Tenofovir disoproxil Teva 245 mg Film-coated Tablets (tenofovir disoproxil) Abbreviated Prescribing Information.
Please refer to the Summary of Product Characteristics (SmPC) for full details of prescribing information.

Presentation: Each film-coated tablet contains tenofovir disoproxil phosphate equivalent to 245 mg of tenofovir disoproxil.

Contraindications: This medicinal product should not be used in patients with a history of anaphylactic shock due to tenofovir disoproxil or other components of the formulation.

Indications: Tenofovir disoproxil Teva is indicated in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults. It is indicated for the treatment of HIV-1 infected adolescents aged 12 to <18 years with a history of tenofovir disoproxil use in patients with severe renal impairment (creatinine clearance <30 ml/min) and long-term safety data has not been evaluated for mild renal impairment (creatinine clearance 30-60 ml/min). Should only be used if the potential benefits of treatment are considered to outweigh the potential risks. Refer to the SmPC for dosing recommendations. Hepatic impairment No dose adjustment necessary.

Contraindications: Hypersensitivity to the active substance or any of the excipients. Special warnings and precautions for use: Please refer to the SmPC for detailed information. HIV antibody testing should be offered to all HIV infected patients before initiating tenofovir disoproxil therapy. HIV-1 while effective viral suppression with tenofovir disoproxil has been proven to substantially reduce the risk of sexual transmission, a residual risk cannot be excluded. Precautions to prevent transmission should be taken in accordance with national guidelines. Chronic Hepatitis B: Patients must be advised that tenofovir disoproxil has not been proven to prevent the transmission of HBV to others through sexual contact or by contact with biologic material. Appropriate precautions must continue to be used.

Renal failure, renal impairment, elevated creatinine, hyperphosphataemia and proximal tubulopathy (including Fanconi syndrome) have been reported with the use of tenofovir disoproxil in clinical practice. It is recommended that creatinine clearance is calculated in all patients prior to initiating therapy and renal function (creatinine clearance and serum phosphorus) is also monitored 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. In patients at risk for renal impairment, a more frequent monitoring of renal function is required. Renal safety with tenofovir disoproxil has only been studied to a very limited degree in adult patients with impaired renal function (creatinine clearance <60 ml/min). In patients with severe renal impairment (creatinine clearance <30 ml/min) and in patients who require haemodialysis use of tenofovir disoproxil is not recommended. If no alternative treatment is available, the dosing interval must be adjusted and renal function should be closely monitored.

Alternative treatment regimens should be considered for patients with severe HIV who are at high risk for kidney disease. There are uncertainties associated with the long term effects of bone and renal toxicity in pancreatic patients. 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. Safety and efficacy data are very limited in liver transplant patients. There are limited data on the safety and efficacy in HBV infected patients with decompensated liver disease and who have a Child-Pugh-Turcotte (CPT) score A.

Spontaneous exacerbations in chronic hepatitis B are relatively common and are characterised by transient increases in aminotransferase levels. Acute exacerbation of hepatitis B has also been reported in patients who have discontinued hepatitis B therapy. Liver flares are especially serious, and sometimes fatal in patients with decompensated liver disease. Patients with liver dysfunctions, including chronic active hepatitis, have an increased frequency of liver function abnormalities during combination antiretroviral therapy (CART) and should be monitored according to standard practice. An increase in weight and in levels of blood lipids and glucose may occur during antiretroviral therapy. In HIV infected patients with severe immune deficiency at the time of institution of CART, an inflammatory reaction to asymptomatic or residual opportunistic pathogens may arise and cause serious clinical disorders, or aggravation of symptoms. Although the anaphylaxis is considered to be multifactorial (including concomitant use, alcohol consumption, severe immunosuppression, higher body mass index), cases of anaphylaxis have been reported, particularly in patients with advanced HIV disease and/or long-term exposure to CART. Elderly patients are more likely to have decreased renal function, and caution should be exercised when treating elderly patients with tenofovir disoproxil. Drug interactions: Interaction studies have only been performed in adults. Potential for CYP3A4-mediated interactions (including) and other medicinal products is low. Concomitant use recommended. Should not be administered concomitantly with other medicinal products containing tenofovir disoproxil. Should not be administered concomitantly with lamivudine, emtricitabine, telbivudine or tenofovir alafenamide. Consult the SmPC in relation to other effects. Overdosage: Monitor for evidence of toxicity, and apply standard supportive treatment as necessary. Can be removed by haemodialysis. Legal category: Medicinal product subject to medical prescription. Marketing authorisation number: PA/1998/0001. Marketing authorisation holder: Teva B.V., Swearingen 5, 2551GA Maarn, Netherlands. Full prescribing information available from Teva Pharmaceuticals Ireland, Pier 1, Wing A, Building 1, Firrhill Business & Technology Park, Dublin, Co. Dublin, Telephone: 1800 201 705. Date of Preparation: July 2017. JEIS/N/17/0015c.

Management of bone effects

Reductions in BMD have been reported in HIV infected adolescents. The BMD Z-scores observed in subjects who received Tenofovir disoproxil Teva were lower than those observed in subjects who received placebo.

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

Dosing recommendations for Tenofovir disoproxil Teva in adolescents

Tenofovir disproxiol Teva 245 mg Film-coated Tablets are indicated for the treatment of chronic hepatitis B in adolescents 12 to <18 years of age and weighing ≥35 kg with compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis.

No data are currently available in children with chronic hepatitis B aged 2 to <12 years or weighing ≥35 kg.

In adolescents 12 to <18 years of age and weighing (greater than/equal to) 35 kg, the recommended dose of Tenofovir disoproxil Teva is 245mg (one tablet) once daily taken orally with food.

No adverse drug reactions to Tenofovir disoproxil Teva should be reported to Teva via email to safety@teva.ie or by telephone to +353 51 321538. You can also report side effects directly via the national reporting system: HPRA Pharmacovigilance, Earlsfort Terrace, Dublin, Ireland. Tel: +353 1 6764971; Fax: +353 1 6762517; Email: medssafety@hpra.ie; Website: www.hpra.ie
If serum phosphate is confirmed to be <3.0 mg/dl (0.96 mmol/l) in any adolescent patient receiving tenofovir disoproxil, 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 tenofovir disoproxil treatment. Also consider interrupting treatment with tenofovir disoproxil in case of progressive decline of renal function when no other cause has been identified.

Use of tenofovir disoproxil should be avoided with concurrent or recent use of a nephrotoxic medicinal product and drugs eliminated by the same route; 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 antiinflammatory drugs (NSAIDs) have been reported in patients treated with tenofovir disoproxil and with risk factors for renal dysfunction. If tenofovir disoproxil is co-administered with an NSAID, renal function should be monitored adequately.

Patients with chronic hepatitis B are at risk of kidney damage in connection with the use of products containing tenofovir disoproxil. There are uncertainties associated with the long term effects of bone and renal toxicity in adolescent patients. Moreover, the reversibility of renal toxicity cannot be fully ascertained.

Therefore, a multidisciplinary approach is recommended for the management of adolescent patients in order to adequately weigh the benefit/risk balance of treatment on a case by case basis, decide the appropriate monitoring during treatment (including decision for treatment withdrawal) and consider the need for supplementation.

Special recommendations relating to adolescent patients being treated with regimens based on tenofovir disoproxil are set out below:

- Check all patients’ creatinine clearance and serum phosphate before starting Tenofovir disoproxil Teva therapy.
- During Tenofovir disoproxil Teva 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 overleaf).
- In patients at risk for renal impairment a more frequent monitoring of renal function is required.
- Tenofovir disoproxil Teva should not be used in adolescents with renal impairment. Tenofovir disoproxil Teva should not be initiated in adolescents with renal impairment and should be discontinued in adolescents who develop renal impairment during Tenofovir disoproxil Teva therapy.
- Avoid concurrent or recent use of nephrotoxic medicinal products
- Tenofovir disoproxil Teva may cause a reduction in bone mineral density (BMD). The effects of Tenofovir disoproxil Teva-associated changes in BMD on long term bone health and future fracture risk are currently unknown in adolescents.
- If bone abnormalities are suspected or detected, consult with an endocrinologist and/or a nephrologist.