PIFELTRO™ (doravirine) Efficacy Profile

In a clinical study with virologically suppressed adults, a doravirine-based fixed-dose combination (FDC) demonstrated a:

Robust Efficacy Profile

- **Primary efficacy outcome:** Proportion of patients with HIV-1 ≥50 copies/mL: 2% for a doravirine-based FDC (ISG at Week 48) vs 1% for baseline regimen (DSG at Week 24). Difference (95% CI): 0.7 (-1.3, 2.6)
- **Additional efficacy outcome:** Proportion of patients with HIV-1 RNA <50 copies/mL in the immediate switch group (ISG) at Week 48 vs the delayed switch group (DSG) at Week 24[a]

HIV-1 RNA <50 copies/mL at week 48

91%

Doravirine-based FDC (ISG, n=447)

HIV-1 RNA <50 copies/mL at week 24

95%

Baseline regimen (DSG, n=223)

- **No virologic data within the time window:** 8% for a doravirine-based FDC (ISG at Week 48) vs 4% for baseline regimen (DSG at Week 24)

[a] DRIVE-SHIFT Study Design: A randomized, international, multicenter, open-label study of adults with virologically suppressed HIV-1 for ≥6 months on 2 NRTIs with a PI plus either ritonavir or cobicistat, or elvitegravir plus cobicistat, or an NNRTI, with no history of virologic failure. Patients either immediately switched to a doravirine-based FDC on Day 1 of the study for 48 weeks (ISG [n=447]) or continued on their baseline regimen and switched after 24 weeks to a doravirine-based FDC (DSG [n=223]).

INDICATIONS AND USAGE

- PIFELTRO is indicated in combination with other antiretroviral (ARV) agents for the treatment of HIV-1 infection in adult patients with no prior ARV treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine.

SELECTED SAFETY INFORMATION

- PIFELTRO is contraindicated when co-administered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers (including the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent mitotane; and the herbal product St. John's wort (*Hypericum perforatum*)), as significant decreases in PIFELTRO plasma concentrations may occur, which may decrease the effectiveness of PIFELTRO.
- Immune reconstitution syndrome can occur, including the occurrence of autoimmune disorders with variable time to onset, which may necessitate further evaluation and treatment.
- Co-administration of PIFELTRO with efavirenz, etravirine, or nevirapine is not recommended.
- If co-administered with rifabutin, increase PIFELTRO dosage to one tablet twice daily (approximately 12 hours apart).
- Consult the full Prescribing Information prior to and during treatment for more information on potential drug-drug interactions.
- The most common adverse reactions with PIFELTRO (incidence ≥5%, all intensities) were nausea (7%), dizziness (7%), headache (6%), fatigue (6%), diarrhea (6%), abdominal pain (5%), and abnormal dreams (5%).
- By Week 96 in DRIVE-FORWARD, 2% of adult subjects in the PIFELTRO group and 3% in the DRV+r group had adverse events leading to discontinuation of study medication.
- By Week 96 in DRIVE-AHEAD, 3% of adult subjects in the DELSTRIGO™ (doravirine/3TC/TDF) group and 7% in the EFV/FTC/TDF group had adverse events leading to discontinuation of study medication.
- In DRIVE-FORWARD, mean changes from baseline at Week 48 in LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) were pre-specified. LDL-C: -4.6 mg/dL in the PIFELTRO group vs 9.5 mg/dL in the DRV+r group. Non-HDL-C: -5.4 mg/dL in the PIFELTRO group vs 13.7 mg/dL in the DRV+r group. The clinical benefits of these findings have not been demonstrated.
- In DRIVE-AHEAD, mean changes from baseline at Week 48 in LDL-C and non-HDL-C were pre-specified. LDL-C: -2.1 mg/dL in the DELSTRIGO group vs 8.3 mg/dL in the EFV/FTC/TDF group. Non-HDL-C: -4.1 mg/dL in the DELSTRIGO group vs 12.7 mg/dL in the EFV/FTC/TDF group. The clinical benefits of these findings have not been demonstrated.

Selected Safety Information continued on next page.

Pifeltro™
doravirine
100 mg tablets

PIFELTRO™ (doravirine) Resistance Profile

In a 48-week study of virologically suppressed adults, a doravirine-based fixed-dose combination (FDC)[b] demonstrated:

Zero cases of doravirine resistance in two subjects in the Immediate Switch Group (ISG)

Among 656 subjects, 8 met protocol defined virologic failure (PDVF) criteria[c]

ISG (n=447)	DSG (n=209)
6 subjects met PDVF criteria	2 subjects met PDVF criteria
2 subjects with resistance data	1 subject failed on baseline regimen before switching to a doravirine-based FDC[d]

ZERO

cases of resistance to doravirine in the two subjects in the ISG

[b] Doravirine-based FDC = doravirine 100 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg tablets
[c] Confirmed HIV-1 RNA ≥50 copies/mL.
[d] This subject developed the RT M184M/I substitution and phenotypic resistance to FTC and 3TC during treatment with their baseline regimen.

3TC, lamivudine; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; DRV+r, darunavir+ritonavir; EFV, efavirenz; FTC, emtricitabine; HIV-1, human immunodeficiency virus type 1; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RNA, ribonucleic acid; TDF, tenofovir disoproxil fumarate; ULN, upper limit of normal range.

SELECTED SAFETY INFORMATION *(continued)*

- In DRIVE-SHIFT, mean changes from baseline at Week 48 in LDL-C and non-HDL-C were pre-specified. LDL-C: -16.3 mg/dL in the DELSTRIGO™ (doravirine/3TC/TDF) group vs -2.6 mg/dL in the PI + ritonavir group. Non-HDL-C: -24.8 mg/dL in the DELSTRIGO group vs -2.1 mg/dL in the PI + ritonavir group. The clinical benefits of these findings have not been demonstrated.
- In DRIVE-AHEAD, neuropsychiatric adverse events were reported in the three pre-specified categories of sleep disorders and disturbances, dizziness, and altered sensorium. Twelve percent of adult subjects in the DELSTRIGO group and 26% in the EFV/FTC/TDF group reported neuropsychiatric adverse events of sleep disorders and disturbances; 9% in the DELSTRIGO group and 37% in the EFV/FTC/TDF group reported dizziness; and 4% in the DELSTRIGO group and 8% in the EFV/FTC/TDF group reported altered sensorium.
- The safety of DELSTRIGO in virologically-suppressed adults was based on Week 48 data from subjects in the DRIVE-SHIFT trial. Overall, the safety profile in virologically-suppressed adult subjects was similar to that in subjects with no ARV treatment history.
- *Serum ALT and AST Elevations:* In the DRIVE-SHIFT trial, 22% and 16% of subjects in the immediate switch group experienced ALT and AST elevations greater than 1.25 X ULN, respectively, through 48 weeks on DELSTRIGO. For these ALT and AST elevations, no apparent patterns with regard to time to onset relative to switch were observed. One percent of subjects had ALT or AST elevations greater than 5 X ULN through 48 weeks on DELSTRIGO. The ALT and AST elevations were generally asymptomatic, and not associated with bilirubin elevations. In comparison, 4% and 4% of subjects in the delayed switch group experienced ALT and AST elevations of greater than 1.25 X ULN through 24 weeks on their baseline regimen.
- There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to PIFELTRO during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.
- Mothers infected with HIV-1 should be instructed not to breastfeed if they are receiving PIFELTRO due to the potential for HIV-1 transmission.

Before prescribing PIFELTRO™ (doravirine), please read the accompanying Prescribing Information. The Patient Information also is available.

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Pifeltro™
doravirine
100 mg tablets