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CATIE-News

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Doravirine (Pifeltro) approved in Canada for HIV treatment

6 November 2018

- **This new anti-HIV drug is approved for use in combination therapy**
- **Doravirine is a highly effective NNRTI ('non-nuke') taken once daily**
- **Clinical trials showed greater tolerance of doravirine than older drugs in its class**

In October 2018 Health Canada approved the use and sale of a new anti-HIV drug, doravirine, to be sold under the brand name Pifeltro. This drug is supplied in 100-mg tablets and is meant to be used as part of combination HIV treatment (ART). Doravirine is taken once daily, with or without food. Made by the pharmaceutical company Merck, doravirine should be available for ordering by pharmacies in early December 2018.

About doravirine

Doravirine was discovered in Canada by Merck scientists, and belongs to a class of drugs called NNRTIs (non-nucleoside reverse transcriptase inhibitors; non-nukes). In general, treatment guidelines recommend that several different classes of anti-HIV drugs be combined to form a regimen.

Effectiveness

Doravirine-based combination therapy has been tested in clinical trials with at least 1,500 people. In these people, doravirine-based combinations were used as initial HIV treatment. Researchers have found that doravirine-based combinations were at least as effective in participants as combination therapy with the non-nuke efavirenz (Sustiva and in Atripla) and combinations based on the protease inhibitor darunavir (Prezista and in Prezcobix and Symtuza)—whether they had high or low viral loads prior to starting treatment.

Additional clinical trials with doravirine-based combination therapy are underway in treatment-experienced HIV-positive people.

Safety

In clinical trials, doravirine was found to be generally safe. Side effects that occurred included the following:

- nausea
- headache
- diarrhea

For the most part, these side effects were generally mild and temporary. However, they were sufficiently bothersome that 2% of clinical trial participants left the studies because of them. Overall, doravirine-based combinations were better tolerated than combinations containing the older drugs efavirenz or darunavir.

Doravirine-based combination therapy reduced levels of LDL-C (so-called bad cholesterol) in the blood compared to regimens containing efavirenz or darunavir.

Note that the HIV-positive people who are typically enrolled in pivotal clinical trials of HIV treatments, including doravirine, 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—that require

medications. As a result, their experience of side effects may be different than those reported in pivotal clinical trials.

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

Special populations

Pregnant women

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

Young people

Doravirine 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 doravirine 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

Merck recommends: “No dose adjustment of doravirine is required in patients with mild, moderate or severe renal impairment.”

People with liver dysfunction

The manufacturer states: “No dose adjustment of doravirine is required in patients with mild or moderate hepatic impairment.”

Drug interactions

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

- 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

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 doravirine.

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 for such coverage to take effect.

If left untreated, HIV infection leads to catastrophic disease that can affect one's ability to work. HIV treatment is also 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 doravirine. This process might not be completed until the autumn of 2019. Check with a pharmacist to find out when doravirine is listed on your region's formulary.

A CATIE factsheet on doravirine is in development.

—Sean R. Hosein

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