Triumeq® (abacavir/dolutegravir/lamivudine) – Expanded indication, new warnings

- On November 21, 2017, the FDA announced the approval of ViiV Healthcare's Triumeq (abacavir/dolutegravir/lamivudine) tablets, for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in pediatric patients weighing ≥ 40 kg.
    - Previously, Triumeq was only approved for the treatment of HIV-1 infection in adults.
    - Triumeq alone is not recommended in patients with resistance-associated integrase substitutions or clinically suspected integrase strand transfer inhibitor resistance because the dose of dolutegravir in Triumeq is insufficient in these subpopulations.
- The approved expanded indication for Triumeq was based on two clinical trials in pediatric patients with HIV-1 infection and weighing ≥ 40 kg.
    - In the first trial, abacavir and lamivudine once daily, in combination with a third antiretroviral drug, were evaluated in HIV-1 infected, treatment-naïve pediatric patients weighing at least 25 kg. At week 96, 67% of subjects achieved HIV-1 RNA less than 80 copies per mL.
    - In the second trial, dolutegravir, in combination with other antiretroviral drugs, was established in treatment-experienced, integrase strand transfer inhibitor-naïve, HIV-1 infected patients 6 years to less than 18 years of age. Overall, 67% of patients weighing ≥ 40 kg achieved virologic suppression at week 48.
- Triumeq carries a boxed warning for hypersensitivity reactions, lactic acidosis and severe hepatomegaly, and exacerbations of hepatitis B.
- The *Warnings and Precautions* section of the Triumeq drug label was also updated with information regarding hepatotoxicity and risk of adverse reactions or loss of virologic response due to drug interactions. In addition, the *Related Products that are Not Recommended* subsection was removed.
- Hepatic adverse events have been reported in patients receiving a dolutegravir-containing regimen.
    - Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of Triumeq. In some cases, the elevations in transaminases were consistent with immune reconstitution syndrome or hepatitis B reactivation particularly in the setting where anti-hepatitis therapy was withdrawn.
    - Cases of hepatic toxicity including elevated serum liver biochemistries, hepatitis, and acute liver failure have also been reported in patients receiving a dolutegravir-containing regimen who had no pre-existing hepatic disease or other identifiable risk factors.
    - Drug-induced liver injury leading to liver transplant has been reported with Triumeq.
    - Monitoring for hepatotoxicity is recommended.
- The concomitant use of Triumeq and other drugs may result in known or potentially significant drug interactions, some of which may lead to:
    - Loss of therapeutic effect of Triumeq and possible development of resistance.
    - Possible clinically significant adverse reactions from greater exposures of concomitant drugs.
    - See table 5 in the label for steps to prevent or manage these possible and known significant drug interactions, including dosing recommendations.
    - Consider the potential for drug interactions prior to and during therapy with Triumeq; review concomitant medications during therapy with Triumeq; and monitor for the adverse reactions associated with the concomitant drugs.

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- The *Adverse Reactions*, *Clinical Pharmacology* and *Clinical Studies* sections were also updated to include data in pediatric patients.
- The recommended dosage of Triumeq in adults and pediatric patients weighing ≥ 40 kg is 1 tablet orally once daily.
    - Triumeq cannot be adjusted for patients weighing less than 40 kg.