

Biktarvy

Summary

Biktarvy contains three medicines—bictegravir, emtricitabine (FTC) and tenofovir alafenamide (TAF). Bictegravir belongs to the class of drugs called integrase inhibitors. TAF and FTC belong to the class of drugs called nucleoside reverse transcriptase inhibitors (“nukes”). Biktarvy is taken at a dose of one pill once daily with or without food. Overall, Biktarvy was well-tolerated in clinical trials. General side effects were uncommon and included headache and diarrhea; these were usually mild and temporary.

What is Biktarvy?

Biktarvy contains three medicines—bictegravir, FTC and TAF. Bictegravir belongs to the class of drugs called integrase inhibitors. TAF and FTC belong to the class of drugs called nucleoside reverse transcriptase inhibitors (“nukes”).

How does Biktarvy work?

The drugs in Biktarvy work by interfering with enzymes needed by HIV called integrase and reverse transcriptase. Using Biktarvy greatly reduces HIV’s ability to infect cells and make copies of itself.

How do people with HIV use Biktarvy?

Biktarvy is meant for use by HIV-positive people (adults and pediatric patients) who weigh at least 25 kg. Gilead, the manufacturer of Biktarvy, recommends that the following be done prior to initiating treatment with Biktarvy:

- testing for hepatitis B virus infection
- assessing levels of creatinine in the blood, as well as levels of glucose and protein in the urine; assessing estimated glomerular filtration rate (eGFR). Also, in patients with chronic kidney disease, Gilead advises to assess the level of phosphorus in the blood.

For more information about HIV treatment, see CATIE’s *Your Guide to HIV Treatment*.

For many people with HIV, the use of ART (HIV treatment or antiretroviral therapy) has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to greatly reduce

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the risk of developing a life-threatening infection or an AIDS-related cancer. Neither Biktarvy nor any other treatment regimen (ART) is a cure for HIV. It is therefore important that you see your doctor for checkups and lab tests on a regular basis.

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. Anxiety and depression

A small proportion of people who took Biktarvy developed anxiety, depression, difficulty concentrating and/or problems with sleep. Anxiety and depression are relatively common in HIV-positive people (regardless of whether they are on treatment or the type of treatment they take). A small proportion of people also reported anxiety and depression when they took medicines similar to bictegravir (integrase inhibitors). If you are taking Biktarvy 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 these symptoms 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
- difficulty falling asleep or staying asleep, or waking up prematurely

- unexpected feelings of sadness
- recurrent nightmares
- prolonged feelings of sadness, anger or depression
- feeling hopeless
- loss of pleasure in everyday activities
- unexpectedly feeling tired or experiencing a lack of energy
- strange thoughts

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

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

2. Pregnancy

Studies of Biktarvy in pregnancy are underway. Interim results from these studies suggest that Biktarvy is safe and effective during pregnancy. For now, Gilead continues to recommend that “Biktarvy should not be used during pregnancy unless the potential benefits outweigh the potential risks to the fetus.” However, some doctors who are experienced in treating people with HIV, including pregnant people, are reassured by the interim data and are prescribing Biktarvy in pregnancy.

If you are taking Biktarvy and are pregnant or want to have a baby, speak to your doctor right away.

3. Liver health

Caution with Biktarvy cessation

TAF and FTC (both of which are in Biktarvy) have activity against hepatitis B virus (HBV). In people who are co-infected with HIV and HBV, if you change your regimen from Biktarvy to something else that does not have TAF or FTC, you can develop worsening HBV infection. This flaring up of HBV may be symptom-free or it may be associated with a wide range of symptoms, including the following:

- yellowing of the skin and the whites of the eye
- loss of appetite

- feeling tired
- muscle, joint, or stomach pain
- upset stomach, nausea, diarrhea, or vomiting
- Blood tests may find that levels of liver enzymes are higher than normal.

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Gilead recommends that if Biktarvy is discontinued and your new regimen does not contain tenofovir and/or FTC that the health and functioning of your liver “should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are co-infected with HIV and HBV.”

Liver injury or dysfunction

Gilead recommends that Biktarvy not be used in people who have severe liver injury (graded as “Child-Pugh C”). Gilead notes that no adjustment of Biktarvy is needed for people who have mild or moderate liver injury or dysfunction.

4. Kidney health

Another older formulation of tenofovir (tenofovir disoproxil fumarate or TDF) has been associated with cases of kidney injury and kidney failure. However, such problems are very rare with Biktarvy as Biktarvy contains the safer, newer formulation of tenofovir called TAF (tenofovir alafenamide). In general, Gilead recommends that Biktarvy not be used in people whose eGFR (estimated glomerular filtration rate) is as follows:

- between 15 and 29 mL/minute
- less than 15 mL/minute and who are not receiving regular dialysis

Gilead cautions that people who take Biktarvy (and other drugs containing tenofovir) and who also take medicines that can injure the kidneys (such as non-steroidal anti-inflammatory drugs) “are at increased risk” for developing kidney injury.

The following drugs and substances have the potential to weaken the health of the kidneys (this list is not exhaustive):

- antibiotics – gentamicin, amikacin, vancomycin, rifampin
- anti-cancer drugs – platinum-containing drugs including cisplatin and carboplatin, Avastin (bevacizumab), gemcitabine
- anti-fungal drugs – amphotericin B, pentamidine
- anti-viral drugs – foscarnet (Foscavir), cidofovir (Vistide), acyclovir, valacyclovir
- non-steroidal anti-inflammatory drugs (NSAIDs) – Aspirin (acetylsalicylic acid), celecoxib (Celebrex), diclofenac (Voltaren), ibuprofen (Advil, Motrin); indomethacin, naproxen, ketorolac (Acular)
- for pain relief – Tylenol (acetaminophen)
- street drugs – cocaine, heroin

Your doctor, nurse or pharmacist may recommend the temporary use of one of these medicines because they are medically necessary. However, chronic use of some of these medicines, such as NSAIDs or acetaminophen, may increase your risk for kidney injury.

Side effects

1. General side effects

In clinical trials, Biktarvy was well tolerated, generally safe and effective. However, as with any treatment, there were side effects but these were uncommon, mild to moderate and usually temporary and included the following:

- headache
- nausea
- diarrhea

Note that the HIV-positive people who are typically enrolled in pivotal clinical trials of HIV treatments, including Biktarvy, are generally young and healthy. Once a drug is approved and more widely available, it gets used by populations who are not usually in pivotal clinical trials. These people may be older and may have other health issues—

such as cardiovascular disease, liver injury, kidney injury, type 2 diabetes, anxiety, depression, and substance use—that require medications or that cause symptoms. As a result, their experience of side effects may be different from those reported in pivotal clinical trials.

2. Weight gain

Some studies with HIV-positive people who used Biktarvy as part of combination treatment found that weight gain occurred. In some people the increased weight gain was modest—a few kilos—while in others it was more substantial. Research suggests that some HIV-positive people with the following features or characteristics tend to gain weight when on ART:

- women
- people of African, Black or Caribbean descent
- people whose CD4+ cell count fell below the 200 cell/mm³ level at some point in the past.

However, some HIV-positive people without these features can also gain weight. The cause of increased weight in HIV-positive people is not clear because studies suggest that HIV-negative people of the same age and gender are also generally gaining weight even though they are not taking ART.

An increase of one or two kilograms in weight over the course of one year is normal when initiating ART and is what has been reported in clinical trials in the current era. However, should you gain more than this amount of weight, speak to your nurse or doctor so that your weight gain can be assessed. Doctors and nurses also consider a person's waist size and/or body mass index (BMI) – this is a number derived by dividing their height by the square of their weight. If your nurse or doctor has found that your BMI is increasing and is outside what is considered healthy then they will investigate possible causes for an increase in weight.

There may be one or more reasons that your BMI is increasing, including the following:

Physical activity – Are you getting enough daily physical activity, including walking and climbing stairs? If not, can you begin a program of exercise?

Speak to your nurse or doctor about what kind of exercise is right for you.

Sleeping problems – Rest and sleep quality are sometimes overlooked aspects of health. A large observational study in HIV-negative people found that people who have sleeping problems tend to gain weight. If you are unexpectedly gaining weight, speak to your doctor or nurse to rule out any sleep problems.

Emotional and mental health – Are there factors in your life that can affect how you respond to stressful events? For instance, when stressed, some people eat more fat and carbohydrate-rich foods as a source of comfort. Repeated engagement in excessive intake of carbohydrates and fatty foods can lead to weight gain over time. Depression can affect appetite—some people gain weight, others lose weight. If you notice weight gain along with changes in your mood, speak to your doctor or nurse.

Metabolic conditions, hormones and arthritis

Some conditions and life-stages are associated with weight gain, including the following:

- diabetes
- problems with the thyroid gland and its hormones
- being post-menopausal
- arthritis

Diet

Not everyone follows a diet that is informed by dietary guidelines. If you have access to subsidized dietary counselling (sometimes this is provided in large hospitals and clinics), you may benefit from consulting a registered dietitian. Registered dietitians can assess the quality and quantity of meals, and if necessary, provide helpful advice about making healthy changes.

Substance use

Alcohol contains calories. Is excess consumption of alcohol an issue for you? Excess consumption of alcoholic beverages could suggest unaddressed mental health and emotional issues.

Prescription medicines

Some prescription medicines (for conditions other than HIV) have the potential to cause changes in weight, particularly increased weight. It can be useful to speak to a pharmacist about all the medicines that you are taking to see if any are associated with changes in weight. You can then discuss any medicines that your pharmacist has identified with your doctor.

Bear in mind

While the above list covers some potential causes of weight gain in HIV-positive people, it is not exhaustive.

3. Uncommon symptoms

The following symptoms were uncommon in clinical trials, affecting less than 2% of Biktarvy users; it is not clear if these symptoms were caused by Biktarvy, the underlying disease process or something else:

- lack of energy
- abdominal pain
- nausea
- vomiting
- muscle soreness
- decreased appetite
- feeling sleepy during the daytime

Drug interactions

Some drugs (including prescribed and over-the-counter), herbs and supplements can interfere with the absorption and/or effectiveness of Biktarvy. Such interference is called a drug interaction. Some

drugs can reduce the levels of the medicines in Biktarvy in your blood. This can make Biktarvy less effective and lead to treatment failure, reducing your future treatment options. Other drugs can raise the levels of medicines in Biktarvy in your blood, resulting in enhanced side effects or new side effects. Therefore, it is important to disclose to your doctor and pharmacist all the supplements, drugs, and herbs you are taking.

This factsheet is not comprehensive and only lists some of the potential and actual drug interactions with Biktarvy. Speak to your pharmacist to find out more about drug interactions with Biktarvy.

Not to be used

Gilead recommends that the following drugs should *not* be used by people taking Biktarvy:

- for treatment of abnormal heart rhythms – dofetilide (Tikosyn)
- for HIV treatment – atazanavir, doravirine, rilpivirine
- anti-seizure drugs – carbamazepine, oxcarbazepine, phenobarbital and phenytoin
- antibiotics – rifampin, rifabutin or rifapentine
- The herb St. John's Wort or its extracts including hypericin and hyperforin

Acid-reducing agents, laxatives, metal supplements and buffered medicines

Gilead recommends that Biktarvy be taken two hours before or two hours after taking medicines or supplements that contain metals (calcium, iron, magnesium or aluminium). Examples of these include:

- Alka-Seltzer
- Calcium and/or magnesium liquid and tablets
- Gaviscon (tablets and syrup)
- Maalox (liquid and tablets)
- Milk of Magnesia
- Pepto-Bismol and Pepto-Bismol Children's

- Roloids
- Tums

As an alternative, people who take supplements or medicines with calcium, magnesium, iron or aluminum, can take them with Biktarvy together with food.

Resistance and cross-resistance

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.

To reduce the risk of developing 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, the level of the medicines in Biktarvy in the blood may fall too low. If this happens, the HIV in your body can become resistant to the medication. If you find you are having problems taking your medications as directed, speak to your doctor, nurse or pharmacist about this. They can find ways to help you.

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 options might be, at some point your doctor can have a small sample of your blood analyzed to test for resistance.

Dosage

Biktarvy is supplied as purplish brown tablets. Each tablet contains 50 mg of bicitgravir, 200 mg of FTC and 25 mg of TAF. Biktarvy is taken once daily with or without food. If you forget to take a dose, Gilead recommends the following:

- If you miss a dose of Biktarvy and you notice after 18 hours, wait and take the next dose at your usual time.
- Do NOT take a double dose (two doses close together).

Availability

Biktarvy is licensed in Canada for the treatment of HIV infection in adults, and children weighing 25 kg or more. Your doctor, nurse or pharmacist can tell you more about the availability and coverage of Biktarvy in your region. CATIE's online resource, *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

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