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(IN REPLY PLEASE QUOTE THIS FILE REF.)

12 Mar 2021

Dear Healthcare Professionals,

**The Food and Drug Administration approved revisions to the TRIUMEQ (abacavir/dolutegravir/lamivudine) and DOVATO (dolutegravir/lamivudine) labels**

Your attention is drawn to the United States Food and Drug Administration's (FDA) announcement that it approved revisions to the TRIUMEQ (abacavir/dolutegravir/lamivudine) and DOVATO (dolutegravir/lamivudine) labels to include dosing in patients with creatinine clearance between 30 and 49 ml per min. Additionally, drug interaction information for TRIUMEQ and riociguat were included in the label. A summary of the major labeling changes for TRIUMEQ is below. Similar changes were made to the DOVATO label.

- Section 2: DOSAGE AND ADMINISTRATION
  2.5 Not Recommended Due to Lack of Dosage Adjustment
  Because TRIUMEQ is a fixed-dose tablet and cannot be dose adjusted, TRIUMEQ is not recommended in patients with creatinine clearance less than 30 ml per minute.

- Section 8: USE IN SPECIFIC POPULATIONS
  8.6 Patients with Impaired Renal Function
  TRIUMEQ is not recommended for patients with creatinine clearance less than 30 ml per min because TRIUMEQ is a fixed-dose combination and the dosage of the individual components cannot be adjusted. If a dose reduction of lamivudine, a component of TRIUMEQ, is required for patients with creatinine clearance less than 30 ml per min, then the individual components should be used.

  Patients with a creatinine clearance between 30 and 49 ml per min receiving TRIUMEQ may experience a 1.6- to 3.3-fold higher lamivudine exposure (AUC) than patients with a creatinine clearance ≥50 mL per min. There are no safety data from randomized, controlled trials comparing TRIUMEQ to the individual components in patients with a creatinine clearance between 30 and

49 ml per min who received dose-adjusted lamivudine. In the original lamivudine registrational trials in combination with zidovudine, higher lamivudine exposures were associated with higher rates of hematologic toxicities (neutropenia and anemia), although discontinuations due to neutropenia or anemia each occurred in <1% of subjects. Patients with a sustained creatinine clearance between 30 and 49 ml per min who receive TRIUMEQ should be monitored for hematologic toxicities. If new or worsening neutropenia or anemia develop, dose adjustment of lamivudine, per lamivudine prescribing information, is recommended. If lamivudine dose adjustment is indicated, TRIUMEQ should be discontinued and the individual components should be used to construct the treatment regimen.

- Section 7: DRUG INTERACTIONS
  Riociguat

  Abacavir: Coadministration with TRIUMEQ resulted in increased riociguat exposure, which may increase the risk of riociguat adverse reactions. The riociguat dose may need to be reduced. See full prescribing information for ADEMPAS (riociguat).

- Section 12: CLINICAL PHARMACOLOGY
  Effect of Abacavir and Lamivudine on the Pharmacokinetics of Other Agents: In vitro studies have shown that abacavir has potential to inhibit CYP1A1 and limited potential to inhibit metabolism mediated by CYP3A4. Lamivudine does not inhibit or induce CYP3A4.

  Abacavir, Dolutegravir, and Lamivudine: Coadministration of a single dose of riociguat (0.5 mg) to HIV-1 - infected subjects receiving TRIUMEQ is reported to increase riociguat AUC(∞) compared with riociguat AUC(∞) reported in healthy subjects due to CYP1A1 inhibition by abacavir. The exact magnitude of increase in riociguat exposure has not been fully characterized based on findings from two studies.

Please refer to the following website in FDA for details:
https://www.fda.gov/drugs/human-immunodeficiency-virus-hiv/food-and-drug-administration-approved-revisions-triumeq-abacavirdolutegravirlamivudine-and-dovato

In Hong Kong, Triumeq Tablets (HK-64012; containing abacavir/dolutegravir/lamivudine) and Dovato Tablets (HK-66511; containing dolutegravir/lamivudine) are pharmaceutical products registered by GlaxoSmithKline Limited. Both products are prescription-only medicines. So far, the Department of Health (DH) has not received any case of adverse drug reaction related to abacavir/dolutegravir/lamivudine and dolutegravir/lamivudine. In light of the above FDA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons

Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Undesirable Medical Advertisements and Adverse Drug Reaction Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Joseph LEE)
for Assistant Director (Drug)