PREFERRED SPECIALTY MANAGEMENT POLICY

POLICY: Human Immunodeficiency Virus – Complera Preferred Specialty Management Policy (Basic Formulary)

- Complera® (emtricitabine/rilpivirine/tenofovir disoproxil fumarate tablets – Gilead)
- Odefsey® (emtricitabine/rilpivirine/tenofovir alafenamide tablets – Gilead)

REVIEW DATE: 05/18/2022

OVERVIEW

Complera is a combination of two nucleoside analog human immunodeficiency virus type-1 (HIV-1) reverse transcriptase inhibitors (NRTIs) [emtricitabine and tenofovir disoproxil fumarate {TDF}] and one non-nucleoside reverse transcriptase inhibitor [NNRTI] (rilpivirine).[1] Complera is indicated for use as a complete regimen for the treatment of **HIV-1 infection** in patients weighing ≥ 35 kg who are:

- Antiretroviral treatment-naïve and with HIV-1 RNA ≤ 100,000 copies/mL at the start of therapy.
- Antiretroviral treatment-experienced to replace a stable antiretroviral regimen virologically suppressed (HIV-1 RNA < 50 copies/mL) patients on a stable antiretroviral regimen for ≥ 6 months with no treatment failure and no known substitutions associated with resistance to the individual components of Complera.

Complera has a limitation of use that more rilpivirine-treated patients with HIV-1 RNA > 100,000 copies/mL at the start of therapy experienced virologic failure (HIV-1 RNA ≥ 50 copies/mL) compared to rilpivirine-treated patients with HIV-1 RNA ≤ 100,000 copies/mL.

Odefsey has the same indication as Complera and contains the same NNRTI, rilpivirine, and one of the same NRTIs, emtricitabine; however the other NRTI differs.[2] Odefsey contains tenofovir alafenamide (TAF) as the third NRTI while Complera contains TDF. TAF and TDF are the two approved forms of tenofovir.[3] TDF has been associated with bone and kidney toxicities, especially when used with a pharmacologic booster (e.g., ritonavir).[3]

GUIDELINES

The **Department of Health and Human Services (DHHS) [January 20, 2022]** Guidelines for Adults and Adolescents with HIV address treatment-initiation in antiretroviral-naïve individuals.[3] Antiretroviral therapy is recommended for all persons with HIV regardless of CD4 cell count.

Complera and Odefsey are <u>not</u> among the recommended initial regimens for individuals with HIV-1 who are treatment-naïve; the guidelines do not distinguish between the two products. All of the recommended initial regimens contain an integrase strand-transfer inhibitor (INSTI). Recommended initial regimens are Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide tablets), Triumeq® (dolutegravir/abacavir/lamivudine tablets) [HLA-B*5701 negative only without chronic hepatitis B virus], Tivicay® (dolutegravir tablets) + emtricitabine or lamivudine + TAF or TDF, or Dovato® (dolutegravir/lamivudine tablets) [HIV RNA ≤ 500,000 copies/mL only without chronic hepatitis B virus and with genotypic resistance testing results].

The International Antiviral Society-USA (IAS-USA) Panel (October 2020) similarly recommends only INSTI-based regimens as initial therapy in antiretroviral therapy-naïve patients.[4] Recommended initial regimens are Biktarvy, Triumeq, or Tivicay + Descovy® (emtricitabine/tenofovir alafenamide tablets),

Tivicay + Truvada® (emtricitabine/tenofovir disoproxil fumarate), Tivicay + Cimduo® (lamivudine/tenofovir disoproxil fumarate), or Dovato. Odefsey is recognized as a potential option for patients who are intolerant to an INSTI in individuals with HIV-1 RNA < 100,000 copies/mL and CD4 cell count of 200 mcL. Complera is not addressed.

According to the **Perinatal Guidelines from the HHS Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (March 17, 2022)** all pregnant women with HIV should initiate antiretroviral therapy as early in pregnancy as possible, regardless of their HIV RNA level or CD4 T lymphocyte count.[6] In general, the recommendations for the use of ARVs in pregnant women are the same as those for women who are not pregnant. However, they may differ in some instances where regimen selection is modified based on concerns about specific drugs or limited experience with newer drugs during pregnancy. Odefsey and Complera are cited as alternative regimens (not preferred) in pregnant women. Preferred antiretroviral regimens in pregnant women are: Norvir® (ritonavir tablet/oral solution/oral powder)-boosted Reyataz® (atazanavir capsule/oral powder) + two NRTIs, Norvir-boosted Prezista® (darunavir tablet/oral suspension) + two NRTIs, Triumeq, Tivicay + two NRTIs, or Isentress + two NRTIs.

According to the **DHHS Guidelines for the Use of ARV Agents in Pediatric HIV Infection (April 11, 2022)** the selection of an initial regimen should be individualized.[14] For treatment-naive children, the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV recommends initiating therapy with three drugs: a two-drug NTRI backbone plus an INSTI, a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a boosted protease inhibitor (PI). Similar to the adult and adolescent guidelines, pediatric guidelines classify treatments as recommended or alternative. When combined with two NRTIs, the following are preferred regimens in children: Viramune® (nevirapine tablets/oral suspension) [age < 14 days], Isentress (age < 4 weeks and weight ≥ 2 kg) [Isentress HD is only indicated for patients ≥ 40 kg], Kaletra® (lopinavir/ritonavir tablets/oral solution/capsules) [age ≥ 14 days to < 4 weeks], Tivicay (≥ 4 weeks and ≥ 3 kg], or Biktarvy (age ≥ 6 weeks and ≥ 14 kg). Rilpivirine-containing regimens (e.g., Complera and Odefsey) are considered alternative options for children and adolescents ≥12 years of age and weighing ≥35 kg with HIV-1 RNA ≤100,000 copies/mL.

POLICY STATEMENT

This Preferred Specialty Management program has been developed to encourage the use of the Preferred Product. The program also directs the patient to try one Preferred Product prior to the approval of a Non-Preferred Product. Requests for the Non-Preferred Product will also be reviewed using the exception criteria (below). All approvals are provided for 1 year.

Automation: Patients with a of one Preferred Product within the 130-day look-back period are excluded from PSM.

Preferred Products: Odefsey
Non-Preferred Products: Complera

RECOMMENDED EXCEPTION CRITERIA

Non-Preferred Product	Exception Criteria
Complera	**1.** Approve for 1 year if the patient meets ONE of the following (A, B, or C): **A)** Patient is currently receiving Complera; OR **B)** Patient is currently taking single-entity or combination products containing rilpivirine, emtricitabine, and tenofovir disoproxil fumarate and is requesting Complera for a single-tablet regimen; OR **C)** Patient has tried the Preferred Product.

REFERENCES

1. Complera® tablets [prescribing information]. Foster City, CA: Gilead Sciences; November 2019.
2. Odefsey® tablets [prescribing information]. Foster City, CA: Gilead Sciences; September 2021.
3. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents. Department of Health and Human Services. Updated January 20, 2022. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/guidelines-adult-adolescent-arv.pdf. Accessed on May 3, 2022.
4. Saag MS, Gandhi RT, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV in adults. 2020 recommendations of the International Antiviral Society USA Panel. *JAMA*. 2020;324(16):1651-1669.
5. Panel on antiretroviral therapy and medical management of children living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Last updated April 11, 2022. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/pediatric-arv/guidelines-pediatric-arv.pdf. Accessed May 3, 2022.
6. Health and Human Services Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission – a working group of the Office of AIDS Research Advisory Council (ORAC). Perinatal Guidelines: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Transmission in the United States. Last updated March 17, 2022. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Perinatal_GL.pdf. Accessed on May 4, 2022.