Amarox

ADVICE FOR HEALTHCARE PROFESSIONALS ON THE USE OF VIRAD (TENOFOVIR DISOPROXIL FUMARATE) FOR THE TREATMENT OF CHRONIC HEPATITIS B AND HIV-1 INFECTION

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This brochure provides important advice on the management of potential renal and bone effects of Virad (tenofovir disoproxil fumarate) with chronic hepatitis B and HIV-1 infection in paediatric and adult patients and on the dosing recommendations for Virad (tenofovir disoproxil fumarate in this population.

Important Points to Consider:

- ✓ Check all patients' creatinine clearance and serum phosphate before starting Virad (tenofovir disoproxil fumarate therapy.
- ✓ During of Virad (tenofovir disoproxil fumarate) 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.
- ✓ Virad (tenofovir disoproxil fumarate) should only be used if the potential benefits of treatment are considered to outweigh the potential risks. In patients with severe renal impairment (creatinine clearance < 30 ml/min) and in patients who require haemodialysis use of Virad (tenofovir disoproxil fumarate) is not recommended. If no alternative treatment is available, the dosing interval must be adjusted and renal function should be closely monitored.
- ✓ Re-evaluate renal function within 1 week if serum phosphate is < 1.5 mg/dl (0.48 mmol/l) or creatinine clearance is decreased to < 50 ml/min during of Virad (tenofovir disoproxil fumarate) therapy.
- ✓ Avoid concurrent or recent use of nephrotoxic medicinal products with of Virad (tenofovir disoproxil fumarate) .
- ✓ Virad (tenofovir disoproxil fumarate) may cause a reduction in bone mineral density (BMD).
- ✓ If bone abnormalities are suspected or detected, then appropriate consultation should be obtained.

Summary of Product Characteristics for Tenofovir Disoproxil 300 mg Film-coated tablets

Monitoring of renal function:

In tenofovir disoproxil clinical studies and post-marketing safety surveillance, rare events of renal failure, renal impairment, and proximal 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 hypophosphataemia.

In children and adolescents:

Here 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.

Patients with impaired renal function:

There are limited data on the safety and efficacy of Virad (tenofovir disoproxil fumarate) in patients with impaired renal function. Therefore, Virad (tenofovir disoproxil fumarate) should only be used if the potential benefits of treatment are considered to outweigh the potential risks. In patients with severe renal impairment (creatinine clearance < 30 ml/min) and in patients who require haemodialysis use of Virad (tenofovir disoproxil fumarate) is not recommended. If no alternative treatment is available, the dosing interval must be adjusted and renal function should be closely monitored. (see the SPC for more information)

The recommendations for monitoring renal function in adult patients without renal risk factors prior to and during Virad (tenofovir disoproxil fumarate) therapy are provided in Table 1. In patients at risk for renal impairment a more frequent monitoring of renal function is required.

Table 1: Monitoring of renal function in adults

	Prior to Tenofovir disoproxil	During 1st 3 months on TDF	>3 months on Tenofovir disoproxil
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

Re-evaluate renal function within one week:

- If serum phosphate is <1.5 mg/dl (0.48 mmol/l) or creatinine clearance is decreased to < 50 ml/min in any adult patient receiving tenofovir disoproxil fumarate.
- If serum phosphate is confirmed to be < 3.0 mg/dl (0.96 mmol/l) in any patient aged 12 to < 18 years.
- If renal abnormalities are suspected, consult a nephrologist.

Re-evaluate measurements of blood glucose, blood potassium and urine glucose concentrations (see section 4.8, proximal tubulopathy).

Consider interrupting treatment with tenofovir disoproxil fumarate:

- In adult patients with creatinine clearance decreased to < 50 ml/min or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l), or when renal function progressively decline and no other cause has been identified.
- In children and adolescents, interrupt treatment in case of progressive decline of renal function when no other cause has been identified.

Use of Virad (tenofovir disoproxil fumarate) 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. 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 Virad (tenofovir disoproxil fumarate) and with risk factors for renal dysfunction. If Virad (tenofovir disoproxil fumarate) is co-administered with an NSAID, renal function should be monitored adequately.

Management of bone effects

Virad (tenofovir disoproxil fumarate) may cause a reduction in BMD. The effects of tenofovir disoproxil fumarate-associated changes in BMD on long-term bone health and future fracture risk are currently unknown.

In HIV infected patients, in a 144-week controlled clinical study that compared Virad (tenofovir disoproxil fumarate) with stavudine in combination with lamivudine and efavirenz in antiretroviral-naïve adult patients, small decreases in bone mineral density (BMD) of the hip and spine were observed in both treatment groups. Decreases in BMD of spine and changes in bone biomarkers from baseline were significantly greater in the Virad (tenofovir disoproxil fumarate) treatment group at 144 weeks. Decreases in BMD of hip were significantly greater in this group until 96 weeks. However, there was no increased risk of fractures or evidence for clinically relevant bone abnormalities over 144 weeks.

Bone abnormalities (infrequently contributing to fractures) may be associated with proximal renal tubulopathy.

If bone abnormalities are detected or suspected, consultation with an endocrinologist and/or nephrologist should be obtained.

Dosing recommendations for Virad (tenofovir disoproxil fumarate)

The recommended dose of Virad (tenofovir disoproxil fumarate) tablets for the treatment of HIV or for the treatment of chronic hepatitis B in adult patients, and in adolescents aged 12 to < 18 years and weighing ≥ 35 kg is 245 mg (one tablet) once daily taken orally with food.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important.

It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via

The National Pharmacovigilance Centre
Saudi Food and Drug Authority
Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa/

Saudi Amarox contact details:
Razan Almalki
Qualified Person for Pharmacovigilance
Al Jamiyah Street, Al Malaz
Riyadh code 12629, Saudi Arabia
E-mail: r.almalki@Amaroxpharma.com
Phone: +966 11 226 8850
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By reporting side effects, you can help provide more information on the safety of Tenofovir disoproxil.

Further information

For further information please refer to the current Virad SmPC.