HIV renal educational brochure for prescribers of paediatric patients

This brochure provides important advice on the management of potential renal and bone effects of tenofovir disoproxil fumarate (TDF) in HIV-1 infected adolescents aged 12 to <18 years, and on the dosing recommendations for TDF in this population. [1]

Important points to consider

- A multidisciplinary approach is recommended for the management of adolescents
- Check all patients' creatinine clearance and serum phosphate before starting TDF therapy
- During TDF therapy, renal function (creatinine clearance and serum phosphate) should be assessed regularly (after two to four weeks of treatment, after three months of treatment and every three to six months thereafter in patients without renal risk factors) (see Table 1)
- In patients at risk for renal impairment a more frequent monitoring of renal function is required
- TDF should not be used in children or adolescents with renal impairment
- Re-evaluate renal function within 1 week if serum phosphate is confirmed to be <3.0 mg/dL (0.96 mmol/L) during TDF therapy
- If renal abnormalities are suspected or detected consult with a nephrologist to consider interrupting TDF therapy. Also consider interrupting treatment with TDF in case of progressive decline of renal function when no other cause has been identified.
- Avoid concurrent or recent use of nephrotoxic medicinal products
- TDF may cause a reduction in bone mineral density (BMD). The effects of TDF associated changes in BMD on long term bone health and future fracture risk are currently unknown in children and adolescents.
- If bone abnormalities are suspected or detected, consult with an endocrinologist and/or a nephrologist

Management of renal effects

There are uncertainties associated with the long-term effects of bone and renal toxicity.
Moreover, the reversibility of renal toxicity cannot be fully ascertained. Therefore, a multidisciplinary approach is recommended to adequately weigh on a case by case basis the benefit/risk balance of treatment, decide the appropriate monitoring during treatment (including decision for treatment withdrawal) and consider the need for supplementation.
In clinical studies and post-marketing safety surveillance of TDF in adults, events of renal failure, renal impairment, and proximal renal tubulopathy (including Fanconi syndrome) have been reported. In some patients proximal renal tubulopathy has been associated with myopathy, osteomalacia (manifested as bone pain and infrequently contributing to fractures), rhabdomyolysis, muscle weakness, hypokalaemia and hypophosphatemia.
TDF is not recommended for use in adolescents with renal impairment. TDF should not be initiated in adolescents with renal impairment and should be discontinued in adolescents who develop renal impairment during TDF therapy.
The recommendations for monitoring renal function in adolescent patients without renal risk factors prior to and during TDF therapy are provided in Table 1 below. In patients at risk for renal impairment a more frequent monitoring of renal function is required.

Table 1: Monitoring of renal function in patients without renal risk factors

	Prior to TDF	During 1st 3 months on TDF	>3 months on TDF
Frequency	At baseline	At 2 to 4 weeks and 3 months	Every 3 to 6 months
Parameter	Creatinine clearance and serum phosphate	Creatinine clearance and serum phosphate	Creatinine clearance and serum phosphate

If serum phosphate is confirmed to be <3.0 mg/dL (0.96 mmol/L), renal function should be re-evaluated within one week, including measurements of blood glucose, blood potassium and urine glucose concentrations. If renal abnormalities are suspected or detected then consultation with a nephrologist should be obtained to consider interruption of TDF treatment. Also consider interrupting treatment with TDF in case of progressive decline of renal function when no other cause has been identified.

Use of TDF should be avoided with concurrent or recent use of a nephrotoxic medicinal product and drugs secreted by the same pathway; if concomitant use is unavoidable, renal function should be monitored weekly.

A higher risk of renal impairment has been reported in patients receiving TDF in combination with a ritonavir or cobicistat boosted protease inhibitor. A close monitoring of renal function is required in these patients. In patients with renal risk factors, the co-administration of TDF with a boosted protease inhibitor should be carefully evaluated.

Cases of acute renal failure after initiation of high dose or multiple non-steroidal anti-inflammatory drugs (NSAIDs) have been reported in patients treated with TDF and with risk factors for renal dysfunction.

If TDF is co-administered with an NSAID, renal function should be monitored adequately.

Management of bone effects

TDF may cause a reduction in BMD.

Reductions in BMD have been reported in paediatric patients. In adolescents, the BMD Z-scores at 48 weeks observed in subjects who received TDF were lower than those observed in subjects who received placebo. In children, the BMD Z-scores observed at 48 weeks in subjects who switched to

TDF were lower than those observed in subjects who remained on their stavudine or zidovudine containing regimen. The effects of TDF associated changes in BMD on long term bone health and future fracture risk are currently unknown. If bone abnormalities are suspected or detected, then consultation with an endocrinologist and/or anephrologist should be obtained.

Dosing recommendations for TDF in Adolescents

Tenofovir 245 mg film-coated tablet is approved, in combination with other antiretroviral medicinal products, for the treatment of HIV-1 infected adolescents aged 12 to < 18 years, with NRTI resistance or toxicities precluding the use of first line agents.

The recommended dose of Tenofovir film-coated tablets for the treatment of HIV-1 infection in adolescents aged 12 to <18 years and weighing ≥35 kg is 245 mg. [1]

Close monitoring of efficacy and safety is needed. [1]

[1)] Summary of Product Characteristics Tenofovir 245 mg film-coated tablets

Please report any adverse events suspected to be caused by the use of Tenofovir Disoproxil Rowex to Rowex Ltd, Bantry, Co Cork. Tel 027 50077; fax 027 50417 or the HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie