RENAL MANAGEMENT AND DOSE ADJUSTMENT ADVICE FOR HEALTHCARE PROFESSIONALS WITH ADULT PATIENTS RECEIVING TENOFOVIR DISOPROXIL FUMARATE

HIV-positive patients are at increased risk of renal impairment, requiring baseline and subsequent renal monitoring.[1] For those adult patients on tenofovir disoproxil fumarate (TDF)-based regimens specific recommendations are detailed below. A separate brochure is available for Stribild.

Important Points to Consider

- ✓ Check all patients' creatinine clearance 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 below)
- ✓ In patients at risk for renal impairment a more frequent monitoring of renal function is required
- ✓ In patients with renal impairment, TDF should only be used if the potential benefits of treatment outweigh the potential risks, and the daily dose of TDF may need to be adjusted (see Table 2 overleaf) or the dosing interval of TDF may need to be prolonged (see Table 3 overleaf)
- ✓ Consider interrupting treatment with TDF in patients with creatinine clearance decreased to <50 mL/min or decreases in serum phosphate to <1.0 mg/dL (0.32 mmol/L).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 renal safety profile

In TDF 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.[2–3]

Monitoring of renal function

The recommendations for monitoring renal function in 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[2–3]

	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	Creatinine clearance and serum phosphate	Creatinine clearance and serum phosphate

If serum phosphate is <1.5 mg/dL (0.48 mmol/L) or creatinine clearance is decreased to <50 mL/min in any patient receiving TDF, renal function should be re-evaluated within 1 week, including measurements of blood glucose, blood potassium and urine glucose concentrations. Consideration should also be given to interrupting treatment with TDF in patients with creatinine clearance decreased to <50 mL/min or decreases in serum phosphate to <1.0 mg/dL (0.32 mmol/L) or in case of progressive decline of renal function when no other cause has been identified.[2–3]

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 must 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.[2–3]

Casesofacuterenalfailureafterinitiationofhighdoseormultiplenon-steroidalanti-inflammatorydrugs (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.[2–3]

Use in Renal Impairment

In patients with renal impairment, TDF should only be used if the potential benefits of treatment outweigh the potential risks, and close monitoring of renal function is recommended. TDF is principally eliminated via the kidney and exposure to tenofovir increases in patients with renal dysfunction. Limited data from clinical studies support once daily dosing of TDF in patients with mild renal impairment (creatinine clearance 50–80 mL/min). Administration of Viread 33mg/g granules to provide a reduced daily dose of TDF is recommended in adult patients with creatinine clearance <50 mL/min, including haemodialysis patients, as shown in Table 2. For patients unable to take Viread 33 mg/g granules, prolonged dosage intervals using Viread 245 mg film-coated tablets may be used (Table 3).

Table 2: Recommended daily dose adjustments for patients with renal impairment[1]

	Creatinine clearance (mL/min)				Haemodialysis patients*
	50–80	30–49*	20-29*	10-19*	
Viread 33 mg/g granules	Administration of 245 mg (7.5 scoops) of granules once daily (no adjustment required)	Administration of 132 mg (4 scoops) of granules once daily.	Administration of 65 mg (2 scoops) of granules once daily.	Administration of 33 mg (1 scoop) of granules once daily.	16.5 mg (0.5 scoop) of granules may be administered following completion of each 4 hour haemodialysis session.

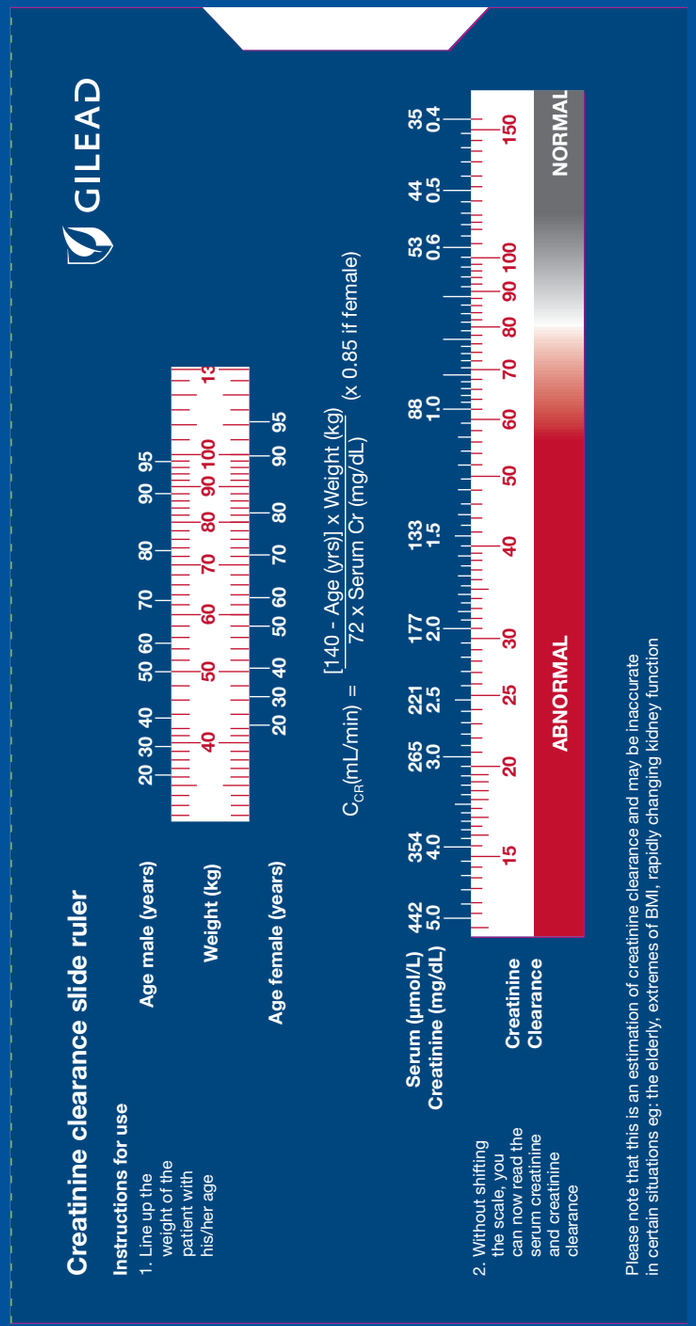
* These dose adjustments have not been confirmed in clinical studies. Therefore, clinical response to treatment and renal function should be closely monitored. No dosing recommendations can be given for non-haemodialysis patients receiving Viread 33 mg/g granules with creatinine clearance <10 mL/min.[3]

The dosing interval adjustment guidelines for patients with creatinine clearance <50 mL/min taking Viread 245 mg film-coated tablets and fixed-dose combinations containing tenofovir disoproxil fumarate are shown in Table 3 below.

Table 3: Dosing interval adjustments for patients with renal impairment[2–3]

	Creatinine clearance (mL/min)			Haemodialysis patients
	50–80	30–49	10–29	
Truvada	Every 24 hours (no adjustment required)	Every 48 hours*	Not recommended for use in patients with severe renal impairment (creatinine clearance <30 mL/min) or in haemodialysis patients	
Viread 245 mg film-coated tablets	Every 24 hours (no adjustment required)	For patients unable to take Viread 33 mg/g granules, administration of Viread 245mg film-coated tablets every 48 hours can be used**	For patients unable to take Viread 33 mg/g granules and with no alternative treatment available, prolonged dose intervals using the 245 mg film-coated tablets may be used: Severe renal impairment – every 72–96 hours (dosing twice a week). Haemodialysis patients – every 7 days following completion of a haemodialysis session.***	

Footnotes can be found on reverse.



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References

1. Gupta SK *et al. Clin Infect Dis* 2005;**40**:1559-1585
2. Truvada Summary of Product Characteristics
3. VIREAD Summary of Product Characteristics

* Dose interval adjustment of Truvada is recommended for patients with creatinine clearance between 30 and 49 mL/min. This dose interval adjustment has not been confirmed in clinical studies and the clinical response to treatment should be closely monitored in these patients. Limited clinical study data suggest that the prolonged dose interval is not optimal and could result in increased toxicity and possibly inadequate response.

** The dose interval adjustment of Viread 245 mg film-coated tablets in patients with moderate (creatinine clearance 30 to 49 mL/min) and severe (below 30 mL/min) renal impairment has not been confirmed in clinical studies and the clinical response to treatment should be closely monitored in these patients. Limited clinical study data suggest that the prolonged dose interval is not optimal and could result in increased toxicity and possibly inadequate response.

*** Assuming 3 haemodialysis sessions per week, each of approximately 4 hours duration or after 12 hours cumulative haemodialysis. No dosing recommendations can be given for non-haemodialysis patients receiving Viread 245 mg film-coated tablets with creatinine clearance <10 mL/min.[5]

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GILEAD

Renal monitoring tool

Prescribing information can be found on the back once unfolded.

VIREAD® PRESCRIBING INFORMATION

Presentation: Viread film-coated tablet containing 245mg of tenofovir disoproxil (as fumarate), equivalent to 300mg of tenofovir disoproxil fumarate, or 136mg of tenofovir. Viread is also available as 33 mg/g granules, 123 mg, 163 mg & 204 mg film-coated tablets. Please refer to the individual SPCs for indications and further information. **Indications:** 1) The treatment of chronic hepatitis B (CHB), in adults with compensated liver disease, with evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis. 2) Evidence of lamivudine-resistant hepatitis B virus. 3) Treatment of CHB in adults with decompensated liver disease. 4) Treatment of CHB in adolescents 12 to < 18 years of age with compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels and histological evidence of active inflammation and/or fibrosis. 5) In combination with other antiretroviral medicinal products for treatment of HIV-1-infected adults. 6) Treatment of HIV 1-infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years. **Dosage & Administration:** Adults: One tablet (245mg) once daily taken with food. Viread available as 33 mg/g granules for the treatment of CHB and HIV-1-infection in adults for whom a solid dosage form is not appropriate. No dose modification necessary in patients with mild to moderate liver disease. Optimal duration of treatment is unknown. Children and adolescents: for the treatment of CHB and HIV-1-infection in adolescents aged 12 to < 18 years and weighing ≥ 35 kg, recommended dose is one tablet (245mg) once daily taken with food. The safety and efficacy of tenofovir disoproxil fumarate in children with CHB aged 2 to < 12 years or weighing < 35 kg and HIV-1-infected children under 2 years of age have not been established. Viread available as 33 mg/g granules for the treatment of CHB and HIV-1 infection in adolescents aged 12 to < 18 years for whom a solid dosage form is not appropriate and for use in HIV-1-infected paediatric patients aged 2 to < 12 years and as reduced tablet strengths for use in HIV-1-infected paediatric patients aged 6 to < 12 years. Not recommended in paediatric patients with renal impairment. No dose adjustment is required in patients with hepatic impairment. Please refer to the SPCs for Viread 33 mg/g granules & 123 mg, 163 mg & 204 mg film-coated tablets. Elderly: Insufficient data are available on which to make dose recommendations for patients over the age of 65 years – caution should be exercised. **Contraindications:** Known hypersensitivity to tenofovir, tenofovir disoproxil fumarate, or any of the excipients. **Warnings and Precautions:** Renal: If Viread is co administered with a non-steroidal anti-inflammatory drug (NSAID), renal function should be monitored adequately. A higher risk of renal impairment has been reported in patients receiving tenofovir disoproxil fumarate in combination with a ritonavir or cobicistat boosted protease inhibitor. A close monitoring of renal function is required in these patients. Renal failure and impairment, elevated creatinine, hypophosphataemia and proximal tubulopathy (including Fanconi syndrome) have been reported with the use of tenofovir disoproxil fumarate in clinical practice. It is recommended that CrCl is calculated in all patients prior to therapy initiation and renal function 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 of renal impairment, a more frequent monitoring of renal function is required. There are limited data on the safety and efficacy of tenofovir disoproxil fumarate in adult patients with impaired renal function. Tenofovir disoproxil fumarate should only be used in these patients if the potential benefits outweigh the risks. Interrupting treatment with tenofovir disoproxil fumarate should also be considered in case of progressive decline of renal function when no other cause has been identified. For adult patients with moderate (CrCl < 30-49 ml/min) or severe (CrCl < 30 ml/min) renal impairment including haemodialysis patients, daily dose adjustment using Viread 33 mg/g granules is recommended. Refer to SPC for dosing and monitoring recommendations. For adult patients with moderate and severe renal impairment who are unable to use the granules formulation, and with no alternative treatment available, prolonged dose intervals using Viread 245 mg film-coated tablets may be used. Refer to SPC for dose adjustment and monitoring recommendations. Not recommended in paediatric patients with renal impairment. Tenofovir disoproxil fumarate should be discontinued in paediatric patients who develop renal impairment during therapy. HIV Co-infection: HIV antibody testing should be offered to all HBV-infected patients before initiating tenofovir disoproxil fumarate therapy. Due to the risk of development of HIV resistance, tenofovir disoproxil fumarate should only be used as part of an appropriate antiretroviral combination regimen in HIV/HBV co-infected patients. Patients must be advised tenofovir disoproxil has not been proven to prevent the risk of transmission of HIV or HBV to others through sexual contact or contamination with blood and appropriate precautions must be used. Exacerbations of hepatitis: Flares on treatment: Spontaneous exacerbations in CHB are relatively common. Patients with cirrhosis may be at higher risk for hepatic exacerbations and therefore should be monitored closely. However it also should be noted that increase in ALT can be part of HBV clearance during therapy with tenofovir. Flares after treatment discontinuation: Acute exacerbations of hepatitis have also been reported in patients who have discontinued hepatitis B therapy. Hepatic function should be monitored at repeated intervals with both clinical and laboratory follow-up for at least 6 months after discontinuation of therapy. Treatment discontinuation is not recommended in patients with advanced liver disease or cirrhosis, since post-treatment exacerbations of hepatitis may lead to hepatic decompensation. Co-infection with hepatitis C or D: There are no data on the efficacy of tenofovir in patients co-infected with hepatitis C or D virus. Hepatic decompensation: There are limited data on the safety and efficacy of tenofovir disoproxil fumarate in HBV-infected patients with decompensated liver disease and who have a Child Pugh Turcotte (CPT) score > 9. These patients may be at higher risk of experiencing serious hepatic or renal adverse reactions. Therefore, hepatobiliary and renal parameters should be closely monitored in this patient population. Hepatic disease: Safety and efficacy data are very limited in liver transplant patients. Other: Lactic acidosis and lipodystrophy – refer to SPC for recommendations regarding monitoring. Viread may cause a reduction in bone mineral density. If bone abnormalities are detected/suspected in paediatric patients, consult an endocrinologist and/or nephrologist. Bone abnormalities (may be associated with proximal renal tubulopathy). Triple nucleoside/nucleotide therapy: Mitochondrial dysfunction. Immune Reactivation Syndrome. Osteonecrosis. Avoid in antiretroviral experienced patients harbouring K65R mutation. Please refer to the summary of product characteristics for further information. **Interactions:** Low potential for CYP450 mediated interactions with other medicinal products. Viread should not be administered concomitantly with other medicinal products containing tenofovir disoproxil fumarate or adefovir dipivoxil, nephrotoxic agents or medicinal products that reduce renal function or compete for active tubular secretion. Monitor renal function if tenofovir disoproxil fumarate administered with tacrolimus. Co-administration with didanosine is not recommended as it may result in a 40-60% increase in systemic exposure to didanosine which may increase the risk of didanosine-related adverse events. Co-administration with 400 mg daily didanosine has been associated with significant decreases in CD4 cell counts. A reduced dose of 250 mg didanosine administered with tenofovir disoproxil fumarate has been associated with reports of high rates of virological failure. Co-administration with lopinavir/ritonavir; 30% increase in tenofovir AUC. Co-administration with atazanavir/ritonavir decreased atazanavir concentrations, but increased exposure to tenofovir. Higher tenofovir concentrations could potentiate tenofovir associated adverse events including renal disorders. Food has been shown to enhance the bioavailability of Viread. Refer to SPC for drug interaction details for protease inhibitors, NRTIs, NNRTIs. **Use in pregnancy and lactation:** The use of Viread may be considered during pregnancy. Viread should not be used during breast feeding. **Side effects:** Very commonly reported adverse events (≥1/10): hypophosphataemia*, dizziness, diarrhoea, vomiting, nausea, rash, asthenia. Common (≥1/100 to <1/10): flatulence, headache, abdominal pain, abdominal distension, fatigue, increased transaminases. Uncommon (≥ 1/1,000 to < 1/100): hypokalaemia*, pancreatitis, rhabdomyolysis*, muscular weakness, increased creatinine. Rare (≥1/10,000, <1/1,000): lactic acidosis, hepatic steatosis, hepatitis, angioedema, osteomalacia*, myopathy*, renal failure, acute renal failure, proximal renal tubulopathy including Fanconi syndrome, acute tubular necrosis, nephritis, nephrogenic diabetes insipidus. The side effects marked * may occur as a consequence of proximal renal tubulopathy. In patients with generally acknowledged risk factors, advanced HIV disease or long-term exposure to combination antiretroviral therapy (CART), cases of osteonecrosis have been reported. Inflammatory reaction to asymptomatic or residual opportunistic infections may arise in patients with severe immunodeficiency at the time of initiation of CART. CART has been associated with metabolic abnormalities such as hypertriglyceridaemia, hypercholesterolaemia, insulin resistance, hyperglycaemia, hyperlactataemia and lipodystrophy. In patients with CHB, exacerbations of hepatitis during treatment may arise. Refer to SPC for full information on adverse events. **Overdosage:** If overdose occurs, monitor for evidence of toxicity. Apply standard supportive treatment if necessary. Tenofovir can be removed by haemodialysis. **Pharmaceutical Precautions:** No special precautions for storage or handling. **Package Quantities:** Bottle of 30 film coated tablets **Marketing Authorisation numbers:** EU/1/01/200/001-009 Further information is available from the marketing authorisation holder: Gilead Sciences International Ltd, Granta Park, Abington, Cambridge CB21 6GT. Telephone: + 44 (0) 8000 113 700. Email: ukmedinfo@gilead.com

CONSULT THE SUMMARY OF PRODUCT CHARACTERISTICS BEFORE PRESCRIBING PARTICULARLY IN RELATION TO SIDE EFFECTS, PRECAUTIONS AND CONTRAINDICATIONS.
Viread is a registered trademark
Date of PI preparation: November 2014.

Suspected adverse drug reactions (ADRs) should be reported to the Medicines Authority Post-Licensing Directorate, 203, Level 3, Rue D'Argens, Gzira GZR 1368, MALTA or at http:/www.medicinesauthority.gov.mt./adrportal

Suspected adverse drug reactions may also be reported to GILEAD SCIENCES INTERNATIONAL LTD via email to csafety@gilead.com or tel: +44 (0) 1223 897500 or to AM MANGION Ltd via email to pv@ammangion.com.mt or tel: (+356) 2397 6333

TRUVADA® PRESCRIBING INFORMATION

Presentation: Truvada film-coated tablet. Each tablet contains 200mg of emtricitabine and 245mg of tenofovir disoproxil (equivalent to 300mg of tenofovir disoproxil fumarate or 136mg of tenofovir). **Indications:** In antiretroviral combination therapy for treatment of HIV-1 infected adults aged 18 years and over. **Dosage & Administration:** Adults: One tablet once daily taken orally with food. Children and adolescents: The safety and efficacy has not been established. No data are available on which to make dose recommendations for patients over the age of 65 years. Limited data from clinical studies support once daily dosing in patients with mild renal impairment (CrCl 50-80ml/min). Dosing interval adjustment required in patients with moderate renal impairment (CrCl between 30 and 49ml/min) – refer to SPC. Not recommended in severe renal impairment (CrCl <30ml/min) or in haemodialysis patients. **Contraindications:** Hypersensitivity to emtricitabine, tenofovir, tenofovir disoproxil fumarate, or any of the excipients. **Warnings and Precautions:** Please refer to the summary of product characteristics for further information. Appropriate precautions must be used to prevent the risk of transmission of HIV to others through sexual contact or contamination with blood. Elderly: Truvada has not been studied in patients over the age of 65. Elderly patients are more likely to have decreased renal function; therefore caution should be exercised when treating elderly patients with Truvada. Renal: Renal failure and impairment, elevated creatinine, hypophosphataemia and proximal tubulopathy (including Fanconi syndrome) have been reported with use of tenofovir disoproxil fumarate in clinical practice. It is recommended that CrCl is calculated in all patients prior to therapy initiation and renal function 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 of renal impairment, a more frequent monitoring of renal function is required. Risk-benefit assessment and monitoring of renal function is needed when Truvada is used in patients with CrCl <60ml/min. Monitor for signs of toxicity and changes in viral load following introduction of Truvada at prolonged dosing intervals. Not recommended where CrCl <30ml/min or in haemodialysis. If CrCl is decreased to <50ml/min or serum phosphate is decreased to <1.5mg/dl, renal function should be re-evaluated within one week. Consideration should also be given to interrupting treatment with Truvada in patients with creatinine clearance decreased to < 50 ml/min or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l). Interrupting treatment with Truvada should also be considered in case of progressive decline of renal function when no other cause has been identified. Refer to SPC for further recommendations regarding monitoring and dose adjustment. Avoid with concurrent or recent use of nephrotoxic medicinal product. If concomitant use of Truvada and nephrotoxic agents is unavoidable, renal function should be monitored weekly. If Truvada is co administered with a non-steroidal anti-inflammatory drug (NSAID), renal function should be monitored adequately. A higher risk of renal impairment has been reported in patients receiving tenofovir disoproxil fumarate in combination with a ritonavir or cobicistat boosted protease inhibitor. A close monitoring of renal function is required in these patients. HBV co-infection: HIV infected patients co infected with HBV virus may experience acute exacerbations of hepatitis associated with immune reactivation syndrome following the initiation of antiretroviral therapy. Co-infected HIV/HBV patients should be closely monitored for at least several months following discontinuation of Truvada for symptoms of exacerbation of hepatitis. Hepatic: Patients with pre-existing liver dysfunction should be monitored; interruption or discontinuation of treatment must be considered if evidence of worsening liver disease. Other: Lactic acidosis and lipodystrophy – refer to SPC for recommendations regarding monitoring and management. Rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption. Mitochondrial dysfunction. Immune Reactivation Syndrome. Osteonecrosis. Decreased bone mineral density and bone abnormalities. Co-administration of tenofovir disoproxil fumarate and didanosine is not recommended as it may result in 40-60% increase in systemic exposure to didanosine which may increase the risk of didanosine-related adverse events. Rare cases of pancreatitis and lactic acidosis, sometimes fatal, have been reported. Co-administration with 400mg daily didanosine has been associated with significant decreases in CD4 cell counts. A reduced dose of 250mg didanosine administered with tenofovir disoproxil fumarate has been associated with reports of high rates of virological failure. Avoid in antiretroviral experienced patients with strains harbouring K65R mutation. **Interactions:** As a fixed combination, Truvada should not be administered concomitantly with medicinal products containing any of the components, emtricitabine or tenofovir disoproxil fumarate. Truvada should not be administered concomitantly with adefovir dipivoxil. Low potential for CYP450 mediated interactions with other medicinal products. Co-administration of Truvada with medicinal products that are eliminated by active tubular secretion or via the anion transporter may lead to an increase in serum concentrations of Emtricitabine or the co-administered product. Avoid concurrent or recent use of nephrotoxic medicinal product. Co-administration with lamivudine not recommended. Co-administration with lopinavir/ritonavir; lead to a 30% increase in tenofovir AUC*. Co-administration with didanosine is not recommended. Co-administration with atazanavir decreased atazanavir concentrations. Co-administration with atazanavir/ritonavir slightly reduced negative impact of tenofovir on atazanavir, but increased exposure to tenofovir*. *Higher tenofovir concentrations could potentiate tenofovir associated adverse events, including renal disorders. **Use in pregnancy and lactation:** The use of Truvada may be considered during pregnancy. Truvada should not be used during breast feeding. **Side effects:** Very common (≥1/10): hypophosphataemia, dizziness, headache, diarrhoea, nausea, vomiting, rash, elevated creatine kinase, asthenia. Common (≥1/100, <1/10): neutropenia, allergic reaction, hypertriglyceridaemia, hyperglycaemia, insomnia, abnormal dreams, flatulence, dyspepsia, abdominal pain, elevated serum lipase, elevated amylase including elevated pancreatic amylase, abdominal distention, hyperbilirubinaemia, increased transaminases, elevated serum aspartate aminotransferase (AST) &/or elevated serum alanine aminotransferase (ALT), pruritus, maculopapular rash, urticaria, vesiculobullous rash, pustular rash and skin discolouration (increased pigmentation), pain. In addition, anaemia was common and skin discoloration very common when emtricitabine was administered to paediatric patients. Uncommon (≥1/1,000, <1/100): anaemia, hypokalaemia, pancreatitis, angioedema, rhabdomyolysis, muscular weakness, increased creatinine, and proteinuria. Rare (≥1/10,000, <1/1,000): lactic acidosis, hepatic steatosis, hepatitis, osteomalacia (manifested as bone pain and infrequently contributing to fractures), myopathy, renal failure (acute and chronic), acute tubular necrosis proximal renal tubulopathy including Fanconi syndrome, nephritis (including acute interstitial nephritis), nephrogenic diabetes insipidus. Some of these side effects may occur as a consequence of proximal renal tubulopathy. Cases of osteonecrosis have been reported, particularly in patients with generally acknowledged risk factors, advanced HIV disease or long term exposure to CART. The frequency of this is unknown. Combination antiretroviral therapy has been associated with metabolic abnormalities and lipodystrophy. Refer to SPC for full information regarding side effects. **Overdosage:** If overdosage occurs, monitor for evidence of toxicity. Apply standard supportive treatment if necessary. Emtricitabine and tenofovir can be partially removed by haemodialysis. **Pharmaceutical precautions:** No special requirements for use and handling. Store in the original package in order to protect from moisture. Keep the bottle tightly closed. **Package Quantities:** Bottle of 30 film-coated tablets. **Marketing Authorisation Number:** EU/1/04/305/001. Further information is available from the marketing authorisation holder: Gilead Sciences International Ltd, Granta Park, Abington, Cambridge CB21 6GT. Telephone: + 44 (0) 8000 113 700. Email: ukmedinfo@gilead.com

CONSULT THE SUMMARY OF PRODUCT CHARACTERISTICS BEFORE PRESCRIBING PARTICULARLY IN RELATION TO SIDE EFFECTS, PRECAUTIONS AND CONTRAINDICATIONS.
Truvada is a trademark
Date of PI preparation: January 2015

Suspected adverse drug reactions (ADRs) should be reported to the Medicines Authority Post-Licensing Directorate, 203, Level 3, Rue D'Argens, Gzira GZR 1368, MALTA or at http:/www.medicinesauthority.gov.mt./adrportal

Suspected adverse drug reactions may also be reported to GILEAD SCIENCES INTERNATIONAL LTD via email to csafety@gilead.com or tel: +44 (0) 1223 897500 or to AM MANGION Ltd via email to pv@ammangion.com.mt or tel: (+356) 2397 6333

Prescribing information can be found within