

Triumeq® (abacavir, dolutegravir and lamivudine) Product Backgrounder for US Media

What is Triumeq® and who is Triumeq for?

- Triumeq (abacavir 600mg, dolutegravir 50mg and lamivudine 300mg) is the first dolutegravir-based fixed-dose combination, offering many people living with HIV the option of a single-pill regimen that combines the integrase strand transfer inhibitor (INSTI) dolutegravir, with the nucleoside reverse transcriptase inhibitors (NRTIs) abacavir and lamivudine.¹
- Triumeq alone is not recommended for use in patients with current or past history of resistance to any components of Triumeq. Triumeq alone is not recommended in patients with resistance-associated integrase substitutions or clinically suspected INSTI resistance because the dose of dolutegravir in Triumeq is insufficient in these populations. Before initiating treatment with abacavir-containing products, screening for the presence of a genetic marker, the HLA-B*5701 allele, should be performed in any HIV-infected patient, irrespective of racial origin. Products containing abacavir should not be used in patients known to carry the HLA-B*5701 allele.¹
- Triumeq is contraindicated in patients with a previous hypersensitivity reaction (HSR) to abacavir, dolutegravir or lamivudine. However, HSR have been observed more commonly with abacavir, some of which have been serious and in rare cases fatal. Clinically it is not possible to determine whether a HSR with Triumeq is caused by abacavir, dolutegravir or lamivudine.¹
- Triumeq is a pill that can be taken with or without food and may be taken at any time of day.¹
- Please refer to the US Prescribing Information for full product information.¹

How does Triumeq work?

- Triumeq contains the INSTI dolutegravir and the NRTIs abacavir and lamivudine.¹
- Two essential steps in the HIV life cycle are replication – when the virus turns its RNA copy into DNA – and integration – the moment when viral DNA becomes part of the host cell's DNA.^{2,3}
- These processes require two enzymes called reverse transcriptase and integrase. NRTIs and integrase inhibitors interfere with the action of the two enzymes to prevent the virus from replicating and further infecting cells.^{2,3}

What role does Triumeq play in the treatment of HIV?

- Triumeq provides many people living with HIV the option of a single-pill regimen containing dolutegravir. Despite the widespread availability of drugs that target HIV,

both in the US and the EU, only between 52% and 58% of people living with HIV are satisfied with the tolerability of their current regimen, signifying the continued need for new treatment options for people living with HIV.^{4,5}

- ViiV Healthcare is committed to delivering advances in care and new treatment options to physicians and people living with HIV. Although single-pill regimens have been available to people living with HIV for some time, Triumeq is the first single-pill regimen containing dolutegravir.

Which clinical trials supported the approval of Triumeq?

- The FDA approval is based primarily upon data from two clinical trials:
 - the Phase III study (SINGLE) of treatment-naïve adults, conducted with dolutegravir and abacavir/lamivudine as separate pills^{6,7}
 - a bioequivalence study of the fixed-dose combination of abacavir, dolutegravir and lamivudine when taken as a single pill compared to the administration of dolutegravir and abacavir/lamivudine as separate pills.⁸
- In the SINGLE study, a non-inferiority trial with a pre-specified superiority analysis, more patients were undetectable (HIV-1 RNA <50 copies/mL) in the dolutegravir and abacavir/lamivudine arm (the separate components of Triumeq) than in the Atripla^{®+} (efavirenz, emtricitabine and tenofovir) arm, the most commonly used single-pill regimen. The difference was statistically significant and met the pre-specified test for superiority. The difference was driven by a higher rate of discontinuation due to adverse events in the Atripla arm.^{6,7}
 - At 96 weeks, 80% of participants on the dolutegravir-based regimen were virologically suppressed compared to 72% of participants on Atripla. Grade 2-4 treatment emergent adverse reactions occurring in 2% or more participants taking the dolutegravir-based regimen were insomnia (3%), headache (2%) and fatigue (2%).⁷
- The bioequivalence study evaluated Triumeq (abacavir, dolutegravir and lamivudine) when taken as a single pill compared to the administration of dolutegravir and abacavir/lamivudine as separate pills. The study was performed according to the usual methods for this type of study.⁸
 - Bioequivalence was demonstrated between the Triumeq single pill and the separate co-administered tablet formulations of dolutegravir and abacavir/lamivudine.⁸
 - Additionally, the effect of food on the plasma pharmacokinetics of the single pill components, abacavir, dolutegravir and lamivudine, was similar to food effects observed with dolutegravir plus abacavir/lamivudine, indicating that the Triumeq single pill may be taken with or without food.⁸

Important Safety Information (ISI) for Triumeq[®] (abacavir, dolutegravir and lamivudine) tablets

The following ISI is based on the Highlights section of the Prescribing Information for Triumeq. Please consult the full Prescribing Information for all the labeled safety information for Triumeq.

BOXED WARNING: RISK OF HYPERSENSITIVITY REACTIONS, LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY AND EXACERBATIONS OF HEPATITIS B

See full Prescribing Information for complete boxed warning.

- Serious and sometimes fatal hypersensitivity reactions have been associated with abacavir-containing products.
- Hypersensitivity to abacavir is a multi-organ clinical syndrome.
- Patients who carry the HLA-B*5701 allele are at high risk for experiencing a hypersensitivity reaction to abacavir.
- Discontinue Triumeq as soon as hypersensitivity reaction is suspected. Regardless of HLA-B*5701 status, permanently discontinue Triumeq if hypersensitivity cannot be ruled out, even when other diagnoses are possible.
- Following a hypersensitivity reaction to abacavir, NEVER restart Triumeq or any other abacavir-containing product.
- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues.
- Severe acute exacerbations of hepatitis B have been reported in patients who are co-infected with Hepatitis B Virus (HBV) and Human Immunodeficiency Virus (HIV-1) and have discontinued lamivudine, a component of Triumeq. Monitor hepatic function closely in these patients and, if appropriate, initiate anti-hepatitis B treatment.

CONTRAINDICATIONS

- Presence of HLA-B*5701 allele.
- Previous hypersensitivity reaction to abacavir, dolutegravir or lamivudine.
- Co-administration with dofetilide.
- Moderate or severe hepatic impairment.

WARNINGS AND PRECAUTIONS

- Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of Triumeq. Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during therapy with Triumeq is recommended in patients with underlying hepatic disease such as hepatitis B or C.

- Hepatic decompensation, some fatal, has occurred in HIV-1/Hepatitis C Virus (HCV) co-infected patients receiving combination antiretroviral therapy and interferon alfa with or without ribavirin. Discontinue Triumeq as medically appropriate and consider dose reduction or discontinuation of interferon alfa, ribavirin or both.
- Immune reconstitution syndrome and redistribution/accumulation of body fat have been reported in patients treated with combination antiretroviral therapy.
- Administration of Triumeq is not recommended in patients receiving other products containing abacavir or lamivudine.

ADVERSE REACTIONS

The most commonly reported ($\geq 2\%$) adverse reactions of at least moderate intensity in treatment-naïve adult subjects receiving Triumeq were insomnia (3%), headache (2%) and fatigue (2%).

DRUG INTERACTIONS

Co-administration of Triumeq with other drugs can alter the concentration of other drugs, and other drugs may alter the concentrations of Triumeq. The potential drug-drug interactions must be considered prior to and during therapy.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Triumeq should be used during pregnancy only if the potential benefit justifies the potential risk.
- **Nursing mothers:** Breastfeeding is not recommended due to the potential for HIV transmission.
- Triumeq is not recommended in patients with creatinine clearance of less than 50 mL per min.
- If a dose reduction of abacavir, a component of Triumeq, is required for patients with mild hepatic impairment, then the individual components should be used.

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¹ Triumeq US label.

² Centers for Disease Control and Prevention. HIV Basics. <http://www.cdc.gov/hiv/basics/index.html>. Accessed July 28, 2014.

³ NHS Choices, HIV and AIDS Overview. <http://www.nhs.uk/conditions/HIV/Pages/Introduction.aspx>. Accessed July 28, 2014.

⁴ The AIDS Treatment for Life International Survey (ALT2010).

<http://www.iapac.org/ATLIS/ATLIS2010/Fact%20Sheet%20Key%20Regional%20Findings%20with%20Stigma%20FINAL.pdf>. Accessed July 28, 2014.

⁵ IAPAC Monthly. Volume 12, Number 5. <http://img.thebody.com/iapac/pdfs/may06.pdf>. Accessed July 28, 2014.

⁶ Walmsley SL, Antela A, Clumeck N *et al*; for the SINGLE Investigators. Dolutegravir plus Abacavir–Lamivudine for the Treatment of HIV-1 Infection. *N Engl J Med*. 2013; 369(19):1807-1818.

⁷ Walmsley S, Berenguer J, Khuong-Josses M, *et al*. Dolutegravir regimen statistically superior to efavirenz/tenofovir/emtricitabine: 96-week results from the SINGLE study (ING114467). Poster presented at: 21st Conference on Retroviruses and Opportunistic Infections; March 3-6, 2014; Boston, MA. Poster 543.

⁸ Weller S, Chen S, Borland J *et al*. Bioequivalence of a Dolutegravir, Abacavir and Lamivudine Fixed-Dose Combination Tablet and the Effect of Food. *JAIDS*. 2014 May
doi:10.1097/QAI.000000000000193.http://journals.lww.com/jaids/Abstract/publishahead/Bioequivalence_of_a_Dolutegravir,_Abacavir_and.97920.aspx.

[†]Atripla is a registered trademark of Bristol-Meyers Squibb and Gilead Sciences LLC.