

# Delstrigo

## Summary

Delstrigo contains three medicines—doravirine, 3TC and tenofovir DF. Doravirine belongs to the class of drugs called non-nucleoside reverse transcriptase inhibitors (“non-nukes”). 3TC and tenofovir DF belong to the class of drugs called nucleoside reverse transcriptase inhibitors (“nukes”). Delstrigo is a complete treatment and is taken at a dose of one pill once daily with or without food. Overall, Delstrigo was well-tolerated in clinical trials. General side effects were uncommon and included dizziness, headache and nausea; these were usually mild and temporary.

## What is Delstrigo?

Delstrigo contains three medicines—doravirine, 3TC and tenofovir DF. Doravirine belongs to the class of drugs called non-nucleoside reverse transcriptase inhibitors (“non-nukes”). 3TC and tenofovir DF belong to a class of drugs called nucleoside reverse transcriptase inhibitors (“nukes”). Delstrigo contains 100 mg of doravirine, 300 mg of 3TC and 300 mg of tenofovir DF.

## How does Delstrigo work?

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

## How do people with HIV use Delstrigo?

Delstrigo is taken at dose of one pill once daily, with or without food. It is a complete treatment for HIV infection.

Delstrigo is meant for people who are aged 12 or older and who weigh at least 35 kg and who do not have past or current evidence of resistance to the medicines in Delstrigo: doravirine, 3TC and tenofovir DF.

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 Delstrigo 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

### Special populations

#### Pregnant people

Delstrigo has not been studied in pregnancy and its safety in pregnant people is not known. Delstrigo's effect on the fetus is not known. If you are pregnant or want to have a baby, let your doctor know.

#### People who are 65 years or older

According to Merck, the manufacturer, "there are limited data on the use of Delstrigo in patients aged 65 years and over. There is no evidence that [older patients] require a different dose than younger adult patients."

#### People with kidney injury or dysfunction

Merck recommends that Delstrigo not be used in people whose estimated glomerular filtration rate (eGFR) is less than 50 mL/minute.

#### People with liver injury or dysfunction

Merck cautions that Delstrigo has not been studied in patients with severe liver injury or dysfunction. Therefore, Merck does not know if doravirine levels will increase significantly in such people. The company notes: "No dose adjustment of doravirine is required in patients with mild or moderate hepatic impairment."

### Driving and operating machinery

According to Merck, some people who use Delstrigo may experience one or more of the following:

- tiredness
- dizziness
- sleepiness

If you experience any of these, do not drive a vehicle or operate machinery. Wait until these symptoms have cleared.

### Side effects

#### General

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

- nausea
- lack of energy
- headache
- dizziness
- feeling sleepy during the daytime

If these side effects persist or are bothersome, let your doctor know.

Note that the HIV-positive people who are typically enrolled in pivotal clinical trials of HIV treatments, including Delstrigo, 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.

### **Kidney injury**

Delstrigo contains tenofovir DF. This drug has been previously associated with kidney injury in some people.

Merck advises that people who are taking Delstrigo should avoid taking medicines that may injure the kidneys. They noted that there have been cases in the past where severe kidney injury or kidney failure have occurred in people who were using regimens containing tenofovir DF and who took drugs that have the potential to injure the kidneys (such as non-steroidal anti-inflammatory drugs). In such cases some people taking tenofovir DF had stable kidney health prior to using drugs that harmed the kidneys.

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 – Cisplatin (cis-platinum), carboplatin, Avastin (bevacizumab), gemcitabine
- anti-fungal drugs – amphotericin B, pentamidine
- anti-viral drugs – foscarnet (Foscavir), cidofovir (Vistide), acyclovir, valacyclovir (Valtrex)
- non-steroidal anti-inflammatory drugs (NSAIDs) – Aspirin (acetylsalicylic acid), celecoxib (Celebrex), diclofenac (Voltaren), ibuprofen (Advil, Motrin); indomethacin, naproxen, ketorolac (Acular),)
- Pain reliever – acetaminophen (Tylenol)
- street drugs – cocaine, heroin

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

In rare cases, kidney injury and dysfunction arising from use of tenofovir DF may be associated with thinner-than-normal bones, bone aches and/or muscle pain or weakness.

Merck recommends that laboratory tests of kidney health and function be carried out prior to starting therapy with Delstrigo.

### **Chronic hepatitis B virus (HBV) infection**

Delstrigo has not been approved for the treatment of people co-infected with HBV. The safety and effectiveness of Delstrigo in co-infected people is not known.

People who stop taking Delstrigo and who have chronic HBV may experience worsening of HBV (flares). Therefore, Merck advises that such people who discontinue Delstrigo be offered a regimen that is effective against this virus.

### **Drug interactions**

Some drugs (including prescribed and over-the-counter), herbs and supplements can interfere with the absorption and/or effectiveness of Delstrigo. Such interference is called a drug interaction. Some drugs can reduce the levels of the drugs in Delstrigo in your blood. This can make Delstrigo less effective and lead to treatment failure, reducing your future treatment options. Other drugs can raise the levels of the drugs in Delstrigo 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.

Drug interactions can occur with:

- anti-seizure drugs – carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- the prostate cancer drug enzalutamide (Xtandi)

- the anti-cancer drug mitotane (Lysodren)
- antibiotics – rifampin, rifapentine
- the herb St. John’s Wort or extracts of this herb including hypericin and hyperforin

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

Many HIV-positive people take acid-reducing agents, including over-the-counter preparations such as Tums or Maalox or a class of drugs called PPIs (proton pump inhibitors), including the following:

- Losec (omeprazole)
- Nexium (esomeprazole)
- Pantoloc (pantoprazole)
- Pariet (rabeprazole)

*None* of these acid-reducing agents interact with Delstrigo.

### Rifabutin

Your doctor may prescribe the antibiotic rifabutin. However, rifabutin can lower levels of some drugs—such as doravirine in Delstrigo—in your body. Merck recommends that if you are taking rifabutin, take one tablet of doravirine (Pifeltro) 12 hours after your last dose of Delstrigo.

### Some modest beneficial effects of doravirine (in Delstrigo)

Note that many people who take HIV treatment gain some weight — usually a few kg and this tends to stabilize after a year or two. However, doravirine (in Delstrigo) has modest effects on weight loss. In studies, some people who have used other regimens and then switched to doravirine-based treatment *lost* a modest amount of weight; a few kg.

Also, levels of cholesterol in the blood may decrease modestly when people switch to a doravirine-based regimen.

### 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 Delstrigo 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

Delstrigo is supplied as yellow, oval-shaped tablets. Each tablet contains 100 mg of doravirine, 300 mg of 3TC and 300 mg of tenofovir DF. Delstrigo is taken once daily with or without a meal.

If you forget to take a dose, Merck has this advice:

- If you miss a dose, take it as soon as you remember. If you do not remember until it is almost time for your next dose, skip the missed dose and take the next dose at your regular time.
- Do not take two doses of Delstrigo at the same time.
- If you are not sure what to do, call your doctor or pharmacist.

## Availability

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