

# Juluca

## Summary

Juluca contains two medicines—dolutegravir and rilpivirine. Dolutegravir belongs to the class of drugs called integrase inhibitors. Rilpivirine belongs to the class of drugs called non-nucleoside reverse transcriptase inhibitors (“non-nukes”). Juluca is taken at a dose of one pill once daily with a meal. Overall, Juluca was well-tolerated in clinical trials. General side effects were uncommon and included headache and diarrhea; these were usually mild and temporary.

## What is Juluca?

Juluca contains two medicines—dolutegravir and rilpivirine. Dolutegravir belongs to the class of drugs called integrase inhibitors. Rilpivirine belongs to the class of drugs called non-nucleoside reverse transcriptase inhibitors (“non-nukes”). Dolutegravir was approved in Canada in 2013 and rilpivirine was approved about a decade ago. What is new is that Juluca combines both of these drugs in one pill.

## How does Juluca work?

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

## How do people with HIV use dolutegravir?

Juluca is meant as a replacement for a more complex regimen in adults. The manufacturer of Juluca, ViiV, recommends that “Prior to initiating Juluca, patients should be on a stable anti-HIV regime for at least six months.” During that time, a person’s viral load should be less than 50 copies/mL or “undetectable.”

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 the risk of developing a life-threatening infection or an AIDS-related cancer. Neither Juluca nor any other treatment regimen (ART) is a cure for HIV. It is

# FACT SHEET

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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

### Pregnancy

In May 2018, regulatory agencies, including Health Canada, the U.S. Food and Drug Administration and the European Medicines Agency, issued cautionary statements because dolutegravir was associated with an apparent increased risk of birth defects in a clinical trial. As a result, ViiV recommends that women who are of “child-bearing potential should undergo pregnancy testing before starting Juluca and Juluca should not be used during the first three months of pregnancy.” Furthermore, ViiV recommends that women of childbearing potential who are taking Juluca “should use effective contraception throughout treatment.”

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

### Anxiety and depression

Although not common in clinical trials, a small proportion of people (less than 2%) who took Juluca developed depression, negative thoughts, anxiety and thoughts of suicide that led to attempted suicide.

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 Juluca 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.

There have been reports of some people developing anxiety and/or depression after initiating treatment with Juluca. 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.

### Skin and hypersensitivity reactions

In large clinical trials with Juluca, about 1% of participants developed rash. All rashes were of mild or moderate severity.

However, over the past decade there are reports of people using dolutegravir or rilpivirine (the drugs in Juluca) who developed severe skin and hypersensitivity reactions. Symptoms of hypersensitivity reactions can include severe rash or rash with a fever, together with lack of energy and painful muscles or joints. In

clinical trials, some severe cases with additional symptoms occurred, such as peeling of the skin, blisters on the lips, swollen eyes and face, stomach cramps and difficulty breathing. The manufacturer advises that Juluca (or any other drugs suspected of causing this reaction) should be discontinued immediately if these symptoms occur, otherwise the hypersensitivity reaction can become life threatening. If symptoms suggestive of hypersensitivity occur, see your doctor immediately or go to the emergency room of your nearest hospital or medical centre.

### Liver health

People who are co-infected with hepatitis B or C viruses or who have elevated levels of liver enzymes in the blood prior to initiating Juluca may be at risk for liver inflammation or injury. According to ViiV, both rilpivirine and dolutegravir use have been linked to “a few cases of [liver injury].” None of the people who developed liver injury had any known pre-existing factors that placed them at heightened risk of liver injury. Therefore, ViiV states that “Appropriate laboratory testing prior to initiating therapy and monitoring for [liver injury] during therapy with Juluca is recommended.”

### Age

Juluca has not been tested in people younger than 18 years. Juluca has also not been tested in large numbers of people who are 65 years or older so its effectiveness and safety in these populations is not known.

### Side effects

#### General

In clinical trials, Juluca was well tolerated, generally safe and effective. However, as with any treatment, there were side effects but these were uncommon 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 Juluca, 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.

### The kidneys

The kidneys filter the blood, put waste materials into urine and reabsorb nutrients and other useful materials back into the blood. Juluca contains dolutegravir and 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 with the integrase inhibitor bictegravir (in Biktarvy).

### Uncommon symptoms

The following symptoms were uncommon in clinical trials, affecting less than 2% of Juluca users; it is not clear if these symptoms were caused by Juluca, 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 Juluca. Such interference is called a drug interaction. Some drugs can reduce the levels of the medicines in Juluca in your blood. This can make Juluca less effective and lead to treatment failure, reducing your future treatment options. Other drugs can raise the levels of medicines in Juluca 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 Juluca. Speak to your pharmacist to find out more about drug interactions with Juluca.

## Not to be used

ViiV recommends that the following drugs should *not* be used by people taking Juluca:

- for treatment of abnormal heart rhythms – dofetilide (Tikosyn)
- anti-seizure drugs – carbamazepine, oxcarbazepine, phenobarbital and phenytoin
- antibiotics – rifampin, rifapentene
- a class of acid-reducing agents called proton pump inhibitors (PPIs) – Losec (omeprazole), Nexium (esomeprazole), Pantoloc (pantoprazole), Pariet (rabeprazole), Prevacid (lansoprazole)
- for inflammation-related conditions – more than one dose of systemic glucocorticoids (e.g. prednisone, cortisone)

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

Juluca should be taken at least 4 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
- Roloids
- Tums
- Zantac (ranitidine), Tagamet (cimetidine)

Alternatively, ViiV recommends that people who take calcium (for reasons other than stomach acid reduction) and/or iron supplements can take these supplements with Juluca “together with a meal.”

## Metformin

The drug metformin is commonly used to help manage blood sugar levels. Dolutegravir, in Juluca, can raise levels of metformin in the body. Your doctor may need to reduce your dose of metformin if you are also taking Juluca.

## 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 dolutegravir and rilpivirine 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

Juluca is supplied as pink tablets. Each tablet contains 50 mg of dolutegravir and 25 mg of rilpivirine. Juluca is taken once daily with a meal. Juluca must be taken with a meal so that it is absorbed.

If you forget to take a dose, ViiV recommends that “you take Juluca with a meal as soon as you remember. If your next dose is due within 12 hours, skip the dose you missed and take the next one at the usual time. Don’t take a double dose to make up for the missed dose.”

## Availability

Juluca is licensed in Canada. Juluca is meant to replace the current HIV treatment in people whose viral loads are less than 50 copies/mL (“undetectable”) and who have been on the same regimen with an undetectable viral load for at least six months. Your doctor or pharmacist can tell you more about the availability and coverage of dolutegravir in your region. CATIE’s online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

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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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