



# WHAT IS ANTIRETROVIRAL THERAPY (ART)

## WHAT IS ART?

ART are medications that treat HIV. The drugs do not kill or cure the virus. However, when taken in combination they can prevent the growth of the virus. When the virus is slowed down, so is HIV disease. Antiretroviral drugs are referred to as ARV. Combination ARV therapy (cART) is referred to as highly active ART (HAART).

## WHAT IS THE HIV LIFE CYCLE?

There are several steps in the HIV life cycle. (See Fact Sheet 400 for a diagram.)

1. Free virus circulates in the bloodstream.
2. HIV attaches to a cell.
3. HIV empties its contents into the cell.
4. The HIV genetic material (RNA) is used by the reverse transcriptase enzyme to build HIV DNA.
5. The HIV DNA is inserted into the cell's chromosome by the HIV integrase enzyme. This establishes the HIV infection in the cell.
6. When the infected cell reproduces, it activates the HIV DNA, which makes the raw material for new HIV viruses.
7. Packets of material for a new virus come together.
8. The immature virus pushes out of the infected cell in a process called "budding."
9. The immature virus breaks free of the infected cell.
10. The new virus matures: raw materials are cut by the protease enzyme and assembled into a functioning virus.

## APPROVED ARV DRUGS

Each type, or "class", of ARV drugs attacks HIV in a different way. The first class of anti-HIV drugs was the **nucleoside reverse transcriptase inhibitors** (also called NRTIs or "nukes".) These drugs block step 4, where the HIV genetic material is used to create DNA from RNA. The following drugs in this class are used:

- Zidovudine (Retrovir, AZT)
- Didanosine (Videx, Videx EC, ddi)
- Stavudine (Zerit, d4T)
- Lamivudine (EpiVir, 3TC)
- Abacavir (Ziagen, ABC)
- Tenofovir, a nucleotide analog (Viread, TDF)
- Combivir (combination of zidovudine and lamivudine)
- Trizivir (combination of zidovudine, lamivudine, and abacavir)
- Emtricitabine (Emtriva, FTC)
- Truvada (combination of emtricitabine and tenofovir)
- Epzicom (combination of abacavir and lamivudine)

**Non-nucleoside reverse transcriptase inhibitors**, also called **non-nukes** or **NNRTIs**

also block step 4 but in a different way. Five have been approved:

- Nevirapine (Viramune, NVP)
- Delavirdine (Rescriptor, DLV)
- Efavirenz (Sustiva or Stocrin, EFV, also part of Atripla)
- Etravirine (Intelence, ETR)
- Rilpivirine (Edurant, RPV, also part of Complera or Epivlera)

**Protease inhibitors or PIs**, block step 10, where the raw material for new HIV virus is cut into specific pieces. Ten protease inhibitors are approved:

- Saquinavir (Invirase, SQV)
- Indinavir (Crixivan, IDV)
- Ritonavir (Norvir, RTV)
- Nelfinavir (Viracept, NFV)
- Amprenavir (Agenerase, APV)
- Lopinavir/ritonavir (Kaletra or Aluvia, LPV/RTV)
- Atazanavir (Reyataz, ATZ)
- Fosamprenavir (Lexiva, Telzir, FPV)
- Tipranavir (Aptivus, TPV)
- Darunavir (Prezista, DRV)

**Entry inhibitors** prevent HIV from entering a cell by blocking step 2 of the life cycle. Two drugs of this type have been approved:

- Enfuvirtide (Fuzeon, ENF, T-20)
- Maraviroc (Selzentry or Celsentri, MVC)

**HIV integrase inhibitors** prevent HIV from inserting its genetic code into the human cell's code in step 5 of the life cycle. The two drugs of this type are:

- Raltegravir (Isentress, RAL)
- Elvitegravir (EVG, part of the combination Stribild,)
- Dolutegravir (Tivicay, DTG)

## HOW ARE THE DRUGS USED?

Antiretroviral drugs are usually used in combinations of three or more drugs from more than one class. This is called "Combination Therapy." Combination therapy helps prevent drug resistance.

Manufacturers of ARVs keep trying to make their drugs easier to take, and have combined some of them into a single tablet regimens. See Fact Sheet 409 for more information on combination medications.

## WHAT IS DRUG RESISTANCE?

When HIV multiplies, many of the new copies have mutations: they are slightly different from the original virus. Some mutant viruses keep multiplying even when you are taking ARV drugs. When this happens, the virus can develop resistance to the drug and ART may stop working. See fact Sheet 126 for more information.

If only one or two ARV drugs are used, it is easy for the virus to develop resistance. For this reason, using just one or two drugs is not recommended. But if three drugs are used, a successful mutant would have to "get around" all of the drugs at the same time. Using combination therapy means that it takes much longer for resistance to develop.

## CAN THESE DRUGS CURE AIDS?

ARVs reduce the viral load, the amount of virus in your bloodstream, but are not a cure. A blood test measures the viral load. People with undetectable viral loads stay healthier longer. They are also less likely to transmit HIV infection to others.

Some people's viral load is so low that it is "undetectable" by the viral load test. This does **not** mean that all the virus is gone, and it does not mean a person is cured of HIV infection. See Fact Sheet 125 for more information on viral load.

## WHEN DO I START?

Current US guidelines say that everyone who is infected with HIV should start ARV therapy. See fact sheet 404 for more information on treatment guidelines. This is an important decision you should discuss with your health care provider.

## WHICH DRUGS DO I USE?

ARV drugs are chosen on the basis of treatment guidelines, HIV drug resistance, your health (for example, kidney or liver disease) and lifestyle factors. While ARV regimens are usually well tolerated, each ARV drug can have side effects. Some may be serious. Refer to the fact sheet for each individual drug. Each person is different, and you and your health care provider will have to decide which drugs to use.

Adherence to ARVs is very important for treatment to work. The viral load test is used to see if ARV drugs are working

## WHAT'S NEXT?

New drugs are being studied in all of the existing classes. Researchers are also trying to develop new types of drugs, such as drugs that will block other steps in the HIV life cycle, and drugs that will strengthen the body's immune defenses.

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