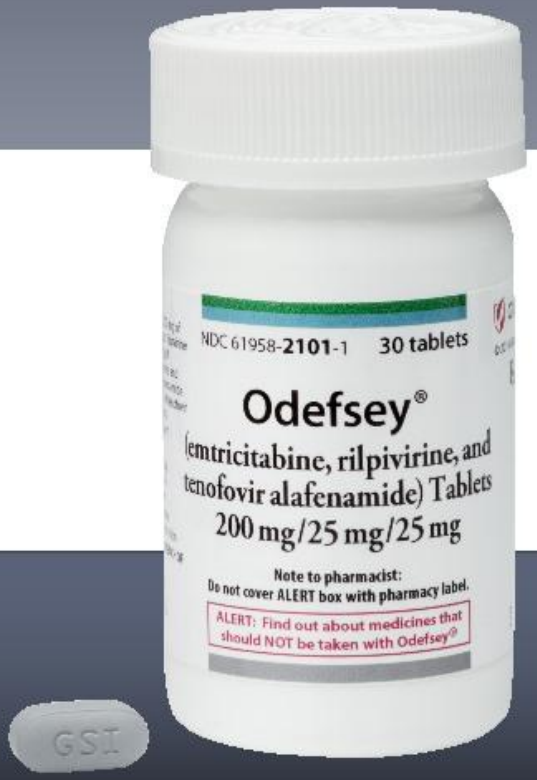
Odefsey

(emtricitabine, rilpivirine, tenofovir alafenamide)



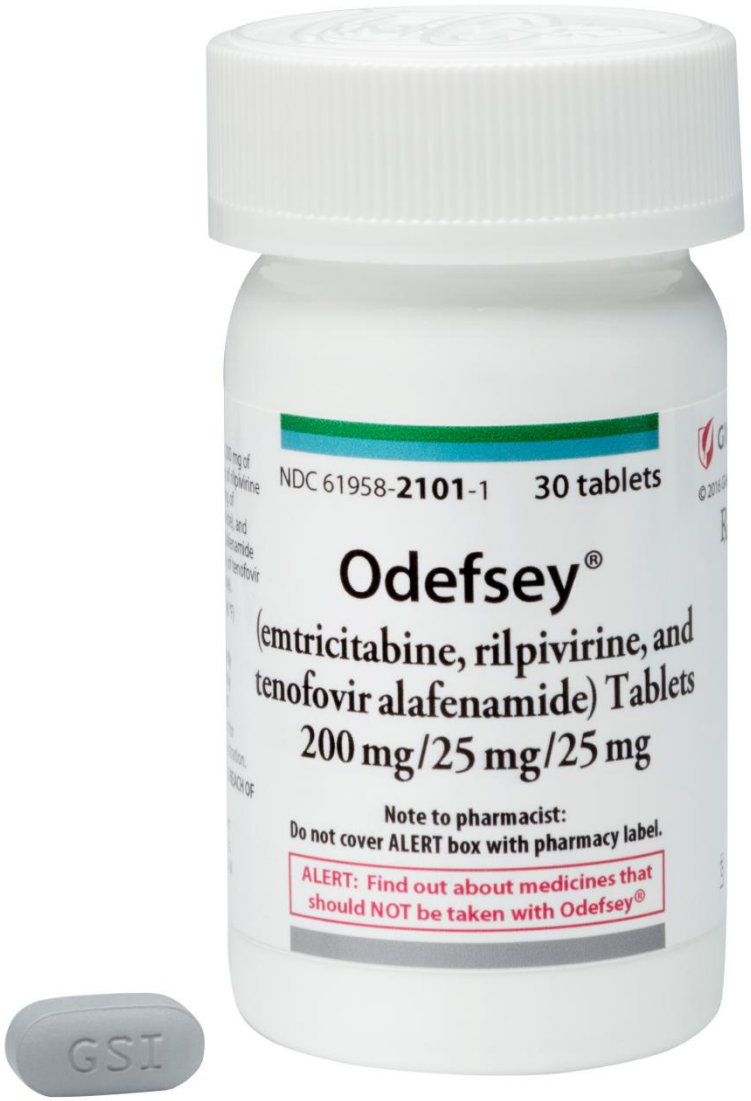
New Product Slideshow

MPR

Introduction

- **Brand name:** Odefsey
- **Generic name:** Emtricitabine, rilpivirine, tenofovir alafenamide (TAF)
- **Pharmacological class:** Nucleoside analog reverse transcriptase inhibitors + non-nucleoside reverse transcriptase inhibitor
- **Strength and Formulation:** 200mg/25mg/25mg; tablets
- **Manufacturer:** Gilead Sciences
- **How supplied:** Bottle—30
- **Legal Classification:** Rx

Odefsey


NDC 61958-2101-1 30 tablets
Odefsey®
(emtricitabine, rilpivirine, and tenofovir alafenamide) Tablets
200 mg/25 mg/25 mg
Note to pharmacist:
Do not cover ALERT box with pharmacy label.
ALERT: Find out about medicines that should NOT be taken with Odefsey®
GSI

Indications

- As a complete regimen for **HIV-1 infection** in patients who are antiretroviral treatment-naïve with HIV-1 RNA ≤100,000 copies/mL or to replace a stable antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA <50 copies/mL) for ≥6 months with no history of treatment failure and no known substitutions associated with resistance to any components of Odefsey

Dosage & Administration

- ≥12yrs (≥35kg): 1 tablet once daily with food

Considerations for Special Populations

- **Pregnancy:** No adequate data available
- **Nursing mothers:** Not recommended
- **Pediatric:** <12yrs (<35kg): not established
- **Geriatric:** No differences observed
- **Renal impairment:** (CrCl<30mL/min): not recommended
- **Hepatic impairment:** Not studied in patients with severe impairment

Contraindications

- Concomitant carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole, dexamethasone (more than a single dose), St. John’s wort

Warnings/Precautions

- **Suspend** therapy if lactic acidosis or hepatotoxicity (eg, hepatomegaly, steatosis) occurs
- Not for treating chronic hepatitis B virus; **test for HBV** before starting therapy and closely monitor patients co-infected with HBV and HIV for several months after stopping treatment (discontinuing therapy may exacerbate HBV infection).
- **Underlying hepatitis B or C**, or marked elevations in liver-associated tests; monitor for hepatotoxicity.

Warnings/Precautions

- Consider monitoring **LFTs** in those without pre-existing hepatic dysfunction or other risks
- Monitor CrCl, urine glucose, urine protein, serum phosphorus (in patients at risk for chronic renal disease); discontinue if significant **renal dysfunction** or Fanconi syndrome occurs)
- Prolongation of **QTc interval** with higher doses
- Promptly evaluate if severe **depressive symptoms** occur

Warnings/Precautions

- History of pathologic **fracture** or risk factors of osteoporosis or bone loss: consider monitoring bone mineral density (BMD); calcium/vitamin D supplement may be beneficial
- Discontinue immediately if severe skin or **hypersensitivity** reactions develop

Interactions

- See **Contraindications**
- Avoid with concurrent or recent use of **nephrotoxic agents**
- Concomitant **antimycobacterials** (eg, rifabutin): not recommended
- May be potentiated by **CYP3A** or **P-gp** inhibitors, antagonized by CYP3A or P-gp inducers.
- Concomitant drugs that strongly affect P-gp activity (eg, cyclosporine) may lead to changes in TAF absorption

Interactions

- Concomitant with drugs known to prolong the **QTc interval** may increase risk of Torsade de Pointes; consider alternatives
- May be potentiated by drugs that decrease **renal function** or compete for active tubular secretion (eg, acyclovir, cidofovir, ganciclovir, valacyclovir, valganciclovir, aminoglycosides, NSAIDs)
- Separate **antacids** by (≥2hrs before or 4hrs after) or **H2-receptor antagonists** by (≥12hrs before or ≥4hrs after) Odefsey

Interactions

- Concomitant **azole antifungals** (eg, fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole); monitor for breakthrough fungal infections
- Concomitant **macrolide** or **ketolide** antibiotics (eg, clarithromycin, erythromycin, telithromycin); consider alternative (eg, azithromycin)
- Concomitant **methadone**; monitor

Adverse Reactions

- Nausea, depressive disorders, insomnia, headache, diarrhea, fatigue; decreased BMD, new onset or worsening renal impairment, fat redistribution, immune reconstitution syndrome.

Mechanism of Action

- **Emtricitabine** inhibits the activity of the HIV-1 reverse transcriptase (RT) by competing with the natural substrate deoxycytidine 5'-triphosphate and by being incorporated into nascent viral DNA, which results in chain termination
- **Rilpivirine** inhibits HIV-1 replication by non-competitive inhibition of HIV-1 RT
- **Tenofovir alafenamide**, a phosphonoamidate prodrug of tenofovir, is intracellularly converted through hydrolysis. Tenofovir diphosphate inhibits HIV-1 replication by incorporation into viral DNA, which results in chain termination

Pharmacokinetics

- **Distribution:** % bound to human plasma proteins
  - Rilpivirine: ~99%
  - Emtricitabine: <4%
  - TAF: ~80%

Pharmacokinetics

- **Metabolism:**
  - Rilpivirine: CYP3A
  - Emtricitabine: not significantly metabolized
  - TAF: cathepsin A (PBMCs); CES1 (hepatocytes) CYP3A (minimal)

Pharmacokinetics

- **Elimination:**
  - Rilpivirine: metabolism; 6% excreted in urine; 85% excreted in feces
  - Emtricitabine: glomerular filtration and active tubular secretion; 70% excreted in urine; 13.7% excreted in feces
  - TAF: metabolism (>80% of oral dose); <1% excreted in urine; 31.7% excreted in feces

Clinical Trials

- Approval is supported by a bioequivalence study demonstrating Odefsey achieved similar drug levels of emtricitabine and TAF in the blood as Genvoya (elvitegravir 150mg/cobicistat 150mg/emtricitabine 200mg/tenofovir alafenamide 10mg) or E/C/F/TAF and similar drug levels of rilpivirine as Edurant (rilpivirine 25mg)

Clinical Trials

- The safety, efficacy and tolerability of Odefsey is supported by clinical studies of rilpivirine-based therapy (administered as R+F/TDF or R/F/TDF) and F/TAF-based therapy (administered as E/C/F/TAF) in a range of patients with HIV including:
  - treatment-naïve adults and adolescents, virologically suppressed adults who switched from PI-, NNRTI- and INSTI-based regimens and virologically suppressed adults with mild-to-moderate renal impairment

New Product Monograph

- For more information view the complete product monograph available at:

http://www.empr.com/odefsey/drugproduct/409/