

BRIEF SUMMARY for TRIUMEQ® (abacavir, dolutegravir, and lamivudine) Tablets (cont'd)

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: **Carcinogenicity:** *Dolutegravir:* Two-year carcinogenicity studies in mice and rats were conducted with dolutegravir. Mice were administered doses of up to 500 mg per kg, and rats were administered doses of up to 50 mg per kg. In mice, no significant increases in the incidence of drug-related neoplasms were observed at the highest doses tested, resulting in dolutegravir AUC exposures approximately 26-fold higher than those in humans at the recommended dose of 50 mg once daily. In rats, no increases in the incidence of drug-related neoplasms were observed at the highest dose tested, resulting in dolutegravir AUC exposures 17-fold and 30-fold higher in males and females, respectively, than those in humans at the recommended dose of 50 mg once daily. *Abacavir:* Abacavir was administered orally at 3 dosage levels to separate groups of mice and rats in 2-year carcinogenicity studies. Results showed an increase in the incidence of malignant and non-malignant tumors. Malignant tumors occurred in the preputial gland of males and the clitoral gland of females of both species, and in the liver of female rats. In addition, non-malignant tumors also occurred in the liver and thyroid gland of female rats. These observations were made at systemic exposures in the range of 7 to 28 times the human exposure at the recommended dose of 600 mg. *Lamivudine:* Long-term carcinogenicity studies with lamivudine in mice and rats showed no evidence of carcinogenic potential at exposures up to 12 times (mice) and 57 times (rats) the human exposures at the recommended dose of 300 mg. **Mutagenicity:** *Dolutegravir:* Dolutegravir was not genotoxic in the bacterial reverse mutation assay, mouse lymphoma assay, or in the in vivo rodent micronucleus assay. *Abacavir:* Abacavir induced chromosomal aberrations both in the presence and absence of metabolic activation in an in vitro cytogenetic study in human lymphocytes. Abacavir was mutagenic in the absence of metabolic activation, although it was not mutagenic in the presence of metabolic activation in an L5178Y mouse lymphoma assay. Abacavir was clastogenic in males and not clastogenic in females in an in vivo mouse bone marrow micronucleus assay. Abacavir was not mutagenic in bacterial mutagenicity assays in the presence and absence of metabolic activation. *Lamivudine:* Lamivudine was mutagenic in an L5178Y mouse lymphoma assay and clastogenic in a cytogenetic assay using cultured human lymphocytes. Lamivudine was not mutagenic in a microbial mutagenicity assay, in an in vitro cell transformation assay, in a rat micronucleus test, in a rat bone marrow cytogenetic assay, and in an assay for unscheduled DNA synthesis in rat liver. **Impairment of Fertility:** Dolutegravir, abacavir, or lamivudine did not affect male or female fertility in rats at doses associated with exposures approximately 44, 9, or 112 times (respectively) higher than the exposures in humans at the doses of 50 mg, 600 mg, and 300 mg (respectively).

PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling (Medication Guide).

Manufactured for:

by:



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TRM:3BRS

Revised: September 2015

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GlaxoSmithKline

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Comprimidos lingüísticos



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Comprimido 1: Paro vs arresto

Es posible que haya oído frases como estas: “el paciente se arrestó” o “el paciente tuvo un arresto respiratorio”. Sea cardíaco o respiratorio, el paciente no sufre un arresto, sino un paro. Recuerde, *arrest* en inglés y *paro* en español. Deje los arrestos a los oficiales de l y y orden.

Comprimido 2: Virus vs viruses

Son innumerables las veces que oímos usar el plural anómalo viruses en español. La razón: El inglés añade “*s*” para formar el plural del sustantivo singular virus. El español usa el artículo para marcar el singular o el plural: “el virus”, “los virus”. Pero aun si no lleva el artículo, virus en singular y virus en plural. Son muchos los virus que atacan al español, protéjase de este.

Comprimido 3: Sistema inmunológico

Por definición, inmunológico significa “perteneciente o relativo a la inmunología” y la inmunología es el “estudio de la inmunidad biológica y sus aplicaciones”. Si partimos del latín, el elemento compositivo “logo” significa a ‘versado’ o ‘especialista’ en el elemento que lo antecede: por ejemplo, cardiólogo, inmunólogo y sus adjetivos, cardiológico e inmunológico, respectivamente. Por eso es más correcto hablar del “sistema inmunitario” pues inmunitario significa a “perteneciente o relativo a la inmunidad”. No obstante, la amplia difusión y aceptación del término “sistema inmunológico” hace que muchas personas estén renuentes a corregirlo. ¡Usted decide!

C. 4: Sistema inmune, enfermedad inmune

¿Alguna vez han pensado en la contradicción que representan frases como estas? Si el sistema fuera inmune nada lo afectaría. Si la enfermedad fuera inmune, no se podría combatir. En realidad, “inmune” en estos y otros casos es una traducción literal del inglés que se podría subsanar usando la frase preposicional “de inmunidad” o, mejor aún, el adjetivo inmunitario. Dígalo correctamente: Sistema inmunitario, enfermedad inmunitaria.