# New Drug Overview

Idvynso (doravirine & islatravir)

RDL Category: Antiretroviral Combinations

## Introduction

**Disease Background:**

- Human Immunodeficiency Virus (HIV) is a virus that kills or damages certain white blood cells that fight infection, called CD4 cells (CD4 T lymphocytes), in the immune system (*HIVinfo.NIH.gov 2025*).
  - In the US, there are about 1.2 million people living with HIV infection; approximately 13% of them are not even aware they are infected with the virus (*HIV.gov 2026*).
  - In addition, an estimated 31,800 new HIV infections transpired in 2022 in the US, which is a 12% decline from 2018.
- The HIV life cycle includes a 7-step process whereby the virus uses the CD4 cells to multiply and distribute throughout the body (*HIVinfo.NIH.gov 2025*).
  - Treatments for HIV targets HIV at various stages of its life cycle and prevents it from multiplying in large numbers. It does not cure the infection but reduces the amount of HIV in the blood.
- Idvynso (doravirine & islatravir) was FDA approved in 2026

**Pharmacology/Usage**

- Idvynso (doravirine & islatravir) is a fixed-dose combination tablet for oral administration containing doravirine (an HIV-1 non-nucleoside reverse transcriptase inhibitor [NNRTI]) and islatravir (an HIV-1 nucleoside analog reverse transcriptase inhibitor [NRTI]).

## Indications

**Table 1. Food and Drug Administration Approved Indications**

| Indication | Idvynso (doravirine & islatravir) |
|---|---|
| • As a complete two-drug regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies/ml) on a stable antiretroviral regimen with no history of virologic treatment failure and no known substitutions associated with resistance to doravirine. | ✔ |

*(Prescribing information: Idvynso 2026)*

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

## Dosing and administration

**Table 2. Dosing and Administration**

| Drug | Available Formulations | Route | Usual Recommended Frequency | Comments |
|---|---|---|---|---|
| Idvynso (doravirine & islatravir) | Film-Coated Tablets:<br><br>100mg doravirine & 0.25mg islatravir. | PO | One tablet PO QD with or without food. | • If co-administered with rifabutin, take one tablet of Idvynso QD as recommended, followed by one tablet |

| Drug | Available Formulations | Route | Usual Recommended Frequency | Comments |
|---|---|---|---|---|
| | | | | of doravirine (Pifeltro brand name) 100mg about 12 hours after the dose of Idvynso for the duration of rifabutin co-administration.<br>• Idvynso is not recommended in patients with eGFR <30ml/min/1.73m$^2$ and has not been studied in participants undergoing dialysis.<br>• Idvynso has not been studied in patients with severe hepatic impairment and therefore is not recommended in these patients. |

See the current prescribing information for full details.

## Clinical Efficacy Summary

- The efficacy of Idvynso is supported by data from 2 randomized, active-controlled, non-inferiority trials (Trial 051 and Trial 052) in virologically-suppressed (HIV-1 RNA less than 50 copies per ml) participants living with HIV.
  - Participants must have been stably suppressed on their baseline regimen for at least 3 months prior to trial entry and had no history of treatment failure.
    - Participants with active HBV infection (hepatitis B surface antigen [HbsAg] positive or HBV DNA positive) were excluded from the trials.
  - In open-labeled Trial 051, participants switched from an oral ART regimen to Idvynso.
    - Participants (N=551) were randomized and switched to QD Idvynso (N=366) or remained on their baseline ART (N=185)
    - At baseline, participants had a mean age of 50 years (range 18 to 83), while 60% were male, 45% were Black/African American, the mean baseline CD4+ T-cell count was 748 cells/mm$^3$, and 80% had baseline CD4+ T-cell count >500 cells/mm$^3$. At enrollment, 64% of the participants were receiving INSTI-based regimens, 5% PI-based regimens (including combinations with INSTI), and 30% other regimens. Approximately 29% of participants in both study arms had evidence of past HBV infection at enrollment.
  - In the double-blind Trial 052, participants switched from bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) to Idvynso.
    - Participants (N=513) were randomized and switched to QD Idvynso (N=342) or remained on BIC/FTC/TAF (N=171)
    - At baseline, participants had a mean age of 48 years (range 19 to 77), 79% of participants were male, 61% were White, the mean baseline CD4+ T-cell count was 717 cells/mm$^3$, and 75% of participants had baseline CD4+ T-cell

count >500 cells/mm$^3$. Approximately 26% of participants in both study arms were HBcAb positive at enrollment. These characteristics were similar between treatment groups.

- The primary endpoint of Trial 051 and Trial 052 was the proportion of participants with HIV-1 RNA ≥50 copies/mL at week 48.
  - Results are presented in the table below, which was adapted from the prescribing information.

**Table 3. Efficacy results**

| | Trial 051 | | Trial 052 | |
|---|---|---|---|---|
| | **Idvynso N=366** | **Baseline ART N=185** | **Idvynso N=342** | **BIC/FTC/TAF N=171** |
| HIV-1 RNA ≥50 copies/mL | 1% | 5% | 1% | 1% |
| Treatment difference | -3.6% | | 0.9% | |
| HIV-1 RNA <50 copies/mL | 96% | 92% | 92% | 94% |
| No virologic data at week 48 window | 3% | 3% | 7% | 5% |
| Discontinued study due to adverse event or death | 1% | 1% | 2% | 2% |
| Discontinued study for other reasons | 2% | 2% | 5% | 4% |
| On study drug but missing data in window | 1% | 1% | - | - |

- In Trial 051, treatment outcomes between treatment groups were similar across subgroups by age, sex, race, and baseline ART regimens. In Trial 052, treatment outcomes between treatment groups were similar across subgroups by age, sex, and race.
- In Trial 051, the mean increase from baseline at week 48 in CD4+ T-cell counts in the Idvynso and baseline ART groups were 5 and 18 cells/mm$^3$, respectively. In Trial 052, the mean increase from baseline at week 48 in CD4+ T-cell counts in the Idvynso and BIC/FTC/TAF groups was 30 and 28 cells/mm$^3$, respectively.

## Clinical guidelines

- There are currently no published guidelines addressing the use of Idvynso.
- **Guidelines for the use of antiretroviral agents in adult and adolescents with HIV; developed by the Health and Human Services (HHS) Panel on Antiretroviral Guidelines for Adults and Adolescents- A Working Group of the National Institutes of Health (NIH) Office of AIDS Research Advisory Council (OARAC)** (*HHS Panel on Antiretroviral Guidelines 2026*)
  - Treatment guidelines promulgated by the NIH are available and are widely accepted as the standard of care for the treatment of HIV infection in the United States. They provide direction for the treatment of patients who are treatment-naïve or treatment experienced, as well as in special populations, such as pregnancy and pediatrics.
  - Recommended initial regimens for most with HIV can be found in the guidelines. Two and three drug regimens are included, including BIC/TAF/FTC (a comparator in a phase 3 Idvynso study). Refer to the guidelines for specific information.

## Safety summary

- **Contraindications:**
  - When co-administered with:
    - Drugs that are strong CYP3A enzyme inducers, as significant decreases in doravirine plasma concentrations may occur, which may decrease the effectiveness of Idvynso.
    - Lamivudine (3TC) or emtricitabine (FTC) as significant decreases in islatravir-triphosphate (ISL-TP) concentrations may occur, which may decrease the efficacy of Idvynso.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Severe skin reactions, including Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN), have been reported during postmarketing experience with doravirine-containing regimens. In addition, Drug Rash with Eosinophilia and Systemic Symptoms (DRESS syndrome) was reported with Idvynso in a clinical trial.
    - Discontinue Idvynso and other medications known to be associated with severe skin reactions, immediately if a painful rash with mucosal involvement, a progressive severe rash, or a rash with constitutional symptoms, eosinophilia, lymphadenopathy, or other organ involvement develops. Clinical status should be closely monitored, and appropriate therapy should be started.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Idvynso) minus reported % incidence for baseline ART for Trial 051. Please note that an incidence of 0% means the incidence was the same as or less than comparator.
    - The most frequently reported adverse events included diarrhea (3%), dizziness (1%), fatigue (1%), abdominal distension (2%), headache (1%), and weight increased (2%).
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Idvynso) minus reported % incidence for BIC/FTC/TAF for Trial 052. Please note that an incidence of 0% means the incidence was the same as or less than comparator.
    - The most frequently reported adverse events included diarrhea (0%), dizziness (1%), fatigue (0%), abdominal distension (1%), headache (1%), and weight increased (<1%).

- **Drug interactions:**
  - As Idvynso is a complete regimen for the treatment of HIV-1 infection, co-administration with other antiretroviral medications for treatment of HIV-1 infection is not recommended.
  - Co-administration with strong CYP3A inducers is contraindicated. At least a 4-week cessation period is recommended prior to initiation of Idvynso.
  - If Idvynso is co-administered with rifabutin, one tablet of doravirine (Pifeltro) should be taken about 12 hours after the dose of Idvynso.
    - Co-administration with other moderate CYP3A inducers is not recommended.
  - Co-administration is contraindicated with lamivudine or emtricitabine.
  - Co-administration with the following nucleoside antimetabolites is not recommended as dCK substrates may cause a decrease in the intracellular concentration of ISL-TP: cladribine, clofarabine, cytarabine, fludarabine, gemcitabine.
  - Co-administration with pentostatin is not recommended as it may cause an increase in plasma concentrations of islatravir.

- The information above was presented in a table in the prescribing information and there is a note at the bottom of the table that says the table is not all inclusive.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are not sufficient human data on use during pregnancy to inform a drug-associated risk of birth defects and miscarriage.
    - There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to Idvynso during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.
  - The safety and efficacy of use in the pediatric population have not been established.

## Conclusion

- Human Immunodeficiency Virus (HIV) is a virus that kills or damages certain white blood cells that help fight infection, called CD4 cells (CD4 T lymphocytes), in the immune system (*HIVinfo.NIH.gov 2025*).
- Idvynso is a two-drug combination of doravirine (a NNRTI) and islatravir (a NRTI) and is indicated as a complete two-drug regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies/ml) on a stable antiretroviral regimen with no history of virologic treatment failure and no known substitutions associated with resistance to doravirine.
  - It is contraindicated when co-administered with drugs that are strong CYP3A enzyme inducers, as well as with lamivudine or emtricitabine.
- The efficacy of Idvynso is supported by data from 2 randomized, active-controlled, non-inferiority trials that included virologically-suppressed participants living with HIV.
  - The primary endpoint of both trials was the proportion of participants with HIV-1 RNA ≥50 copies/mL at week 48.
  - Idvynso was found to be effective as compared to its active-comparators for the primary endpoint.
- Treatment guidelines are available and are widely accepted as the standard of care for the treatment of HIV infection in the United States. Refer to the guidelines found online.

- There is no evidence to suggest that Idvynso is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Idvynso be placed on the RDL as non-recommended.

- **RDL Placement:**
  - ☐ Recommended
  - ☒ Non-Recommended

## References


- Idvynso. Package insert. Merch Sharp & Dohme LLC; April 2026.
- HIVinfo.NIH.Gov. HIV Overview. Updated April/May 2025. Accessed June 4, 2026. Website: https://hivinfo.nih.gov/understanding-hiv/fact-sheets.
- HIV.gov. US Statistics, Data & Trends: Fast Facts. Updated February 25, 2026. Accessed June 4, 2026. Website: https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Updated May 27, 2026. Accessed June 4, 2026. Website: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new.


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