Dolutegravir-Abacavir-Lamivudine (Triumeq)

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Drug Summary

Dolutegravir-abacavir-lamivudine is a single-tablet regimen that is used primarily for treatment-naïve individuals; it should not be offered to individuals who are positive for HLA-B*5701 due to risk of a life-threatening abacavir hypersensitivity reaction. It has high potency, a relatively robust barrier to resistance (due to the dolutegravir component), good tolerability, and few drug interactions. It may be especially advantageous for individuals with renal insufficiency or risk factors for renal disease or osteoporosis, as it avoids the use of tenofovir DF. In certain treatment-experienced individuals, dolutegravir-abacavir-lamivudine may provide an option for switch or simplification of therapy. Abacavir can cause a life-threatening hypersensitivity reaction in individuals who are HLA-B*5701 positive; all patients need to undergo testing for HLA-B*5701 prior to receiving dolutegravir-abacavir-lamivudine and those who test positive for HLA-B*5701 should not receive this single tablet regimen. Dolutegravir blocks tubular secretion of creatinine and therefore causes a small increase in serum creatinine in the first 4 to 8 weeks of use; this increase is benign and does not indicate a change in true creatinine clearance.

Key Clinical Trials

In antiretroviral-naïve individuals, dolutegravir plus abacavir-lamivudine demonstrated superior virologic responses when compared with efavirenz-tenofovir disoproxil fumarate (DF)-emtricitabine [SINGLE], with superiority largely driven by the greater tolerability of the dolutegravir plus abacavir-lamivudine regimen. In a comparison of 2 NRTIs plus either dolutegravir or raltegravir in treatment-naïve patients, virologic responses in the subset of patients who received dolutegravir plus abacavir-lamivudine were equivalent to those receiving raltegravir plus either tenofovir DF-emtricitabine or abacavir-lamivudine [SPRING-2]. In a similarly designed trial, treatment-naïve adults were randomized to receive two NRTIs plus either dolutegravir or ritonavir-boosted darunavir; this analysis demonstrated superior virologic response in the group that received dolutegravir plus two NRTIs (including dolutegravir with abacavir-lamivudine) when compared with those who received darunavir plus two NRTIs [FLAMINGO]. Individuals taking standard 3-drug antiretroviral therapy with suppressed HIV RNA levels (and no evidence of drug resistance mutations) were randomized to continue current therapy or switch to dolutegravir-abacavir-lamivudine; after 24 weeks there were equivalent rates of virologic suppression in the two groups [STRIIVING].
Adverse Effects

Abacavir can cause a life-threatening hypersensitivity reaction; this reaction manifests as flu-like symptoms with or without rash and gastrointestinal symptoms, all of which worsen with each dosage. This hypersensitivity reaction may occur in individuals who are positive for HLA-B*5701. Screening for HLA-B*5701 should be done before initiating dolutegravir-abacavir-lamivudine. Other possible abacavir-related side effects include rash, malaise, fatigue, anxiety, and increases in hepatic aminotransferase levels. The use of abacavir is contraindicated in patients with moderate or severe hepatic impairment. Some studies have shown that abacavir increases the risk of ischemic cardiovascular events, whereas other trials have failed to confirm this finding. Lamivudine is well tolerated and does not frequently cause adverse events. Adverse effects with dolutegravir are usually mild and include headaches, insomnia, and psychiatric symptoms. Dolutegravir inhibits tubular secretion of creatinine and may increase serum creatinine (average increase of 0.12 mg/dL); it has no effect on actual (measured) glomerular filtration rate.

Dolutegravir Safety Alert: On May 18, 2018, an FDA Safety Alert was posted that warned of potential serious neural tube birth defects in infants born to mothers who received dolutegravir at the time of becoming pregnant or early in the first trimester. On May 30, 2018, the HHS Antiretroviral Guideline Panels issued Recommendations Regarding Dolutegravir that address the use of dolutegravir in adults and adolescents with HIV who are pregnant or of child-bearing potential.

Use In Pregnancy

Note: On May 18, 2018, an FDA Safety Alert was posted that warned of potential serious neural tube birth defects in infants born to mothers who received dolutegravir at the time of becoming pregnant or early in the first trimester. On May 30, 2018, the HHS Antiretroviral Guideline Panels issued Recommendations Regarding Dolutegravir that address the use of dolutegravir in adults and adolescents with HIV who are pregnant or of child-bearing potential.

The information in the May 30, 2018 HHS Antiretroviral Guideline Panels recommendations regarding dolutegravir should take priority over content listed below as outlined in the October 19, 2017 version in the HHS Perinatal Guidelines.

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), the fixed dose medication dolutegravir-abacavir-lamivudine is designated in the category Alternative Integrase Inhibitor Regimens for Initial Combination Regimens for Antiretroviral-Naive Pregnant Women (only for women who are HLAB*5701 negative). This recommendation is based on the classification of dolutegravir as an alternative integrase inhibitor in pregnancy; the abacavir-lamivudine component of this regimen is in the category of Preferred Initial Regimens in Pregnancy as a Preferred Two-NRTI Backbone (only for women who are HLAB*5701 negative). Note that for pregnant women with acute HIV, a dolutegravir-based regimen is considered a preferred regimen.

- For additional information regarding the safety and toxicity of dolutegravir-abacavir-
lamivudine in pregnancy see the HHS Perinatal Guidelines summaries on Dolutegravir, Abacavir, and Lamivudine.

Resistance

For a listing of the most common clinically significant mutations associated with dolutegravir (DTG) resistance, see the INSTI Resistance Notes on the Stanford University HIV Drug Resistance Database.

For a listing of the most common clinically significant mutations associated with abacavir (ABC) and/or lamivudine (3TC) resistance, see the NRTI Resistance Notes on the Stanford University HIV Drug Resistance Database.

Key Drug Interactions

For complete information on dolutegravir-abacavir-lamivudine-related drug interactions, see the Drug Interactions section in the Dolutegravir-Abacavir-Lamivudine (Triumeq) Prescribing Information.

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