BRITISH COLUMBIA
CENTRE *for* EXCELLENCE
in HIV/AIDS

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Dear Doctor,

Stribild™ is now approved as "extended access" in the BC Centre for Excellence in HIV/AIDS Drug Treatment Program (DTP). Stribild™ is a fixed dose combination product containing elvitegravir 150mg/cobicistat 150mg with standard dose tenofovir/emtricitabine. Elvitegravir/cobicistat can be regarded as an alternative third agent (in the same category as raltegravir) for antiretroviral naïve patients for whom the tenofovir/emtricitabine backbone is considered appropriate. It is currently only available as a co-formulation. The fixed-dose combination does not allow for elvitegravir dose adjustments, therefore it should not be administered with protease inhibitors.

Elvitegravir is a novel HIV integrase strand transfer inhibitor (InSTI) that can be dosed in a once daily fashion [1]. Elvitegravir is metabolized via the cytochrome P (CYP) 450 3A4 isoenzyme pathway and requires use of a co-administered boosting agent in a similar fashion to protease inhibitors. Initial pharmacokinetic evaluation revealed an increase in plasma half-life from 3.5 to 9.5 hours, and a three-fold increase in area under the concentration-time curve (AUC) when elvitegravir was co-administered with ritonavir [1]. Absorption is improved with food. Elvitegravir undergoes predominantly hepatobiliary clearance.

Cobicistat is a novel pharmacokinetic booster without intrinsic antiviral activity [2]. Cobicistat predominantly inhibits CYP3A4, with weak inhibition of CYP2D6, and as such drug-drug interactions may preclude concomitant administration with medications which are cleared through the CYP3A4 pathway [3]. The use of cobicistat 150mg daily as a pharmacokinetic enhancer for elvitegravir (as a single tablet co-formulated with tenofovir/emtricitabine) was assessed in a cross-over study in a comparison to ritonavir-boosted elvitegravir with tenofovir/emtricitabine [4], and showed that boosting with cobicistat resulted in higher AUC and similar trough concentrations of elvitegravir.

Note that cobicistat acts to inhibit creatinine secretion and can lead to an increase in creatinine values in subjects receiving cobicistat within the first few weeks of therapy (average 11-13 mmol/L), with stabilization in the creatinine

values thereafter. This can affect evaluation of estimated Glomerular Filtration Rate (eGFR) (average 13-14 mL/min) but is thought not to affect actual GFR. .Stribild should be used with caution in patients with diminished renal function, in particular in those individuals with estimated creatinine clearance <50 ml/min.

In treatment naïve individuals, the co-formulated elvitegravir tablet was compared to efavirenz/tenofovir/emtricitabine [7], and to atazanavir/ritonavir and shown to be non-inferior with plasma viral load (pVL) < 50 copies/mL in 87.6% of those receiving elvitegravir vs. 84.1% using efavirenz (48 weeks), and 89.5% vs. 86.8% (elvitegravir and atazanavir/ritonavir).

Elvitegravir has been compared to raltegravir in treatment-experienced patients with pVL > 1,000 copies/mL and either at least 6 months experience or evidence of resistance to at least 2 other drug classes The proportion of individuals achieving virologic suppression at week 48 was 59% vs. 58% in the elvitegravir and raltegravir arms, respectively (difference 1.1% [95% CI -6.0% to 8.2%]) within the pre-specified interval of 10% for non-inferiority. Proportions of individuals with virologic failure demonstrating documented resistance was similar between arms.

Elvitegravir/cobicistat has more gastrointestinal (GI) side effects (diarrhea and nausea) than efavirenz, and fewer neuropsychiatric symptoms. GI side effects with elvitegravir/cobicistat are similar to those with atazanavir/ritonavir.

All Stribild™ drug requests must specifically include the justification for use. Any requests that do not include this information will be forwarded back to the prescriber and the drug request will be held until this information is received.

Yours sincerely,

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