STRIBILD®

(elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/ tenofovir disoproxil (as fumarate) 245 mg)

Today, approximately 34 million people worldwide are living with HIV,[1] including 2.3 million in the European region, where more than 120,000 new cases of HIV infection were reported in 2010 alone.[2]

HIV therapy has transformed dramatically since the first AIDS cases were reported three decades ago. Early treatment regimens were complex and burdensome, consisting of 20-30 pills that had to be taken throughout the day. Treatment today has been simplified with fixed-dose combination therapies, including once-daily single tablet regimens containing a complete course of HIV therapy in one pill.

Single tablet regimens reduce pill burden and can make it easier for patients to be consistently adherent to a fully suppressive regimen. This in turn supports optimal health outcomes and helps to minimize the risk of drug resistance.[3,4] Owing to these benefits, single tablet regimens have rapidly become preferred therapies and are recommended by European AIDS Clinical Society (EACS) guidelines.[5] There is also growing recognition of the benefits of simplified therapies from national organizations, including the British HIV Association, the German AIDS Society (Deutsche AIDS-Gesellschaft), Spain's AIDS Study Group (GeSIDA) and Italy's Ministry of Health.[6,7,8,9]

About Stribild®

Please visit **www.ema.europa.eu** for full prescribing information, including Important Safety Information.

- Stribild (elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/ tenofovir disoproxil (as fumarate) 245 mg) is a complete once-daily single tablet regimen for the treatment of HIV-1 infection in adult patients who are antiretroviral-naïve or are infected with HIV-1 without known mutations associated with resistance to any of the three antiretroviral agents in Stribild. Stribild received marketing authorisation from the European Commission in May 2013 and is the third single tablet HIV regimen developed by Gilead.
- A complete course of HIV therapy consisting of three or more medicines with at least two mechanisms of action can help lower HIV-1 viral load and increase the number of CD4 cells, which is a marker of immune system health.
- Stribild combines four compounds in a once-daily tablet: elvitegravir, cobicistat, Emtriva® (emtricitabine) and Viread® (tenofovir disoproxil (as fumarate)).
- Elvitegravir and cobicistat are new agents in HIV therapy. Elvitegravir is an integrase inhibitor and works by blocking the ability of the virus to integrate into the genetic material of human cells. Cobicistat is a "boosting" agent that works by inhibiting cytochrome P450 3A (CYP3A), an enzyme that metabolizes drugs in the body. Cobicistat has no known anti-HIV activity.
- Emtriva and Viread have been used in HIV treatment regimens for a decade. Emtriva is a nucleoside reverse transcriptase inhibitor (NRTI) and Viread is a nucleotide reverse transcriptase inhibitor (NtRTI). They work by blocking reverse transcriptase, an enzyme that HIV depends on to replicate and invade immune system cells.
- Stribild is dosed as one tablet taken orally once daily with food.

Clinical Profile[10]

- The approval of Stribild was supported by 48-week data from two pivotal Phase 3 studies in which Stribild met its primary objective of non-inferiority compared to two leading HIV treatment regimens: Atripla® (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil (as fumarate) 245 mg) (Study 102) and ritonavir-boosted atazanavir plus Truvada® (emtricitabine/tenofovir disoproxil (as fumarate)) (Study 103).

- In these studies, Stribild was associated with a lower incidence of certain central nervous system side effects, cholesterol elevations and rash compared to Atripla, and a favorable triglycerides profile compared to a regimen of ritonavir-boosted atazanavir plus Truvada.
- The most frequently reported adverse reactions occurring in more than 10 percent of patients taking Stribild in Studies 102 and 103 were diarrhoea and nausea.
- In November 2012, additional data from these clinical trials found that Stribild maintained high antiviral efficacy through two years (96 weeks) of treatment.
- Stribild does not cure HIV infection, nor has it been shown to reduce the risk of transmission of HIV to others.

EU Important Product Information About Stribild[11]

- Lactic acidosis, usually associated with hepatic steatosis, has been reported with the use of nucleoside analogues. Lactic acidosis has a high mortality and patients at increased risk should be followed closely.
- Stribild should not be taken with any of the following due to the potential for serious and/or life threatening events or loss of virologic response and possible resistance to Stribild:
    - alpha 1 adrenoreceptor antagonists: alfuzosin
    - antiarrhythmics: amiodarone, quinidine
    - anticonvulsants: carbamazepine, phenobarbital, phenytoin
    - antimycobacterials: rifampicin
    - ergot derivatives: dihydroergotamine, ergometrine, ergotamine
    - gastrointestinal motility agents: cisapride
    - herbal products: St. John's wort (*Hypericum perforatum*)
    - HMG Co-A reductase inhibitors: lovastatin, simvastatin
    - neuroleptics: pimozide
    - PDE-5 inhibitors: sildenafil for treatment of pulmonary arterial hypertension
    - sedatives/hypnotics: orally administered midazolam, triazolam
- As a fixed combination, Stribild should not be administered concomitantly with other medicinal products containing tenofovir disoproxil (as fumarate), lamivudine or adefovir dipivoxil used for the treatment of hepatitis B virus infection.
- Emtricitabine and tenofovir disoproxil (as fumarate) are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion. Renal failure, renal impairment, elevated creatinine, hypophosphataemia and proximal tubulopathy (including Fanconi syndrome) have been reported with the use of tenofovir disoproxil (as fumarate).
- Patients who have previously discontinued treatment with tenofovir disoproxil (as fumarate) due to renal toxicity should not be treated with Stribild.
- Patients should have creatinine clearance calculated and urine glucose and urine protein determined prior to initiating Stribild therapy.
- Stribild should not be initiated in patients with creatinine clearance below 70 mL/min. It is recommended that Stribild is not initiated in patients with creatinine clearance < 90 mL/min unless, after review of the available treatment options, it is considered that Stribild is the preferred treatment for the individual patient.
- Creatinine clearance, serum phosphate, urine glucose and urine protein should be monitored every 4 weeks during the first year and then every 3 months. More frequent monitoring of renal function should be considered in patients at risk for renal impairment.
- Cobicistat inhibits the tubular secretion of creatinine and may cause modest increases in serum creatinine and modest declines in creatinine clearance. Patients who experience a confirmed increase in serum creatinine of greater than 26.5 µmol/L (0.3 mg/dL) from baseline should be closely monitored for renal safety.

- Renal function should be re-evaluated within 1 week if serum phosphate is < 0.48 mmol/L (1.5 mg/dL) or creatinine clearance decreases to < 70 mL/min during Stribild therapy.

- If creatinine clearance is confirmed as < 50 mL/min or serum phosphate decreases to < 0.32 mmol/L (1.0 mg/dL) then Stribild should be discontinued.

- There are currently inadequate data to determine whether co-administration of tenofovir disoproxil (as fumarate) and cobicistat is associated with a greater risk of renal adverse reactions compared with regimens that include tenofovir disoproxil (as fumarate) without cobicistat.

- Stribild should be avoided with concurrent or recent use of a nephrotoxic medicinal product due to the increased risk of renal adverse reactions (with the TDF component of Stribild).

- Bone abnormalities (infrequently leading to fractures) may be associated with proximal renal tubulopathy and appropriate consultation should be obtained if suspected.

- Stribild has not been studied in patients with severe hepatic impairment (CPT Score C).

- Discontinuation of Stribild therapy in patients co-infected with HIV and hepatitis B virus (HBV) may be associated with severe acute exacerbations of hepatitis. Patients co-infected with HIV and HBV who discontinue Stribild should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, initiation of hepatitis B therapy may be warranted. In patients with advanced liver disease or cirrhosis, treatment discontinuation is not recommended since post treatment exacerbation of hepatitis may lead to hepatic decompensation.

- Immune Reactivation Syndrome has been reported in patients treated with combination therapy, including the components of Stribild.

- Combination therapy has been associated with the redistribution of body fat (lipodystrophy) in HIV patients. The long-term consequences of these events are currently unknown.

This fact sheet does not include all data contained in the Summary of Product Characteristics (SmPC) for Atripla, Emtriva, Stribild, Truvada or Viread. Please see the complete SmPCs for further details, available at www.ema.europa.eu.

For more information on Gilead Sciences, please visit the company's web site at www.gilead.com or call the Gilead Public Affairs Department at +44 (0)208 587 2349.

References

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[10] Stribild SMPC. May 2013. Available at www.ema.europa.eu.

[11] Stribild SMPC. May 2013. Available at www.ema.europa.eu.

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