PREFERRED SPECIALTY MANAGEMENT POLICY

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

- Biktarvy® (bictegravir/emtricitabine/tenofovir alafenamide tablets – Gilead)
- Genvoya® (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide tablets – Gilead)
- Stribild® (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate tablets – Gilead)

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OVERVIEW

Stribild is a four-drug combination of elvitegravir, a human immunodeficiency virus (HIV) integrase strand transfer inhibitor (INSTI), cobicistat, a cytochrome P450 (CYP)3A inhibitor, and emtricitabine and tenofovir disoproxil fumarate (TDF), both HIV nucleoside reverse transcriptase inhibitors (NRTIs).[1] It is indicated as a complete regimen for the treatment of **HIV-1 infection** in adults and pediatric patients ≥ 12 years of age weighing ≥ 35 kg who are:

- Antiretroviral treatment-naïve; OR
- Antiretroviral treatment-experienced and virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Stribild to replace the current antiretroviral regimen.[1]

Biktarvy and Genvoya are among the other available single-tablet/fixed-dose, complete INSTI-based regimens.[2,3] Table 1 provides the indications for Biktarvy, Genvoya, and Stribild, the products within this *Preferred Specialty Management Policy*.

Genvoya and Stribild contain the same INSTI backbone, elvitegravir, but different NRTI backbones. Stribild contains TDF while Genvoya contains tenofovir alafenamide (TAF).[1,3] Biktarvy contains a different INSTI backbone than Genvoya and Stribild, but similar to Genvoya contains TAF. TAF and TDF are the two approved forms of tenofovir.[4] TDF has been associated with bone and kidney toxicities, especially when used with a pharmacologic booster. TAF is less likely to cause kidney and bone toxicities than TDF. TDF is associated with lower lipid levels than TAF. Biktarvy and Genvoya are not recommended in patients with severe renal impairment (estimated creatinine clearance [CrCl] 15 to < 30 mL/min) or end-stage renal disease (estimated CrCl < 15 mL/min) who are not receiving chronic hemodialysis.[2,3] In addition, Biktarvy is not recommended in patients with end-stage renal disease who are receiving chronic hemodialysis who have no antiviral treatment history.[2] Stribild should not be started in patients with an estimated CrCl < 70 mL/min and should be discontinued if the estimated CrCl declines to < 50 mL/min during treatment with Stribild.[4]

Two randomized double-blind Phase III clinical trials compared the safety and efficacy of Genvoya and Stribild in antiretroviral-naïve adults with estimated glomerular filtration rate ≥ 50 mL/min (n = 1,73).[6] Genvoya was virologically non-inferior to Stribild at Week 48 (92% vs. 90% of patients, respectively, achieved plasma HIV RNA < 50 copies/mL). Genvoya was superior to Stribild at Week 144 (84.2% vs. 80% of patients, respectively, achieved plasma HIV RNA < 50 copies/mL), largely driven by a higher rate of treatment discontinuation in the Stribild arm. Patients in the Genvoya group had significantly smaller reductions in bone mineral density at the spine and hip than those in the Stribild arm through 144 weeks.[4] They also had smaller changes in estimated glomerular filtration rate and renal biomarkers and fewer

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clinically significant renal events through Week 96. Conversely, levels of fasting low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides increased more in the Genvoya group than in the Stribild group at 96 weeks, with no change in total cholesterol to high-density lipoprotein ratio.

Table 1. Biktarvy, Genvoya, and Stribild Indications.[1-3]

Name	Indication
INSTI-Based Single-Tablet Regimens	
Biktarvy® (bictegravir 50 mg/emtricitabine 200 mg/TAF 25 mg tablets)	A complete regimen for the treatment of HIV-1 infection in adults and pediatric patients ≥ 14 kg: (1) Who have no ARV treatment history. (2) To replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy.
Genvoya® (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/TAF 10 mg tablets)	A complete regimen for the treatment of HIV-1 infection in adults and pediatric patients ≥ 25 kg: (1) Who have no ARV treatment history. (2) To replace the current ARV regimen in those who are virologically-suppressed (HIV-1 RNA < 50 copies/mL) on a stable ARV regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya.
Stribild® (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/TDF 300 mg tablets)	A complete regimen for the treatment of HIV-1 infection in adults and pediatric patients ≥ 12 years of age weighing ≥ 35 kg: (1) Who have no ARV treatment history. (2) To replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ARV regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Stribild.

HIV – Human immunodeficiency virus; TDF – Tenofovir disoproxil fumarate; ARV – Antiretroviral; TAF – Tenofovir alafenamide; INSTI – Integrase strand-transfer inhibitor.

GUIDELINES

The **Department of Health and Human Services (DHHS) (January 21, 2022)** Guidelines for Adults and Adolescents with HIV address treatment-initiation in ARV-naïve individuals. ARVs is recommended for all persons with HIV regardless of CD4 cell count.[4]

All of the recommended initial regimens contain an INSTI. Stribild is <u>not</u> one of the recommended initial regimens for individuals with HIV-1 who are treatment naïve. Genvoya and Stribild are considered regimens recommended in "certain clinical situations". The rationale for the lower rating for Genvoya and Stribild is because both of these products contain cobicistat, a pharmacoenhancer that inhibits CYP3A4 and increases the likelihood of drug-drug interactions. In addition, elvitegravir, the INSTI component of both products has a lower barrier to resistance than dolutegravir and bictegravir. Recommended initial regimens are Biktarvy, 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) only recommends INSTI-based regimens as initial therapy in antiretroviral treatment-naïve patients (Biktarvy, Triumeq, or Tivicay + Descovy® [emtricitabine/tenofovir alafenamide tablets], Tivicay + Truvada® [emtricitabine/tenofovir disoproxil fumarate], Tivicay + Cimduo® [lamivudine/tenofovir disoproxil fumarate], or Dovato).[5]
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 ARV therapy as early in pregnancy as possible, regardless of their HIV RNA level or

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CD4 T lymphocyte count.[8] 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. Neither Genvoya nor Stribild are recommended in pregnant women; data are insufficient for Biktarvy. 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® (dolutegravir/abacavir/lamivudine tablets), 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.[7] 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). Genvoya is not a preferred INSTI-based regimen because of the lower barrier to resistance of elvitegravir compared to bictegravir (and dolutegravir), and the potential for multiple drug–drug interactions from cobicistat. Stribild as a fixed-dose combination is placed as a preferred or alternative regimen in the guidelines; however, among NRTIs, TDF-containing regimens are considered alternative recommendations.

POLICY STATEMENT

This Preferred Specialty Management program has been developed to encourage the use of Preferred Products. The program also directs the patient to try one Preferred Product prior to the approval of a Non-Preferred Product. Requests for Non-Preferred Products 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: Biktarvy, Genvoya
Non-Preferred Products: Stribild

RECOMMENDED EXCEPTION CRITERIA

Non-Preferred Product	Exception Criteria
Stribild	**1.** Approve for 1 year if the patient meets ONE of the following (A or B): **A)** Patient is currently receiving Stribild; OR **B)** Patient has tried one Preferred Product.

REFERENCES

1. Stribild® tablets [prescribing information]. Foster City, CA: Gilead; September 2021.
2. Biktarvy® tablets [prescribing information]. Foster City, CA: Gilead; October 2021.
3. Genvoya® tablets [prescribing information]. Foster City, CA: Gilead; January 2022.

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4. 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. January 21, 2022. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/guidelines-adult-adolescent-arv.pdf. Accessed on May 4, 2022.
5. 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.
6. Arribas JR, Thompson M, Sax PE, et al. Brief report: randomized, double-blind comparison of tenofovir alafenamide (TAF) vs tenofovir disoproxil fumarate (TDF), each coformulated with elvitegravir, cobicistat, and emtricitabine (E/C/F) for initial HIV-1 treatment: week 144 results. *J Acquir Immune Defic Syndr*. 2017;75(2):211-218.
7. 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 5, 2022.
8. 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 5, 2022.

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