazil have started providing DTG nationwide and Kenya, has started a pilot programme (similar programmes are planned in Uganda and Nigeria). South Africa will change its first-line to DTG-based in 2018.

Up until now, the “early adopter” countries have used DTG from the originator company (Brazil and Botswana) or more recently as a single generic formulation plus two NRTIs (Kenya was the first country to introduce generic DTG).

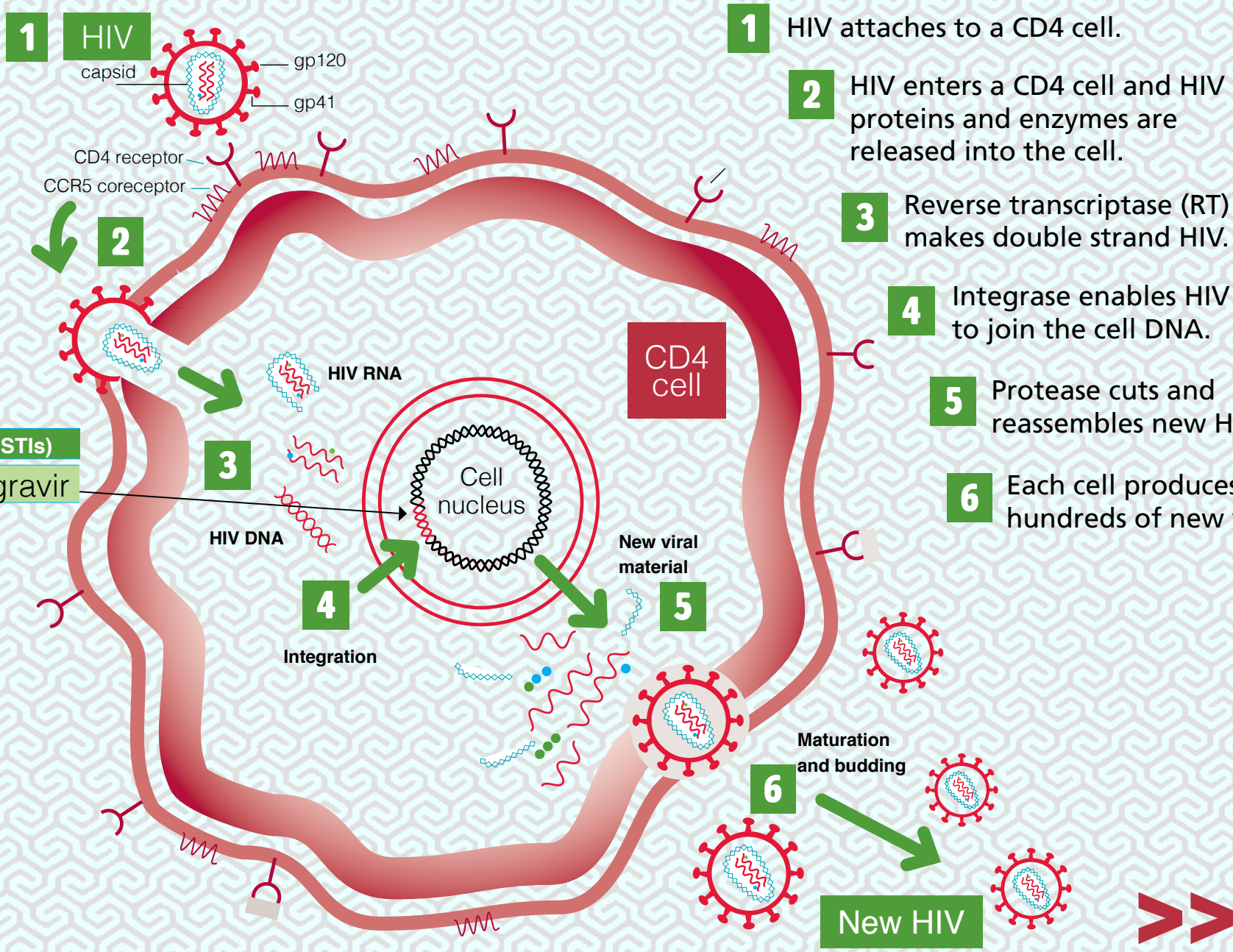
TLD will encourage more countries to change their first-line regimen to a DTG-based one.

What is dolutegravir?

dol-you-TEG-rah-veer

DTG is an integrase inhibitor. When HIV infects a cell, it combines its genetic code into the cell's own code – this is called integration. DTG blocks integration, so HIV can't make more copies of itself.

DOLUTEGRAVIR: TARGETS INTEGRASE IN THE HIV LIFECYCLE



1 HIV attaches to a CD4 cell.

2 HIV enters a CD4 cell and HIV proteins and enzymes are released into the cell.

3 Reverse transcriptase (RT) makes double strand HIV.

4 Integrase enables HIV to join the cell DNA.

5 Protease cuts and reassembles new HIV.

6 Each cell produces hundreds of new virions.

HIV i-Base (www.i-Base.info)

Why is dolutegravir better than efavirenz?

DTG is more effective and seems to have fewer side effects than EFV. It is less easy to get resistance to DTG.

What is the dose of dolutegravir?

The standard dose of DTG is 50 mg once daily for people who are taking first-line HIV treatment.

Does dolutegravir need to be taken with food?

For most people, DTG can be taken with or without food

What are the side effects of dolutegravir?

There have been reports of central nervous system (CNS) side effects (similar to efavirenz but far less frequent).

These includes mood changes and difficulty sleeping. Although these are not common, occasionally people might need to change to another ARV. Some people find it better to take DTG in the morning than the evening.

More severe CNS side effects, including depression and feelings of wanting to commit suicide, have been very rare with DTG.

Immune Reconstitution Inflammatory Syndrome (IRIS) happens mostly in people with low CD4 cell count starting ART. As integrase inhibitors drive down viral load faster than other ARV classes, IRIS might be more likely in people taking them with low CD4. There have been some reports of an increased risk.

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Can you take DTG in pregnancy?

One of the reasons that WHO and other guidelines do not yet recommend DTG universally first-line is that not very much was known about its safety in pregnancy.

More recently there have been reassuring reports from women who have taken DTG in pregnancy. These include 845 women in Botswana.

There are also several studies looking at DTG-based ART in pregnancy.

As DTG is used in more countries (both low- and high-income) more information will be available.

Countries are starting to be more comfortable about recommending and providing DTG in pregnancy and guidelines will be updated as there is more information.

What about with TB medicine?

Another reason that DTG was not part of the preferred WHO regimen was lack of information on giving it with first-line TB treatment. Rifampicin, one of the medicines used in first-line TB treatment, can reduce the levels of other medicines, including DTG.

As with pregnancy we will learn more about using DTG and TB treatment together.

Where countries are using them together this “interaction” between DTG and rifampicin is overcome by adding an extra DTG pill. So DTG is given twice daily (once within TLD and once as a single dose).

As we learn more about using TLD with TB treatment the guidelines will be updated.

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What about other medicines and supplements?

There are interactions between DTG with some supplements, heartburn treatment, laxatives and multivitamins, including calcium supplements. To overcome this DTG should be taken two hours before or six hours after these medicines.

Another important interaction is that DTG doubles levels of metformin – to treat type 2 diabetes – and requires careful monitoring.

Less well understood are interactions with traditional herbal medicines or imbiza. We don't know what these imbiza can do. They might weaken the impact of the ARVs or using them together might make the ARVs or imbiza more toxic.

Can children take dolutegravir?

Currently adolescents aged 12–18 can take the adult formulation of TLD.

Children 6 years old and weighing at least 15 kilos can take DTG. But there are not yet suitable generic FDCs. Manufacturers are working on DTG containing formulations for children aged 6–12. And research is ongoing in children and babies less than 6 years old.

Eventually DTG might be available to treat even the youngest babies with HIV.

What will TLD look like?

As with all ARVs and FDCs there will be different versions made be different generic manufacturers. So, the pill one person takes might not look exactly the same as the pill a different person takes in another country, district or clinic.

Sometimes your own TLD might change the way it looks a bit and have a different packet.

Here are pictures of the first generic versions of TLD.

We will add more versions of TLD as they become available.

About this booklet

This booklet is for HIV treatment activists and communities in South Africa. These might be: HIV positive people who are starting treatment with TLD, activists training their communities about this new FDC and those working to make sure that it is available, and community health workers. The booklet gives information about TLD. It is produced by the Treatment Action Campaign (TAC) and i-Base.

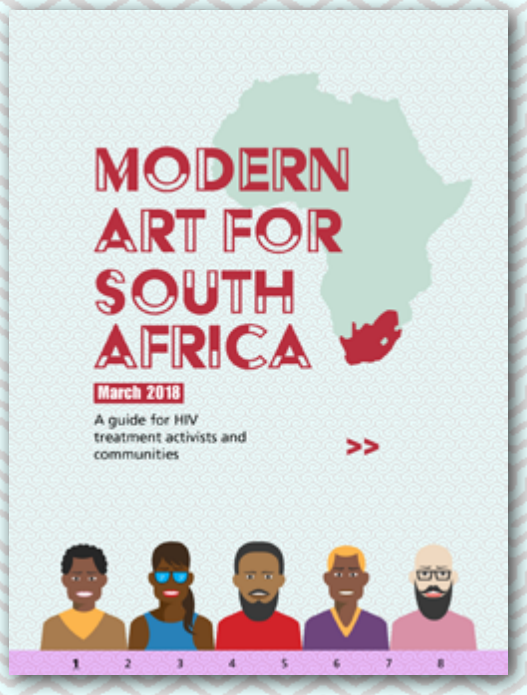
For further information:

i-Base has a Q&A service to answer your questions about HIV and treatment. **http://i-base.info/qa/**

They answer questions from all over the world. They use everyday language to answer your question personally. If you have questions about TLD or any other HIV treatment, please contact them.

TAC also has a Facebook page dedicated to answering your questions. You can send them a direct message. Or you can call the TAC office on 011 100 4721.

https://facebook.com/QuestionsAndAnswersAboutHivtbInSouthAfrica/



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