Tenofovir disoproxil fumarate

ATC codes: J05AF07

Indication	Human immunodeficiency virus disease without mention of tuberculosis or malaria, clinical stage unspecified ICD11 code: 1C62.Z
INN	Tenofovir
Medicine type	Chemical agent
List type	Core
Formulations	**Oral > Solid:** 300 mg tablet (equivalent to 245 mg tenofovir disoproxil)
EML status history	First added in 2007 (TRS 946)
Sex	All
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Tenofovir disoproxil fumarate
DrugBank	Tenofovir disoproxil fumarate (Tenofovir disoproxil)

Summary of evidence and Expert Committee recommendations

In 2002, the following NRTIs were added to the core Model List: abacavir, didanosine, lamivudine, stavudine and zidovudine. In 2005, the Expert Committee considered an application from the manufacturer for tenofovir (TDF) as an additional NRTI. At that time the application was based mainly on unpublished studies and the Committee deferred a decision on the product until the data were publicly available. The application has since been resubmitted. Tenofovir is listed in current WHO treatment guidelines for adults and children (1,2) as one option for first-line combination treatment as part of the NRTI backbone, and as an alternative to abacavir (ABC). The application provides an updated summary of the evidence, but as noted by the Committee, did not adequately cover all published literature. Some of the supporting evidence is still in the form of conference proceedings and abstracts. The trials presented are restricted to phase III clinical trials comparing TDF to stavudine, or TDF plus TFC to zidovudine/lamivudine FDC or trials with TDF as an add-on treatment in patients with virological failure. The main evidence in the application consists of data from four key regulatory trials. There are ongoing trials in the African region and also in children, but there is as yet no approval for use of TDF in populations younger than 18 years of age. The application provided an updated review of safety information, dated October 2005. The concerns noted by the Committee in 2005 were the potential for renal toxicity, interactions, lactic acidosis, bone problems and liver problems. Although the supplement to the application provides lists of references that are related to these problems, there was no synthesis or overview of the information provided. The expert review prepared for the Committee summarized the information in the references, and notes that several other relevant publications have not been considered. Overall, renal problems with tenofovir appear to be real but rare and the uncertainty is therefore the level of monitoring that would be required. Changes in bone density do not appear to be clinically

relevant and may be reversible. The data on interactions is based on the product information document and may or may not be sufficient for global use. Lactic acidosis and lipodystrophy may be less of a problem with tenofovir than other currently available antiretrovirals (ARVs), especially stavudine. In summary, tenofovir has been found to be effective in terms of effect on standard end-points such as viral load measures, for the treatment of HIV-infected adults, when used in combination with other ARVs. The safety profile is now better characterized than when it was considered in 2005, and considerable data are in the public domain. It is not yet approved for use in children. There are ongoing trials of its use in resource-poor settings. The Committee recommended adding tenofovir to the core Model List and noted that the monitoring requirements for this medicine are no different to those for other ARVs. References: 1. Antiretroviral therapy for HIV infection in adults and adolescents in resource limited settings: toward universal access. Recommendations for a public health approach – 2006 revision. Geneva, Switzerland, World Health Organization, 2006 (http://www.who.int/hiv/pub/guidelines/adult/en/index.html). 2. Antiretroviral therapy of HIV infection in infants and children in resource limited settings: towards universal access. Geneva, World Health Organization (http://www.who.int/hiv/pub/guidelines/art/en/index.html).

