

# Doravirine (*Pifeltro*)

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## Drug Summary

Doravirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that is well tolerated and dosed once daily, with or without food. Doravirine is indicated for adults with no prior antiretroviral treatment history or to replace the current antiretroviral regimen in those who have suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine. Doravirine retains activity in the presence of several common NNRTI drug-resistant mutations (e.g. K103N and G190A) and thus may have clinical utility for some individuals with HIV that is resistance to other NNRTIs, depending on the specific NNRTI mutations present. Several key reverse transcriptase mutations cause more than 100-fold reduced susceptibility of HIV to doravirine: (1) Y188L alone or in combination with K103N or V106I, (2) V106A in combination with G190A and F227L, or (3) E138K in combination with Y181C and M230L. In addition, treatment failure with doravirine can result in emergence of resistance-associated substitutions that may confer cross-resistance to efavirenz, etravirine, nevirapine, and rilpivirine.

Unlike the NNRTI rilpivirine, there are no CD4 count or HIV RNA level restriction for the use of doravirine. In addition, doravirine does not have restrictions for use in combination with proton pump inhibitors. Doravirine in combination with two NRTI's was studied in head-to-head randomized clinical trials as a comparison to efavirenz plus two NRTI's or boosted darunavir plus two NRTI's, but doravirine has not been studied head-to-head versus integrase strand transfer inhibitors. In addition, the only single-tablet coformulation with doravirine includes the NRTI backbone tenofovir DF-lamivudine, which may limit its utility as a single-tablet regimen. Overall, doravirine is a well-tolerated NNRTI that currently is indicated for use only in antiretroviral-naïve individuals, but, in the future it is likely that doravirine will be used more often for antiretroviral-experienced individuals, especially those with resistance to NNRTIs.

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## Key Clinical Trials

In the phase 3, randomized-controlled DRIVE AHEAD trial, investigators compared doravirine-tenofovir DF-lamivudine to efavirenz-tenofovir DF-emtricitabine as therapy for treatment-naïve individuals [[DRIVE AHEAD](#)]. A total of 364 adults were randomized to each arm and 48 weeks results demonstrated non-inferiority of the doravirine regimen by FDA snapshot (proportion of participants with HIV RNA below 50 copies/mL was 84.3% in the doravirine arm versus 80.8% in the efavirenz arm by intention-to-treat analysis). Results also showed that less rash, central nervous side effects, and lipid changes occurred in the doravirine arm and there were overall fewer treatment discontinuations due to adverse effects as compared to the efavirenz arm. In the phase 3 DRIVE FORWARD study, doravirine was compared to ritonavir-boosted darunavir as initial antiretroviral therapy, each with two NRTIs [[DRIVE FORWARD](#)]. In the primary analysis, there were 383 participants in each arm; at 48 weeks, doravirine was non-inferior to ritonavir-boosted darunavir (HIV RNA less than 50 copies/mL in 83.8% versus 79.9%, respectively). Overall rates of drug-related adverse events were similar between the two arms, though lipid parameters were more favorable in the doravirine group. In the open-label, active-controlled, non-inferiority DRIVE SHIFT trial, investigators enrolled 670 adults who had suppressed HIV RNA levels for at least 6 months and randomized them (2:1) to switch to once-daily single-tablet regimen of doravirine plus tenofovir DF plus lamivudine or to continue on their current antiretroviral regimen [[DRIVE SHIFT](#)]. Participants enrolled were taking two nucleoside reverse transcriptase inhibitors (NRTIs) plus either (1) a boosted protease inhibitor, (2) boosted elvitegravir, or (3) a non-nucleoside reverse transcriptase inhibitor.

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## Adverse Effects

The adverse reactions that have occurred in 5% or more of persons taking doravirine are nausea, dizziness, headache, fatigue, diarrhea, abdominal pain, and abnormal dreams.

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## Use In Pregnancy

Doravirine has not been adequately studied for use in pregnancy.

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## Resistance

For a listing of the most common clinically significant mutations associated with doravirine (DOR) resistance, see the [NNRTI Resistance Notes on the Stanford University HIV Drug Resistance Database](#).

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## Key Drug Interactions

For complete information on doravirine-related drug interactions, see the [Drug Interactions section in the](#)

[Doravirine \(Pifeltro\) Prescribing Information.](#)

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