**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all the information needed to use COMPLERA safely and effectively. See full prescribing information for COMPLERA.**

**COMPLERA® (emtricitabine, rilpivirine, tenofovir disoproxil fumarate) tablets, for oral use**
**Initial U.S. Approval: 2011**

**WARNING: POSTTREATMENT ACUTE EXACERBATION OF HEPATITIS B**
***See full prescribing information for complete boxed warning.***

**Severe acute exacerbations of hepatitis B virus (HBV) have been reported in patients coinfected with HIV-1 and HBV who have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), two of the components of COMPLERA. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue COMPLERA. If appropriate, initiation of anti-hepatitis B therapy may be warranted. (5.1)**

----------**RECENT MAJOR CHANGES**----------
Warnings and Precautions
Immune Reconstitution Syndrome (5.9) 11/2019

----------**INDICATIONS AND USAGE**----------
COMPLERA, a combination of two nucleoside analog HIV-1 reverse transcriptase inhibitors (emtricitabine and tenofovir disoproxil fumarate) and one non-nucleoside reverse transcriptase inhibitor (rilpivirine), is indicated for use as a complete regimen for the treatment of HIV-1 infection in patients weighing at least 35 kg (1) as initial therapy in those with no antiretroviral treatment history and with HIV-1 RNA less than or equal to 100,000 copies/mL at the start of therapy, or (2) or to replace a stable antiretroviral regiment in those who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen for at least 6 months with no treatment failure and no known substitutions associated with resistance to the individual components of COMPLERA. (1, 14)

Limitations of Use:

- More rilpivirine-treated subjects with HIV-1 RNA greater than 100,000 copies/mL at the start of therapy experienced virologic failure (HIV-1 RNA ≥50 copies/mL) compared to rilpivirine-treated subjects with HIV-1 RNA less than or equal to 100,000 copies/mL. (1, 14)

----------**DOSAGE AND ADMINISTRATION**----------

- Testing: Prior to or when initiating COMPLERA, test for hepatitis B virus infection. Prior to initiation and during treatment with COMPLERA, on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus. (2.1)
- Recommended dosage in adults and pediatric patients weighing at least 35 kg: One tablet taken orally once daily with food. (2.2)
- For pregnant patients who are already on COMPLERA prior to pregnancy and who are virologically suppressed (HIV-1 RNA less than 50 copies per mL), one tablet taken once daily may be continued. Lower exposures of rilpivirine were observed during pregnancy; therefore, viral load should be monitored closely. (2.3)
- Renal impairment: Not recommended in patients with estimated creatinine clearance below 50 mL per minute. (2.4)
- Recommended dosage with rifabutin coadministration: an additional 25 mg tablet of rilpivirine (Edurant) once per day taken concomitantly with COMPLERA and with a meal for the duration of the rifabutin coadministration. (2.5, 7.6, 12.3)

----------**DOSAGE FORMS AND STRENGTHS**----------
Tablets: 200 mg of emtricitabine, 25 mg of rilpivirine, and 300 mg of tenofovir disoproxil fumarate. (3)

----------**CONTRAINDICATIONS**----------
COMPLERA is contraindicated when coadministered with drugs which may result in loss of virologic response and possible resistance to COMPLERA. (4)

----------**WARNINGS AND PRECAUTIONS**----------

- Skin and Hypersensitivity Reactions: Severe skin and hypersensitivity reactions have been reported during postmarketing experience, including cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Immediately discontinue treatment if hypersensitivity or rash with systemic symptoms or elevations in hepatic serum biochemistries develops and closely monitor clinical status, including hepatic serum biochemistries. (5.2)
- Hepatotoxicity: Hepatic adverse events have been reported in patients receiving a rilpivirine-containing regimen. Monitor liver-associated tests before and during treatment with COMPLERA in patients with underlying hepatic disease or marked elevations in liver-associated tests. Also consider monitoring liver-associated tests in patients without risk factors. (5.3)
- Depressive disorders: Severe depressive disorders have been reported. Immediate medical evaluation is recommended for severe depressive disorders. (5.4)
- New onset or worsening renal impairment: Can include acute renal failure and Fanconi syndrome. Avoid administering COMPLERA with concurrent or recent use of nephrotoxic drugs. (5.5)
- Decreases in bone mineral density (BMD): Consider monitoring BMD in patients with a history of pathologic fracture or other risk factors of osteoporosis or bone loss. (5.6)
- Concomitant use of COMPLERA with drugs with a known risk to prolong the QTc interval of the electrocardiogram may increase the risk of Torsade de Pointes. (5.7)
- Lactic acidosis/severe hepatomegaly with steatosis: Discontinue treatment in patients who develop symptoms or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity. (5.8)
- Immune reconstitution syndrome: May necessitate further evaluation and treatment. (5.9)

----------**ADVERSE REACTIONS**----------

- Most common adverse reactions to rilpivirine (incidence greater than or equal to 2%, Grades 2–4) are depressive disorders, insomnia, and headache. (6.1)
- Most common adverse reactions to emtricitabine and tenofovir disoproxil fumarate (incidence greater than or equal to 10%) are diarrhea, nausea, fatigue, headache, dizziness, depression, insomnia, abnormal dreams, and rash. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD-5 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**

----------**DRUG INTERACTIONS**----------

- COMPLERA is a complete regimen for the treatment of HIV-1 infection; therefore, coadministration with other antiretroviral medications for treatment of HIV-1 infection is not recommended. (7.1)
- Consult the Full Prescribing Information prior to and during treatment for important drug interactions. (4, 5.7, 7)

----------**USE IN SPECIFIC POPULATIONS**----------

- Pregnancy: Monitor viral load closely during pregnancy as rilpivirine exposures were generally lower during pregnancy. (2.3, 8.1, 12.3)
- Lactation: Breastfeeding not recommended due to the potential for HIV-1 transmission. (8.2)
- Pediatrics: Not recommended for patients weighing less than 35 kg. (8.4)

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.**

**Revised: 11/2019**

**Patient Information**
**COMPLERA® (kom-PLEH-rah)**
**(emtricitabine, rilpivirine, tenofovir disoproxil fumarate)**
**tablets**

**Important: Ask your healthcare provider or pharmacist about medicines that should not be taken with COMPLERA**. For more information, see the section "What should I tell my healthcare provider before taking COMPLERA?"

**What is the most important information I should know about COMPLERA?**

**COMPLERA can cause serious side effects, including:**

**Worsening of Hepatitis B virus (HBV) infection.** Your healthcare provider will test you for HBV before starting treatment with COMPLERA. If you have HBV infection and take COMPLERA, your HBV may get worse (flare-up) if you stop taking COMPLERA. A "flare-up" is when your HBV infection suddenly returns in a worse way than before.

- Do not stop taking COMPLERA without first talking to your healthcare provider.
- Do not run out of COMPLERA. Refill your prescription or talk to your healthcare provider before your COMPLERA is all gone.
- If you stop taking COMPLERA, your healthcare provider will need to check your health often and do blood tests regularly for several months to check your HBV infection. Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking COMPLERA.

For more information about side effects, see the section "**What are the possible side effects of COMPLERA?**".

**What is COMPLERA?**

COMPLERA is a prescription medicine that is used to treat Human Immunodeficiency Virus-1 (HIV-1) in people weighing at least 77 lb (35 kg) who:

- have **never** taken HIV-1 medicines before, **and** who have an amount of HIV-1 in their blood (this is called 'viral load') that is no more than 100,000 copies/mL before they start taking COMPLERA,

  **or**

- in certain people who have a viral load that is less than 50 copies/mL when they start taking COMPLERA, to replace their current HIV-1 medicines.

HIV-1 is the virus that causes AIDS (Acquired Immune Deficiency Syndrome). COMPLERA does not cure HIV-1 or AIDS.

COMPLERA contains 3 medicines (emtricitabine, rilpivirine, tenofovir disoproxil fumarate) combined in one tablet. Emtricitabine (EMTRIVA®) and tenofovir disoproxil fumarate (VIREAD®) are HIV-1 nucleoside analog reverse transcriptase inhibitors (NRTIs). Rilpivirine (Edurant®) is an HIV-1 non-nucleoside analog reverse transcriptase inhibitor (NNRTI).

It is not known if COMPLERA is safe and effective in children less than 12 years of age or who weigh less than 77 lb (35 kg).

**Who should not take COMPLERA?**

**Do not take COMPLERA if you also take:**

- anti-seizure medicines:
  - carbamazepine
  - oxcarbazepine
  - phenobarbital
  - phenytoin
- anti-tuberculosis (anti-TB) medicines:
  - rifampin
  - rifapentine
- proton pump inhibitor (PPI) medicine for certain stomach or intestinal problems:
  - dexlansoprazole
  - esomeprazole
  - lansoprazole
  - omeprazole
  - pantoprazole sodium
  - rabeprazole
- more than 1 dose of the steroid medicine dexamethasone or dexamethasone sodium phosphate
- St. John's wort (*Hypericum perforatum*)

**What should I tell my healthcare provider before taking COMPLERA?**

**Before taking COMPLERA, tell your healthcare provider about all your medical conditions, including if you:**

- have liver problems, including hepatitis B or C virus infection
- have kidney problems
- have a history of depression or suicidal thoughts
- have bone problems
- are pregnant or plan to become pregnant. It is not known if COMPLERA can harm your unborn child. Tell your healthcare provider if you become pregnant during treatment with COMPLERA.

  **Pregnancy Registry.** There is a pregnancy registry for those who take COMPLERA during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk with your healthcare provider about how you can take part in this registry.
- are breastfeeding or plan to breastfeed. Do not breastfeed if you are taking COMPLERA.
  - You should not breastfeed if you have HIV-1 because of the risk of passing HIV-1 to your baby.
  - At least two of the medicines contained in COMPLERA can be passed to your baby in your breast milk.
  - Talk with your healthcare provider about the best way to feed your baby during treatment with COMPLERA.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Some medicines interact with COMPLERA. Keep a list of your medicines to show your healthcare provider and pharmacist when you get a new medicine.

- You can ask your healthcare provider or pharmacist for a list of medicines that can interact with COMPLERA.
- Do not start taking a new medicine without telling your healthcare provider. Your healthcare provider can tell you if it is safe to take COMPLERA with other medicines.

**How should I take COMPLERA?**

- Take COMPLERA exactly as your healthcare provider tells you to take it.
- **Take COMPLERA with food.** Taking COMPLERA with food is important to help get the right amount of medicine in your body. A protein drink does not replace food. If your healthcare provider decides to stop COMPLERA and you are switched to new medicines to treat HIV-1 that include rilpivirine tablets, the rilpivirine tablets should be taken only with a meal.
- Do not change your dose or stop taking COMPLERA without first talking with your healthcare provider. Stay under the care of your healthcare provider during treatment with COMPLERA.
- If you miss a dose of COMPLERA within 12 hours of the time you usually take it, take your dose of COMPLERA **with food** as soon as possible. Then, take your next dose of COMPLERA at the regularly scheduled time. If you miss a dose of COMPLERA by more than 12 hours of the time you usually take it, wait and then take the next dose of COMPLERA at the regularly scheduled time.
- Do not take more than your prescribed dose to make up for a missed dose.
- If you take too much COMPLERA, contact your local poison control center or go to the nearest hospital emergency room right away.
- When your COMPLERA supply starts to run low, get more from your healthcare provider or pharmacy. It is very important not to run out of COMPLERA. The amount of virus in your blood may increase if the medicine is stopped for even a short time.

**What are the possible side effects of COMPLERA?**

**COMPLERA can cause serious side effects, including**:

- **See "What is the most important information I should know about COMPLERA?"**

  **Severe skin rash and allergic reactions.** Skin rash is a common side effect of COMPLERA. Rash can be serious. Call your healthcare provider right away if you get a rash. In some cases, rash and allergic reaction may need to be treated in a hospital. **If you get a rash with any of the following symptoms, stop taking COMPLERA and call your healthcare provider or get medical help right away:**
  - fever
  - skin blisters
  - mouth sores
  - redness or swelling of the eyes (conjunctivitis)
  - swelling of the face, lips, mouth, tongue or throat
  - trouble breathing or swallowing
  - pain on the right side of the stomach (abdominal) area
  - dark or "tea colored" urine

- **Severe liver problems.** In rare cases, severe liver problems can happen that can lead to death. Tell your healthcare provider right away if you get these symptoms: skin or the white part of your eyes turns yellow, dark “tea-colored” urine, light-colored stools, loss of appetite for several days or longer, nausea, or stomach-area pain.
- **Change in liver enzymes**. People with a history of hepatitis B or C virus infection or who have certain liver enzyme changes may have an increased risk of developing new or worsening liver problems during treatment with COMPLERA. Liver problems can also happen during treatment with COMPLERA in people without a history of liver disease. Your healthcare provider may need to do tests to check your liver enzymes before and during treatment with COMPLERA.
- **Depression or mood changes. Tell your healthcare provider right away if you have any of the following symptoms:**
  - feel sad or hopeless
  - feel anxious or restless
  - have thoughts of hurting yourself (suicide) or have tried to hurt yourself
- **New or worse kidney problems, including kidney failure,** can happen in some people who take COMPLERA. Your healthcare provider should do blood tests to check your kidneys before starting treatment with COMPLERA. If you have had kidney problems in the past or need to take another medicine that can cause kidney problems, your healthcare provider may need to do blood tests to check your kidneys during your treatment with COMPLERA.
- **Bone problems** can happen in some people who take COMPLERA. Bone problems include bone pain, softening, or thinning (which may lead to fractures). Your healthcare provider may need to do additional tests to check your bones.
- **Too much lactic acid in your blood (lactic acidosis).** Too much lactic acid is a serious but rare medical emergency that can lead to death. Tell your healthcare provider right away if you get these symptoms: weakness or being more tired than usual, unusual muscle pain, being short of breath or fast breathing, stomach pain with nausea and vomiting, cold or blue hands and feet, feel dizzy or lightheaded, or a fast or abnormal heartbeat.
- **Changes in your immune system (Immune Reconstitution Syndrome)** can happen when you start taking HIV-1 medicines. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your healthcare provider right away if you start having new symptoms after starting your HIV-1 medicine.

The most common side effects of rilpivirine, one of the medicines in COMPLERA, include:

- depression
- trouble sleeping
- headache

The most common side effects of emtricitabine and tenofovir disoproxil fumarate, two of the medicines in COMPLERA, include:

- diarrhea
- nausea
- tiredness
- headache
- dizziness
- depression
- trouble sleeping
- abnormal dreams
- rash

These are not all the possible side effects of COMPLERA.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**How should I store COMPLERA?**

- Store COMPLERA at room temperature between 68 °F to 77 °F (20 °C to 25 °C).
- Keep COMPLERA in its original container and keep the container tightly closed.
- Do not use COMPLERA if the seal over the bottle opening is broken or missing.

**Keep COMPLERA and all other medicines out of reach of children.**

**General information about safe and effective use of COMPLERA**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use COMPLERA for a condition for which it was not prescribed. Do not give COMPLERA to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about COMPLERA that is written for health professionals.

For more information, call 1-800-445-3235 or go to www.COMPLERA.com.

**What are the ingredients of COMPLERA?**

**Active ingredients:** emtricitabine, rilpivirine hydrochloride, and tenofovir disoproxil fumarate.

**Inactive ingredients:** croscarmellose sodium, lactose monohydrate, magnesium stearate, microcrystalline cellulose, polysorbate 20 povidone, pregelatinized starch. The tablet film coating contains FD&C Blue #2 aluminum lake, FD&C Yellow #6 aluminum lake, hypromellose, iron oxide red, lactose monohydrate, polyethylene glycol, titanium dioxide, triacetin.

Manufactured and distributed by: Gilead Sciences, Inc. Foster City, CA 94404



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