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CATIE-News

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Delstrigo approved in Canada for HIV treatment

22 November 2018

- **Health Canada has approved a new three-in-one daily pill to treat HIV**
- **Delstrigo contains two older drugs plus the new drug doravirine**
- **Discovered in Canada, doravirine is effective and generally well tolerated**

In November 2018, Health Canada approved the use and sale of a new treatment for HIV infection—a pill called Delstrigo—that contains the following three medicines:

- doravirine
- tenofovir DF
- 3TC (lamivudine)

These three drugs are a complete treatment in one pill, taken once daily with or without food. According to Merck, the manufacturer of Delstrigo, this pill is meant to be used in adults "without past or present evidence of viral resistance to doravirine, tenofovir DF or 3TC."

Delstrigo should be available for ordering by wholesalers and pharmacies by mid-December 2018.

Something new, something old

Delstrigo contains the drug doravirine, which was discovered in Canada by Merck scientists and belongs to a class of drugs called NNRTIs (non-nucleoside reverse transcriptase inhibitors; non-nukes). Doravirine was recently approved in Canada for use in HIV combination treatment.

Delstrigo also contains two other drugs—tenofovir DF and 3TC. Both of these drugs have been in use for many years as part of HIV treatment in combination with other drugs. They belong to a class of drugs called NRTIs (nucleotide/nucleoside reverse transcriptase inhibitors; nukes).

Effectiveness

Delstrigo has been tested in a clinical trial (called Drive-Ahead) with 728 adults who had not previously received HIV treatment. This randomized double-blind trial compared Delstrigo against Atripla (efavirenz + tenofovir DF + FTC). About 85% of participants were men and 15% were women. Upon entering the study, the average profile of participants was 30 years old with a CD4+ count of 362 cells and a viral load of less than 100,000 copies/mL. After 48 weeks, Delstrigo was found to be at least as effective as Atripla, with 84% of Delstrigo users achieving and maintaining a viral load less than 50 copies/mL (compared to 81% of Atripla users). Drive-Ahead is expected to continue for a total of 144 weeks.

Other trials with doravirine-containing regimens are planned or underway.

Safety

In the Drive-Ahead trial, Delstrigo was found to be generally safe and well tolerated. The most common side effect of the drug was dizziness, affecting 7% of people.

About 2% of participants quit taking Delstrigo because of side effects such as dizziness, abnormal dreams, nausea

and rash. In contrast, about 7% of participants who took Atripla quit due to side effects.

When researchers compared the brain-related side effects (such as dizziness, difficulty sleeping and problems with concentration and thinking clearly) of both regimens, Delstrigo was found to cause significantly fewer side effects than Atripla.

Delstrigo had minimal impact on levels of lipids (cholesterol and triglycerides) in fasting blood samples.

Note that the HIV-positive people who are typically enrolled in pivotal clinical trials of HIV treatments, including Delstrigo, are generally young and relatively 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/or may have other health issues—such as cardiovascular disease, liver injury, kidney injury, type 2 diabetes, anxiety, depression—that require medications. As a result, their experience of side effects may be different from those reported in pivotal clinical trials.

Also, as with any newly licensed treatment, the full range of side effects associated with Delstrigo, especially rare and long-term ones, may not be known for at least another five years. However, data collected so far suggest that Delstrigo is generally safe.

Special populations

Pregnant women

Delstrigo has not been studied in pregnant women and its safety in this population is not known.

Young people

Delstrigo has not been studied in people under 18 years old.

People who are 65 or older

According to 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 people whose estimated glomerular filtration rate (eGFR) is less than 50 ml/minute “should not receive Delstrigo.”

People with liver injury or dysfunction

The manufacturer states: “No dose adjustment of Delstrigo is required in patients with mild or moderate hepatic impairment. Delstrigo has not been studied in patients with severe hepatic impairment.”

People with hepatitis B virus co-infection

Delstrigo is not approved for the treatment of HIV-positive people who are co-infected with hepatitis B virus.

Prior to initiating treatment with Delstrigo

Delstrigo contains tenofovir DF. Previous studies that have not included Delstrigo or doravirine have found that the use of tenofovir DF is linked to an increased risk for kidney injury in some HIV-positive people. Although the risk of kidney injury is generally low among people new to HIV treatment and has not been reported in Drive-Ahead, Merck recommends: “Prior to or when initiating treatment with Delstrigo and periodically during Delstrigo therapy, patients at risk for renal dysfunction should additionally be tested for phosphorus [levels in the blood and, levels of glucose and protein in the urine].”

Drug interactions

Merck cautions that some drugs should not be used by people taking Delstrigo, as they can significantly reduce the amount of doravirine in the blood. This reduction can weaken the anti-HIV effects of doravirine and the other drugs in Delstrigo and lead to treatment failure. Here are some of the drugs that Delstrigo users should avoid:

- anti-seizure drugs – carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- the prostate cancer drug enzalutamide (Xtandi)
- the anti-cancer drug mitotane (Lysodren)
- the antibiotics rifampin and rifapentine
- the herb St. John's wort or extracts of this herb including hypericin and hyperforin

A note on acid-reducing agents

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

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

None of these acid-reducing agents interact with Delstrigo.

Pharmacists are a great source of information about drug interactions.

Access

After Health Canada licenses a treatment, physicians can prescribe it but initially patients must pay for it themselves unless they have a private insurance plan that covers the cost. Usually it takes between three and six months after licensure for such coverage to take effect.

If left untreated, HIV infection leads to catastrophic disease that can affect one's ability to work. However, HIV treatment is expensive. Therefore, in Canada, provincial and territorial ministries of health heavily subsidize the cost of anti-HIV medications. Each ministry has a listing for the drugs for which it is prepared to pay. These listings are called formularies.

In the months ahead, Merck and provincial and territorial ministries of health will be negotiating the price of Delstrigo. This process might not be completed until late 2019. Check with a pharmacist to find out when Delstrigo is listed on your region's formulary.

A CATIE factsheet on Delstrigo is in development.

—Sean R. Hosein

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