From TreatmentUpdate 212

Genvoya approved in Canada—What you need to know

On November 27, 2015, Health Canada licensed the sale and use of a new anti-HIV treatment sold under the brand name Genvoya and made by the pharmaceutical company Gilead Sciences. Genvoya is a complete treatment in one pill that comes in the form of green capsule-shaped tablets. The dose of Genvoya used by adults with HIV is one tablet once daily with food. Genvoya was generally well tolerated in clinical trials; general and usually temporary side effects included headache, tiredness or lack of energy, nausea and diarrhea. Genvoya should be available for ordering by pharmacies late in January 2016.

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

The only new drug listed above is TAF. This is a new formulation of an older drug called tenofovir DF (tenofovir disoproxil fumarate). TAF is meant to eventually replace tenofovir DF. In clinical trials, TAF was found to be safe and generally well tolerated with fewer side effects than tenofovir DF. Further details on side effects appear later in this issue of TreatmentUpdate.

Genvoya is the first pill to be licensed in Canada that contains TAF.

Studies

In clinical trials (for details, see TreatmentUpdate 211) Genvoya has been tested in more than 3,000 HIV-positive people. Researchers found that Genvoya was an effective regimen against HIV. Genvoya, which contains TAF, was found to be as good as other regimens that contained the older formulation, tenofovir DF. Genvoya was generally well tolerated and safe; because it contains TAF, it has a reduced potential for causing side effects affecting the kidney and bones compared to regimens that include tenofovir DF. Genvoya was effective both in people new to anti-HIV therapy and in those who are treatment-experienced.

Common 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.

Uncommon side effects

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

- abdominal pain
• indigestion
• flatulence
• rash
• vomiting

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) and the anti-HIV drug dolutegravir (Tivicay and in Triumeq).

Lipid levels

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

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, 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. Women

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.

Genvoya’s safety has not been studied in pregnant women. Gilead Sciences recommends: “Genvoya should not be used in pregnant women unless the potential benefits outweigh the potential risks to the fetus.”

5. 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. 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 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.

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

Understanding 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, supplements or herbs, and street drugs. Pharmacists in particular can be very helpful in checking for the possibility of drug interactions.

Genvoya and drug interactions

Gilead Sciences recommends that the following medicines 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)
• cholesterol-lowering medicines (statins) – lovastatin and simvastatin
• drugs for prostate problems – alfuzosin
• drugs for pulmonary hypertension – Revatio (sildenafil)

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, Gilead Sciences recommends that you take Genvoya and antacid “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) – dexamethasone
• 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, Tizac), felodipine, isradipine, nicardipine (Cardene SR), nifedipine (Procardia), nisoldipine (Sular), verapamil (Calan, Verelan, Covera-HS)
• drugs to treat pulmonary arterial hypertension (PAH) – bosentan
• hepatitis C treatments – Harvoni (sofosbuvir + ledipasvir), boceprevir
• sedatives – buspirone, zolpidem (Ambien)
• anti-TB drugs – rifabutin or rifapentine

Gilead notes that the following drugs do not have any “clinically significant interactions” with Genvoya:

• entecavir
• famciclovir
• methadone
• ribavirin
Resistance and other integrase inhibitors

Genvoya is meant to be taken once daily every day 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, dolutegravir (Tivicay and in Triumeq). Only 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.

Dosing

Gilead Sciences recommends that adults and adolescents who are at least 12 years and who weigh at least 35 kg can use Genvoya.

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

Gilead Sciences 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.” But, 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.”

Access

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.

In the months ahead, Gilead Sciences and provincial and territorial formularies will be negotiating the price of Genvoya. Your pharmacist or doctor can tell you when Genvoya is listed on your region’s formulary.

—Sean R. Hosein

REFERENCES:


**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.

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