Genvoya

FACT SHEET

Published
2021

Summary

Genvoya is a complete treatment in one pill that comes in the form of green tablets. The dose of Genvoya used by adults with HIV is one tablet once daily with food. Genvoya was well tolerated in clinical trials; most side effects were mild, usually temporary and included headache, tiredness or lack of energy, nausea and diarrhea.

Inside Genvoya

Each tablet of Genvoya contains the following medicines:

- elvitegravir 150 mg – an integrase inhibitor
- cobicistat 150 mg – a boosting agent; cobicistat raises and maintains the level of elvitegravir in the blood so that it can be taken only once a day
- FTC (emtricitabine) 200 mg – a nucleoside analogue ("nuke") that works against HIV
- TAF (tenofovir alafenamide) 10 mg – another nuke that works against HIV

How do people with HIV use Genvoya?

Because it contains three anti-HIV drugs, Genvoya is considered antiretroviral therapy, or ART. For more information on ART, see CATIE's *Your Guide to HIV Treatment*.

Genvoya is meant for use by people who weigh at least 25 kg.

Neither Genvoya nor any other anti-HIV medication 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.

CONTACT US

by e-mail
info@catie.ca

by mail
555 Richmond Street West
Suite 505, Box 1104
Toronto ON M5V 3B1

CATIE
Canada's source for HIV and hepatitis C information

Common side effects

1. General side effects

In clinical trials Genvoya was generally well tolerated. General side effects included the following:

- headache
- tiredness or lack of energy
- nausea
- diarrhea

These side effects are usually temporary.

2. Weight gain

Some studies with HIV-positive people who used dolutegravir 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/mm^3 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 take into account 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:

- pre-diabetes and 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. The kidneys

The kidneys filter blood and then put waste materials into urine and reabsorb nutrients and other useful materials back into the blood.

Genvoya, because it contains cobicistat, can interfere with the ability of the kidneys to release the waste product creatinine into urine. Therefore, a small but persistent increase of creatinine levels in the blood is generally seen in people who use Genvoya. This small increase is not considered harmful and is usually reversible once a person stops taking Genvoya. Furthermore, this particular effect on the kidneys does not appear to affect the ability of these organs to filter other substances. This effect on the kidneys by cobicistat is also seen with the anti-ulcer drug cimetidine (Tagamet).

4. Lipid levels

In clinical trials, Genvoya users developed small increases in the levels of cholesterol and triglycerides in their blood.

Uncommon side effects

Fewer than 1% of participants in clinical trials experienced the following side effects:

- abdominal pain
- indigestion
- flatulence
- rash
- vomiting

Warnings

1. Lactic acidosis

Genvoya contains TAF and FTC. Both of these medicines may be associated with a build-up of the waste product lactic acid in the blood. People who are obese or who have used nukes for many years may be at increased risk of developing lactic acidosis. 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 Genvoya and do not resolve, call your doctor right away.

2. Liver problems—enlarged liver and fatty liver

In rare cases, people who take Genvoya may develop swollen liver (hepatomegaly) or fatty liver (steatosis). Obesity and the use of nukes over many years may be risk factors for enlarged and fatty liver in people with HIV. People who develop these specific liver problems may also develop the following symptoms:

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

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

3. Other liver problems—hepatitis viruses

The safety of Genvoya in people co-infected with HIV and hepatitis B virus (HBV) is not known. Genvoya contains tenofovir (in the form of TAF), which has anti-HBV activity. Co-infected people who take Genvoya and then stop it may notice symptoms of their hepatitis B infection worsen. If you have this co-infection, talk to your doctor before you start Genvoya. 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 (including hepatitis C virus) and who take potent combination anti-HIV therapy (ART) can be 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 hepatitis B, speak to your doctor about getting a vaccine to protect you from it. There is no vaccine for preventing hepatitis C virus infection.

4. Pregnancy

In clinical trials with Genvoya, the proportion of women enrolled was relatively small. However, no side effects were more common in women than in men. According to the manufacturer, Gilead Sciences, "there are not sufficient data to recommend the routine initiation of Genvoya in women during pregnancy. Genvoya should not be used in pregnant women unless the potential benefits outweigh the potential risks to the fetus and mother."

There are reports that less than normal levels of elvitegravir have occurred in pregnancy when this drug is used with the booster cobicistat. If this happens, HIV could become detectable and there would be an increased risk of the baby being born with HIV. Gilead recommends that doctors "closely monitor viral load during pregnancy, if Genvoya is continued to be used."

5. Medicines and kidney injury

In addition to tenofovir (in Genvoya), 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)

6. Monitoring kidney health

Genvoya contains TAF. There have been reports of kidney injury in a minority of TAF users. Therefore the manufacturer of Genvoya, Gilead Sciences, recommends that doctors do the following:

- Prior to or when starting therapy with Genvoya, request eGFR (estimated glomerular filtration rate) and levels of glucose (sugar) and protein in the urine. Genvoya should not be started in patients who have an eGFR of 15 to less than 30 mL/min or in patients whose eGFR is less than 15 mL/min who are not receiving regular dialysis

7. Bone health

Genvoya contains tenofovir in the form of TAF.

Before you start taking Genvoya, 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 and 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.

In clinical trials with Genvoya, nearly 30% of participants lost more than 3% of their bone density in their hip and spine after taking this medicine for three years.

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 Genvoya or any other anti-HIV therapy. If your bones are thin, talk to your doctor about your intake of calcium and vitamin D3. Regular monitoring of bone density may also be useful.

8. Pancreatitis

Gilead Sciences, warns that "caution should be exercised" when using Genvoya 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 Genvoya.

According to the U.S. National Institutes of Health (NIH) the most common risk factor for pancreatitis is drinking excess alcohol. 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

9. Emotional issues—anxiety and depression

Genvoya is similar to another fixed-dose combination treatment called Stribild (the only difference between these pills is that Genvoya contains TAF, and Stribild contains tenofovir DF instead of TAF). After the licensure of Stribild, reports emerged of very rare cases of depression associated with the use of Stribild. Stribild and Genvoya both contain 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.

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 Genvoya 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.

Drug interactions

Sometimes one drug can interfere with the body's processing of another drug. Such an effect is called a drug-drug interaction or, more simply, a drug interaction. This can cause higher-than-normal levels of one or both drugs in the blood, resulting in side effects or worsening of pre-existing side effects. Alternatively, the interference of one drug on another can cause the levels of one or both drugs to fall below normal levels. This can result in the drug(s) losing effectiveness. In the case of anti-HIV meds, this fall in drug levels can cause HIV to develop the ability to resist one drug and, likely, other related drugs. This drug resistance limits future treatment options.

To minimize the development of drug resistance, all prescribed medicines should be taken every day, exactly as directed.

Always tell your doctor, nurse and pharmacist about **all** the drugs you are taking—prescription and over-the-counter drugs, supplements or herbs, and street drugs. Pharmacists in particular can be very helpful in checking for the possibility of drug interactions.

Here are recommendations from the manufacturer about potentially significant drug interactions with Genvoya. The following medicines should NEVER be used by someone who is taking Genvoya because they could lead to serious or life-threatening effects or they can weaken the anti-HIV activity of Genvoya:

- anti-asthma drugs – salmeterol (Advair, Serevent)
- antihistamines – astemizole, terfenadine
- anti-tuberculosis (TB) drugs – rifampin
- anti-migraine drugs (ergot derivatives) – dihydroergotamine (Migranal), ergotamine (Ergomar), ergonovine, methylergonovine
- anti-anxiety drugs – midazolam (Versed), triazolam (Halcion)
- anti-seizure drugs – carbamazepine, phenobarbital, phenytoin

- gastrointestinal motility drugs – cisapride (Prepulsid)
- antifungal drugs – voriconazole (Vfend), posaconazole (Posanol)
- antipsychotic drugs – pimozide (Orap)
- herbs – St. John's wort and its extracts (such as hypericin and hyperforin)
- some cholesterol-lowering medicines – lovastatin and simvastatin; lomitapide
- drugs for prostate problems – alfuzosin
- drugs for pulmonary hypertension – sildenafil (Revatio)
- transplant medicines – Genvoya contains cobicistat. This can raise levels of transplant medicines, such as tacrolimus (Advagraf, Prograf), to dangerous levels in the blood and cause kidney injury.

Commonly used drugs and their interactions

Acid-reducing agents can lower levels of elvitegravir (in Genvoya) if taken at the same time as Genvoya. Therefore, the manufacturer recommends that you take Genvoya and acid-reducing agents "at least two hours" apart from each other.

Genvoya can raise the level of erectile dysfunction drugs—such as sildenafil (Viagra), tadalafil (Cialis) and vardenafil (Levitra)—in the blood, leading to side effects. Gilead provides the following advice for dosing these drugs in Genvoya users:

- sildenafil – no more than 25 mg in a 48-hour period should be used
- tadalafil – no more than 10 mg in a 72-hour period should be used
- vardenafil – no more than 2.5 mg in a 72-hour period should be used

Other drug interactions

In some cases, with advice and monitoring by your doctor and the use of lab and other tests, it can be possible for you to use some of the drugs listed below. Your doctors, including in some cases your specialist and pharmacist, can advise you how to take Genvoya safely with these drugs. The following drugs can interact with Genvoya and/or vice versa:

- abnormal heart rhythm drugs – amiodarone, bepridil, digoxin, disopyramide, flecainide, systemic lidocaine, mexiletine, propafenone, quinidine
- antibiotics – clarithromycin (Biaxin) and telithromycin
- some antidepressants
- antifungal agents – itraconazole, ketoconazole, voriconazole
- cholesterol drugs – atorvastatin, lovastatin, rosuvastatin, simvastatin
- corticosteroids (inhaled) – fluticasone
- corticosteroids (systemic) – dexamethaxone
- hormonal contraceptives (the Pill) – norgestimate + ethinyl estradiol
- drugs to prevent blood clots – warfarin
- drugs to treat higher-than-normal blood pressure – amlodipine (Norvasc), diltiazem (Cardizem, Tiazac), felodipine, isradipine, nicardipine (Cardene SR), nifedipine (Procardia), nisoldipine (Sular), verapamil (Calan, Verelan, Covera-HS)
- drugs to treat pulmonary arterial hypertension (PAH) – bosentan
- sedatives – buspirone, zolpidem (Ambien)
- anti-TB drugs – rifabutin or rifapentine

The manufacturer notes that the following drugs do not have any "clinically significant interactions" with Genvoya:

- entecavir
- famciclovir
- methadone
- ribavirin
- sertraline

The above lists are not exhaustive. Consult your pharmacist if you have questions about potential drug interactions with Genvoya.

Resistance and other integrase inhibitors

Genvoya is meant to be taken once daily with food. If you have problems taking Genvoya exactly as directed, speak to your doctor and pharmacist. They can help you find ways to stick to your drug regimen. If you do not take Genvoya once every day, the level of anti-HIV drugs in your body will be reduced. When this happens, HIV can develop the ability to resist the medicines that make up Genvoya, which means that the medicines will no longer work. This could weaken your immune system and affect your body's ability to fight infections. Also, the development of HIV that is resistant to one or more of the medicines inside Genvoya can reduce your future treatment options.

The U.S. Department of Health and Human Services (DHHS) has been producing comprehensive HIV treatment guidelines for many years. These guidelines recommend that patients have resistance testing done prior to starting ART. Such testing can help reveal if HIV in your body has any resistance to the drugs in Genvoya.

Genvoya contains the integrase inhibitor elvitegravir. HIV that is resistant to elvitegravir is also usually resistant to another integrase inhibitor called raltegravir (Isentress). HIV that is resistant to elvitegravir or raltegravir is usually sensitive to another integrase inhibitor, bictegravir (in Biktarvy) and dolutegravir (Tivicay and in Dovato, Juluca and Triumeq). A combination of resistance testing of a sample of your blood and a review of your treatment history can help your doctor determine which treatments are best for you.

Dosage

The manufacturer recommends that adults and adolescents who are at least 12 years old and who weigh at least 25 kg can use Genvoya.

The recommended dose is one tablet once daily with food. The type of food does not matter.

The manufacturer advises the following when it comes to missed doses: if you miss "a dose of Genvoya within 18 hours of the time it is usually taken, [you] should take Genvoya with food as soon as possible, and then take the next dose of Genvoya at the regularly scheduled time." If you miss a dose of Genvoya "by more than 18 hours, [you] should not take the missed dose but resume the usual dosing schedule."

Availability

Once Health Canada licenses a drug, physicians can prescribe it but patients must pay for it unless they have a private insurance plan that provides coverage. If left untreated, HIV infection leads to catastrophic disease that can affect one's ability to work and requires expensive care. Therefore, in Canada, provincial and territorial ministries of health heavily subsidize the cost of anti-HIV medications. Each ministry has a listing of drugs for which it is prepared to pay. These listings are called formularies. CATIE's online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

Your pharmacist or doctor can tell you when Genvoya is listed on your region's formulary.

References

1. Gilead Sciences Canada. Genvoya (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide). *Product Monograph*. 13 November, 2020.

Author(s): **Hosein SR**

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.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to consult as broad a range of sources as possible. Users relying on this information do so entirely at their own risk. Neither CATIE, nor any of its partners, funders, employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE do not necessarily reflect the policies or opinions of CATIE nor the views of its partners and funders.

Permission to reproduce

Production of this document has been made possible through a financial contribution from the Public Health Agency of Canada. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.

CATIE fact sheets are available for free at **www.catie.ca**

CATIE
Canada's source for HIV and hepatitis C information

CONTACT US

by e-mail
info@catie.ca

by mail
555 Richmond Street West
Suite 505, Box 1104
Toronto ON M5V 3B1