Triumeq

Summary

Triumeq is the name given to a pill containing the following three anti-HIV drugs: dolutegravir, abacavir and 3TC. Although Triumeq is generally well-tolerated, general side effects are uncommon and can include nausea, vomiting, diarrhea, headache and difficulty falling asleep. These are usually temporary and mild. Triumeq is a complete treatment in one pill and is taken once daily. Triumeq can be taken day or night, with or without food.

What is Triumeq?

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

- Dolutegravir (Tivicay and in Juluca), which belongs to a group or class of drugs called integrase inhibitors
- abacavir (Ziagen), which belongs to a group of drugs called nucleoside analogues or nukes
- 3TC (lamivudine), which belongs to a group of drugs called nukes

Triumeq is used as a once-daily, complete treatment for HIV infection.

How does Triumeq 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 three medicines in Triumeq interfere with enzymes needed by HIV, including an enzyme called reverse transcriptase and another one called integrase. These enzymes are used by HIV-infected cells to make more copies of HIV.

Since the drugs in Triumeq inhibit, or reduce, the activity of these enzymes, Triumeq causes HIV-infected cells to slow down or stop producing new viruses.

How do people with HIV use Triumeq?

Triumeq is a combination of three anti-HIV drugs. Such combinations are called antiretroviral therapy, or ART. For more information on ART, see CATIE’s Your Guide to HIV Treatment.
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 greatly reduce the risk of developing a life-threatening infection. Neither Triumeq nor any other anti-HIV medication 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. Hypersensitivity testing

Before you first begin taking Triumeq, check with your doctor to find out if you have been screened for possible hypersensitivity to abacavir, one of the drugs in Triumeq. This screening is written as HLA-B*5701 and is done with a simple blood test. If you test positive for abacavir hypersensitivity then you cannot use Triumeq, or any other medicine that contains abacavir such as these:

- Kivexa
- Ziagen
- Trizivir

If you test negative, then your risk of having a hypersensitivity reaction is greatly reduced. Speak to your doctor about your abacavir hypersensitivity results and whether it is safe for you to use Triumeq. For more information, see CATIE’s fact sheet Abacavir hypersensitivity screening.

#### About hypersensitivity

In up to 8% of people with HIV who use abacavir, an exaggerated reaction against abacavir by the immune system—abacavir hypersensitivity—can occur. This reaction is very serious and can be fatal.

Although the hypersensitivity reaction can occur at any time while a person is taking abacavir, on average it occurs within the first six weeks of use. The manufacturer, ViiV Healthcare, states that you should stop using abacavir if you have signs or symptoms from two or more of the following groups:

- Fever
- Rash
- Gastrointestinal symptoms (including nausea, vomiting, diarrhea or belly pain)
- General symptoms (including fatigue, lack of energy, achiness)
- Respiratory symptoms (sore throat, shortness of breath, cough, unusual findings on X-rays of the chest)

If you develop symptoms from two or more of these groups while you are taking abacavir or any drug containing abacavir, you should stop taking this medicine and contact your doctor right away. If your doctor confirms that a hypersensitivity reaction to abacavir has indeed occurred, then abacavir should never be restarted, as a fatal reaction could occur within hours. You should also never take any other drug that contains abacavir.

#### 2. Pregnancy

In May 2018, regulatory agencies issued cautionary statements because dolutegravir was associated with an apparent increased risk of birth defects in a clinical trial:


If you are taking Triumeq and are pregnant or want to have a baby, speak to your doctor.
3. Lactic acidosis and hepatic steatosis

Two related conditions, lactic acidosis (a build-up of lactic acid in the blood) and hepatic steatosis (excess fat in the liver), have occurred in some people who have used nucleoside analogues. These conditions can be serious or fatal. They have mostly been seen in women and people who are overweight or who have been on nucleosides a long time, and can cause the following symptoms:

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

If any of these symptoms occur without apparent reason, call your nurse or doctor right away.

Lactic acidosis is rare. If you do develop any of these symptoms, it does not necessarily mean you have lactic acidosis, but you should still let your doctor know right away.

4. Cardiovascular risk

There are conflicting data from some studies about a link between heart attacks and the initial use of abacavir-containing products (Ziagen and in Triumeq, Kivexa and Trizivir). However, a review by the U.S. Food and Drug Administration (FDA) of randomized clinical trials has not found any link between abacavir use and an increased risk of heart attack. Another large observational study, the French Hospital Database also assessed the risk of heart attack among its participants who used abacavir. French researchers found that after adjusting for use of cocaine (a powerful stimulant that by itself can cause heart attacks), exposure to abacavir was not linked to an increased risk for heart attacks.

All of the available data make it difficult to draw firm conclusions about the possible role of abacavir and heart attacks.

Therefore, as a precaution, before starting Triumeq, let your doctor know if you have any of these risk factors for cardiovascular disease:

- your close family members (mother, father, brother, sister) have a history problems such as heart attack or stroke
- have risk factors for cardiovascular disease such as high blood pressure, abnormal cholesterol or triglyceride levels in your blood, or have diabetes or pre-diabetes
- you use tobacco
- you use cocaine or club drugs or inject street drugs

Your doctor can help you find ways to reduce your risk factors for cardiovascular disease. Your doctor can also help you decide if Triumeq is right for you.

5. Hepatitis B

If someone with hepatitis B infection is taking 3TC—a component of Triumeq—the hepatitis can grow worse or “flare up” if the medication is stopped. People who stop taking Triumeq should be carefully monitored. If you are co-infected with HBV, talk to your doctor about how best to treat this co-infection.

Side effects

1. General

Triumeq is generally well-tolerated. However, like many medicines, Triumeq can be associated with these symptoms:

- nausea
- vomiting
- diarrhea
- headache
- abdominal discomfort/pain
If these persist or are bothersome tell your doctor right away.

2. Older people

Triumeq has not been studied in large numbers of people aged 65 or older. Older people may have major organ systems (heart, liver, kidneys and so on) that do not work as well as in healthy younger people. Older people may also be taking multiple medicines that have the potential to interact with Triumeq. The manufacturer therefore advises doctors that in people aged 65 or older Triumeq should be used with caution.

3. Liver

The manufacturer does not recommend that Triumeq be used in people whose livers have a “moderate to severe” degree of dysfunction.

4. The kidneys

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

Triumeq contains dolutegravir. This drug 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 dolutegravir users. This small increase is not considered harmful. Furthermore, this effect on creatinine does not appear to affect the ability of the kidneys to filter other substances. Such an effect on creatinine is also seen with the anti-ulcer drug cimetidine (Tagamet) and with the boosting agent cobicistat, found in Stribild and Prezcobix.

However, the manufacturer recommends that Triumeq not be used by people whose kidneys are not functioning normally. That is, people whose eGFR (estimate glomerular filtration rate) is less than 50 mL/min should not use Triumeq.

Uncommon side effects

Triumeq is a relatively new formulation and it contains a relatively new drug (dolutegravir) and as it becomes more widely used in the community, more side effects may appear.

Side effects that were rare (less than 1%) in clinical trials included the following:
• feeling sleepy in the day time
• muscle weakness
• muscle pain

Emotional issues—Anxiety and depression

Note that all integrase inhibitors, including dolutegravir, 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 dolutegravir 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:
• become easily upset or angry
• feel fearful
• excessive worry
• have unexpected feelings of sadness
• have prolonged feelings of sadness, anger or depression
• feel hopeless
• have loss of pleasure in everyday activities
• unexpectedly feel tired or experience a lack of energy
• have difficulty falling asleep, staying asleep or waking up prematurely
• have 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

In general, integrase inhibitors such as dolutegravir (one of the drugs in Triumeq) tend not to interfere with many other drugs (raising or lowering their levels in the blood). Dolutegravir causes few interactions with other drugs. However, there are other medicines that interfere with dolutegravir levels in the blood, usually decreasing them. Bear in mind that as dolutegravir and Triumeq become more widely used in the community, there may be reports of new drug interactions.

The manufacturer has not specifically conducted drug interaction studies with Triumeq. It has instead done drug interaction studies with a combination of the drugs used in Triumeq (dolutegravir + abacavir + 3TC).

Here are recommendations from the manufacturer about potentially significant drug interactions with the dolutegravir (in Triumeq):

Other HIV drugs

Etravirine (Intelence) – this drug can reduce the concentration of dolutegravir in the blood. Therefore, the manufacturer recommends that dolutegravir should not be used with etravirine unless it is also taken with one of the following combinations of drugs:

• atazanavir (Reyataz) + ritonavir (Norvir)
• darunavir (Prezista) + ritonavir
• lopinavir + ritonavir (in Kaletra)

Nevirapine (Viramune) – dolutegravir should not be used with nevirapine, as there is not enough information to make dosing recommendations.

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

Dolutegravir should be taken 2 hours before or 6 hours after taking these medicines.

Examples of acid-reducing agents include:

• Alka-Seltzer
• Gaviscon (tablets and syrup)
• Maalox (liquid and tablets)
• Milk of Magnesia
• Pepto-Bismol and Pepto Bismol Children’s
• Rolaid
• Tums

Metal supplements include those containing iron, calcium and magnesium.

Abnormal heart rhythm drugs

The drug dofetilide (Tikosyn) is prescribed to treat abnormal heart rhythms. Dolutegravir can raise levels of dofetilide. Although dofetilide is not approved in Canada, many Canadians travel to the U.S. where it is approved and may be prescribed this medicine. The manufacturer warns that dofetilide should never be used by patients who are taking dolutegravir, as high concentrations of dofetilide can occur causing serious injury.

Anti-seizure drugs

Oxcarbazepine, carbamazepine (Tegretol), phenobarbital, phenytoin (Dilantin) – dolutegravir should not be used with these drugs as there is not enough information to make dosing recommendations.

Antibiotics

Rifampin – this drug reduces the concentration of dolutegravir in the blood. The manufacturer recommends that dolutegravir at a dose of 50 mg twice daily should be used if rifampin must also be taken. However, the manufacturer also notes that in the case of patients who have used integrase inhibitors in the past and who have
HIV that may be or is suspected to be resistant to integrase inhibitors, doctors and nurses should seek alternative antibiotics to rifampin where possible.

**Diabetes drugs**

Metformin – as dolutegravir can raise levels of metformin in the blood, the manufacturer recommends close monitoring of patients when they are starting or stopping therapy with dolutegravir. The manufacturer also suggests that it may be necessary to reduce the dose of metformin in some dolutegravir users.

**Herbs**

St. John's wort (or compounds found in St. John's wort such as hypericin, hyperforin) can significantly reduce dolutegravir levels and this herb should not be used. Although St. John's wort is the only herb listed here, note that other herbs are likely to interact with dolutegravir.

Here are recommendations from the manufacturer about potentially significant drug interactions with abacavir (in Triumeq):

- Methadone – for most people no adjustment to their dose of methadone is needed.
- Alcohol – although drinking alcohol can increase the concentration of abacavir in the blood, this is not considered clinically meaningful.

These additional drugs should not be taken by someone using Triumeq – abacavir (Ziagen), Combivir, and Trizivir.

Here are recommendations from the manufacturer about potentially significant drug interactions with 3TC (in Triumeq):

- FTC (emtricitabine, Emtriva and in Hepsera, Truvada, Complera, Stribild and Atripla) – these drugs should not be taken by Triumeq users.

**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. Triumeq is a complete treatment in one pill.

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 medicines 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. Should the HIV in your body become resistant to dolutegravir, your doctor can recommend a new treatment combination for you.

For patients whose integrase inhibitor regimens are failing, doctors can request laboratory testing of their blood to assess the degree of resistance to integrase inhibitors. This will help doctors determine whether or not an integrase inhibitor can be used in future regimens.

In 2013, a study in the U.S. with about 3,000 HIV-positive participants who were undergoing testing of their blood for the presence of HIV resistance was completed. Researchers found that resistance to integrase inhibitors was present in 16% of participants. Their results suggested that, in most cases, dolutegravir would have “full or partial activity” against most strains of HIV with integrase resistance. However, 2% of all participants (or 12% of participants with HIV resistant to the integrase inhibitors raltegravir or elvitegravir) had “high-level resistance to dolutegravir.”
Dosage

Triumeq is available as a purple film-coated tablet. It contains the following drugs:

- dolutegravir – 50 mg
- abacavir – 600 mg
- 3TC – 300 mg

Triumeq is approved for use by adults 18 years of age or older. It is a complete regimen in one pill. It is meant to be taken once daily, day or night, without food or water restrictions.

If you miss a dose, the manufacturer recommends that you take it “as soon as you remember, but if your next dose is due within four hours, skip the dose you missed and take your next one at the usual time. Then continue your treatment as before.”

If you continue to miss doses, speak to your doctor, nurse or pharmacist about ways of helping you stick to a regular schedule of pill-taking.

Availability

Triumeq is licensed in Canada for the treatment of HIV infection in adults. Your doctor can tell you more about the availability and coverage of Triumeq 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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