Consumer Update **Jan 2022**

Tenofovir Alafenamide: Risk of Renal impairment including renal failure, proximal

EDA performs Label Update to include the following:

Warnings

Use in Renal Impairment

Post marketing cases of renal impairment, including acute renal failure, proximal renal tubulopathy (PRT), and Fanconi syndrome have been reported with tenofovir alafenamide containing products; while most of these cases were characterised by potential confounders that may have contributed to the reported renal events, it is also possible these factors may have predisposed patients to tenofovir-related adverse events.

Patients taking tenofovir prodrugs who have impaired renal function and those taking nephrotoxic agents, including non-steroidal anti-inflammatory drugs, are at increased risk of developing renal-related adverse reactions.

Background:

Tenofovir alafenamide is a phosphonamidite prodrug of tenofovir (2'-deoxyadenosine monophosphate analogue). Tenofovir alafenamide enters primary hepatocytes by passive diffusion and by the hepatic uptake transporters OATP1B1 and OATP1B3. Tenofovir alafenamide is primarily hydrolyzed to form tenofovir by carboxylesterase 1 in primary hepatocytes. Intracellular tenofovir is subsequently phosphorylated to the pharmacologically active metabolite tenofovir diphosphate. Tenofovir diphosphate inhibits HBV replication through incorporation into viral DNA by the HBV reverse transcriptase, which results in DNA chain termination.

- Tenofovir has activity that is specific to hepatitis B virus and human immunodeficiency virus (HIV-1 and HIV-2). Tenofovir diphosphate is a weak inhibitor of mammalian DNA polymerase that include mitochondrial DNA polymerase ɤ and there is no evidence of mitochondrial toxicity in vitro based on several assays including mitochondrial DNA analyses.
- Many Case Reports have been received worldwide for TAF causing renal problems as renal failure, proximal Renal tubulopathy and Fanconi Syndrome.

References: *TGA (Click here)*