Stribild

FACT SHEET

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Summary

Stribild is the name of a pill containing three anti-HIV drugs: tenofovir DF, FTC, elvitegravir and one additional drug, cobicistat, which boosts the level of elvitegravir. Stribild is a complete treatment for people with HIV. Common side effects include diarrhea, nausea and headache. Stribild is taken once daily with food. To help integrate Stribild into your life it may be simplest to take Stribild with a meal.

What is Stribild?

Stribild is the name of a pill that contains the following three anti-HIV drugs:

- elvitegravir, which belongs to a group of drugs called integrase inhibitors
- tenofovir DF (Viread), which belongs to a group of drugs called nucleotide analogues ("nukes")
- FTC (emtricitabine, Emtriva), which belongs to a group of drugs called nucleoside analogues ("nukes")

Stribild also contains cobicistat (Tyboost), which belongs to a group of drugs called pharmacokinetic enhancers or boosters.

Stribild is meant to be used as a once-daily complete treatment for HIV infection.

How does Stribild work?

When HIV infects a cell, it takes control of that cell. HIV then forces the cell to make many more copies of the virus. To make these copies, the cell uses proteins called enzymes. When the activity of these enzymes is reduced, the production of HIV slows.

All the anti-HIV medicines in Stribild interfere with enzymes used by HIV-infected cells to make more HIV.

Since Stribild inhibits, or reduces, the activity of these enzymes, Stribild causes HIV-infected cells to reduce their production of new copies of HIV.

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How do people with HIV use Stribild?

Stribild is taken once daily with food. To help integrate Stribild into your life, it may be simplest to take Stribild once daily with a meal. Stribild contains multiple drugs, and is a complete treatment for HIV. Such combinations are called antiretroviral therapy, or ART.

For many people with HIV, the use of ART has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to reduce the risk of developing a life-threatening infection. Neither Stribild nor any other anti-HIV treatment is a cure for HIV. It is therefore important that you see your doctor regularly so that he/she monitors your health.

Evidence shows that HIV-positive people who are on ART, engaged in care, and have an ongoing undetectable viral load are substantially less likely to transmit HIV to others, be it through sex, when sharing equipment to use drugs or during pregnancy and birth. In fact, the evidence for sexual transmission shows that people on ART who maintain an undetectable viral load do not pass HIV to their sexual partners. For further information see the CATIE fact sheet *HIV treatment and an undetectable viral load to prevent HIV transmission*. However, it is still a good idea to use condoms because they can reduce your risk for getting and passing on other sexually transmitted infections.

Warnings

1. Lactic acidosis

Stribild contains tenofovir and FTC. Both of these medicines are associated with the build-up of the waste product lactic acid in the blood. Symptoms of excess amounts of lactic acid in the blood can include the following:

- nausea
- vomiting
- abdominal pain
- diarrhea
- unexpected tiredness
- unexpected muscle pain
- feeling cold, especially in the arms and legs
- feeling dizzy or light-headed

If these symptoms occur while you are taking Stribild, call your doctor right away.

2. Liver problems—enlarged liver and fatty liver

In rare cases, people who take Stribild can develop swollen liver (hepatomegaly) or fatty liver (steatosis). People who develop these specific liver problems may also develop the following symptoms:

- yellowing of the skin and whites of the eyes
- nausea
- vomiting
- abdominal pain

If any of these symptoms develop, contact your doctor right away.

3. Other liver problems—hepatitis viruses

The safety of Stribild in people co-infected with HIV and hepatitis B is not known. Stribild contains tenofovir DF, which has anti-HBV activity. Co-infected people who take Stribild and then stop it may notice their hepatitis B infection worsen. If you have this co-infection, talk to your doctor before you start Stribild. If you later need to change your therapy, remind your doctor that you have hepatitis B.

People who are co-infected with HIV and hepatitis-causing viruses and who take ART are at increased risk for liver injury. It is important to have regular blood tests so that your doctor can assess the health of your liver. If lab tests reveal that you do not have HBV, speak to your doctor about getting a vaccine to protect you from HBV.

4. Medicines and kidney injury

In addition to tenofovir (in Stribild), there are other medications that are processed by the kidneys and have the potential to cause or amplify kidney injury.

Many of these medications are antibiotics and can be grouped as follows:

- beta-lactams – penicillin and amoxicillin
- quinolones – ciprofloxacin and related compounds
- aminoglycosides – amikacin and gentamicin
- macrolides – erythromycin
- tetracyclines – minocycline
- anti-tuberculosis agents – rifampin and ethambutol
- other antibiotics – co-trimoxazole (Septra/Bactrim), vancomycin (Vanocin)

Bear in mind that there are other medications that can have the potential to cause kidney dysfunction, including (but not limited to) the following:

- antiviral agents – acyclovir (Zovirax), valacyclovir (Valtrex), cidofovir (Vistide), foscarnet (Foscavir), indinavir (Crixivan)
- antifungal agents – amphotericin B (Fungizone), intravenous pentamidine
- anti-seizure drugs – phenytoin, carbamazepine, valproic acid
- drugs commonly used for relief from pain, inflammation and fever – acetaminophen (Tylenol), ibuprofen (Advil, Motrin), indomethacin (Indocid), naproxen (Naprosyn, Aleve)
- transplant drugs – cyclosporine (Neoral, Sandimmune), tacrolimus (Advagraf, Prograf)

5. Monitoring kidney health

Stribild contains tenofovir DF and cobicistat. An analysis of data from several thousand HIV-positive people has found that when boosting agents such as cobicistat or ritonavir were used in regimens containing tenofovir DF, there was a statistically increased risk for thinning bones, bone fractures and kidney injury. Cases of kidney injury including severe kidney injury have been reported in people who used Stribild. The manufacturer of Stribild, Gilead Sciences, recommends that doctors do the following:

- Prior to starting therapy with Stribild, request eGFR (estimated glomerular filtration rate) and levels of glucose (sugar) and protein in the urine. Stribild should not be started in patients who have an eGFR less than 70 mL/min.
- Routinely monitor eGFR alongside glucose and protein levels in the urine of patients while they are taking Stribild.
- In patients at risk for kidney injury, measure the level of phosphorus in the blood.
- Advise patients to stop taking Stribild if eGFR falls below 50 mL/min.

Should the amount of creatinine in the blood rise above 0.4 mg/dL (35.36 micromol/Litre) then patients should be "closely monitored for [kidney injury]."

6. Dizziness

Some Stribild users have reported dizziness. People who take Stribild may also develop difficulty concentrating or feel sleepy during the daytime. If any of these problems occur, let your doctor know and avoid driving or operating machinery.

7. Pancreatitis

Gilead Sciences, warns that "caution should be exercised" when using Stribild in patients with a history of pancreatitis (inflammation of the pancreas gland) or who are at risk for pancreatitis. There have been reports of pancreatitis in some people who have used tenofovir, one of the drugs in Stribild.

According to the U.S. National Institutes of Health (NIH) the most common risk factor for pancreatitis is alcoholism. Other risk factors can include the following:

- a close relative (mother, father, brother or sister) with pancreatitis
- cystic fibrosis

- excessive levels of calcium in the blood
- very high levels of cholesterol or triglycerides in the blood

Symptoms of pancreatitis can include the following:

- nausea
- vomiting
- abdominal pain
- weight loss
- diarrhea
- oily stools

8. Pregnancy

According to the manufacturer of Stribild, "There are not sufficient data to recommend the routine initiation of Stribild in women during pregnancy." The U.S. Food and Drug Administration has reported that the level of elvitegravir in pregnant women who use Stribild is not sometimes sufficient to suppress HIV viral load. If this happens, there is a risk that the baby could become infected with HIV. Gilead Sciences recommends "Stribild should not be used in pregnant women unless the potential benefits outweigh the potential risks to the fetus." They also recommend that if treatment is initiated, doctors should "closely monitor viral load during pregnancy."

9. Emotional issues —Anxiety and depression

After the licensure of Stribild, reports emerged of very rare cases of depression associated with the use of Stribild. Stribild contains the integrase inhibitor elvitegravir. Note that all integrase inhibitors have been associated with rare cases of anxiety and depression. Whether these drugs caused anxiety or depression is not clear. In some reports, the rare cases of anxiety and/or depression associated with the use of integrase inhibitors occurred mainly in people who had a history of these issues.

Anxiety and depression are relatively common in HIV-positive people (regardless of whether they are on treatment or the type of treatment that they take). If you are taking Stribild and think that you may have developed anxiety or depression, speak to your doctor right away. Your doctor can help determine if you have anxiety or depression and if there is any relationship between them and the medicines that you are taking.

Symptoms of anxiety and depression can include the following:

- becoming easily upset or angry
- feeling fearful
- excessive worry
- having unexpected feelings of sadness
- having prolonged feelings of sadness, anger or depression
- feeling hopeless
- having loss of pleasure in everyday activities
- unexpectedly feeling tired or experiencing a lack of energy
- having difficulty falling asleep, staying asleep or waking up prematurely
- having strange thoughts

If you have any of these feelings, contact your doctor or nurse.

If you have thoughts of harming yourself or others, dial 911 right away.

10. Special populations

Stribild has not been well-studied in people over the age of 65 years. Therefore it is not clear if they will respond differently to the drug than younger people.

Stribild has not been studied in people under the age of 18 years.

Side effects

This is not a complete list of side effects – consult your doctor, nurse or pharmacist for further information.

1. General side effects

These can include nausea, vomiting and headache.

2. Bone health

Stribild contains tenofovir DF. In experiments on monkeys using tenofovir at doses 10- to 30-times greater than the dose that would be used in people, the animals' bones became thinner over a period of one year.

Before you start taking Stribild, tell your doctor if you have bone problems, thinner-than-normal bones (osteopenia or osteoporosis) or if your parents, brothers or sisters have bone problems.

In clinical trials of regimens containing tenofovir, thinner bones in the spine and elsewhere, as well as bone pain have been reported in some participants. Thinner bones are generally weaker and are at increased risk for breaking (fractures) should accidents or trauma occur.

Researchers are not certain why bone thinning occurs in some people exposed to tenofovir. One theory is that bones became thinner because tenofovir appears to have caused kidney injury. The kidneys filter blood, putting waste materials into the urine and returning nutrients back to blood. In cases of tenofovir-associated bone loss, injured kidneys may not be able to restore bone-building nutrients back to the blood.

An analysis with data from several thousand HIV-positive people has found that when boosting agents, such as cobicistat (in Stribild) or ritonavir were used in regimens containing tenofovir DF, there was a statistically increased risk for thinning bones, bone fractures and kidney injury.

Bear in mind that some people with HIV can develop thinner-than-normal bones without ever using tenofovir. This sometimes occurs in people who use ART for the first time. The decrease in bone density tends to stabilize within a couple of years after starting ART. It may be useful for you to discuss with your doctor the possibility of having bone density assessments done before you begin taking Stribild or any other anti-HIV therapy. If your bones are thin, talk to your doctor about your intake of calcium and vitamin D_3. Regular monitoring of bone density may also be useful.

For more information about vitamin D and bones, see CATIE's *A Practical Guide to Nutrition for People Living with HIV*.

Drug interactions

Always consult your doctor and pharmacist about taking any other prescription or nonprescription medication, including herbs, supplements and street drugs.

Some drugs can interact with the drugs in Stribild, increasing or decreasing their levels in your body. Increased drug levels can cause you to experience side effects or make pre-existing side effects worse. On the other hand, if drug levels become too low, HIV can develop resistance and your future treatment options may be reduced.

It may also be necessary to avoid drugs that do not affect levels of the medications contained in Stribild, but cause similar side effects.

If you must take a drug that has the potential to interact with your existing medications, your doctor can do the following:

- adjust the dose of either your anti-HIV drugs or other medications; or
- prescribe different anti-HIV drugs for you.

The following lists of drugs interact or have the potential to interact with one or more of the drugs in Stribild. These lists are not exhaustive.

The manufacturer recommends that the following drugs should **not** be taken by people using Stribild because this could lead to serious, even life-threatening interactions or affect Stribild's ability to control HIV:

- anti-asthma drugs – salmeterol (Advair, Serevent)
- antihistamines – astemizole, terfenadine
- anti-TB drugs – rifampin
- anti-migraine drugs (ergot derivatives) – dihydroergotamine (Migranal), ergotamine (Ergomar), ergonovine, methylergonovine

- anti-anxiety drugs – midazolam (Versed), triazolam (Halcion)
- gastrointestinal motility drugs – cisapride (Prepulsid)
- antifungal drugs – voriconazole (Vfend), posaconazole (Posanol)
- antipsychotic drugs – pimozide (Orap)
- herbs – St John's wort, or its extracts such as hypericin or hyperforin
- cholesterol-lowering medicines (statins) – lovastatin and simvastatin
- drugs for pulmonary hypertension – Revatio (sildenafil)

Other drug interactions

Antacids can reduce the absorption of elvitegravir (in Stribild) if taken at the same time. Therefore, Gilead Sciences recommends that you take Stribild and antacids at least two hours apart.

Cobicistat can raise the levels of the transplant drugs cyclosporine and tacrolimus in the blood.

There are many potential interactions between the drugs in Stribild and other medicines. Always consult your pharmacist and doctor before taking other medicines, including over the counter drugs, herbs and supplements.

Resistance, cross-resistance and treatment interruption

Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes, called mutations, can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you. The use of a combination of drugs, such as Stribild, can delay the development of drug resistance.

All anti-HIV drugs should be taken every day exactly as prescribed and directed. If doses are delayed, missed or not taken as prescribed, levels of the drugs in Stribild in the blood may fall too low. If this happens, resistant virus can develop. If you find you are having problems taking your medications as directed, speak to your doctor and nurse about this. They can find ways to help you.

Therefore, if you are taking Stribild and need to interrupt your therapy, speak to your specialist about ways to minimize the chance that HIV in your body might become resistant to the drugs that are in Stribild.

If you miss taking your dose of Stribild within 12 hours of the time that you usually take it, Gilead Sciences recommends that you take it with a meal as soon as possible and "then take the next dose of Stribild at the regularly scheduled time." If you miss taking your dose of Stribild by more than 12 hours, Gilead recommends that you do not take the missed dose but wait until the next scheduled dose to take Stribild.

If you continue to have problems taking Stribild as directed, talk to your doctor and pharmacist.

When HIV becomes resistant to one drug in a class, it sometimes becomes resistant to other drugs in that class. This is called cross-resistance. Feel free to talk with your doctor about your current and future treatment options. To help you decide what these future therapies might be, at some point, your doctor can have a small sample of your blood analyzed using resistance testing.

Should HIV in your body become resistant to the medicines in Stribild, your doctor, with the help of resistance testing, can recommend a new treatment regimen for you.

Dosage and formulations

Stribild comes in the form of tablets. Each tablet contains the following medications:

- elvitegravir – 150 mg
- cobicistat – 150 mg
- FTC – 200 mg
- tenofovir – 300 mg

The adult dose is one tablet once daily with food. Taking Stribild with a meal at the same time every day is probably the easiest way to integrate Stribild into your life.

Availability

Stribild is licensed in Canada for the treatment of HIV infection in adults. Your doctor can tell you more about the availability and coverage of Stribild in your region. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

References

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Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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