Journal of Virus Eradication

Volume 3

www.viruseradication.com

Issue 2

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Switch your treatment-experienced patients to

THE ONLY TREATMENT OPTION THAT **TARGETS CCR5-TROPIC VIRAL ENTRY**



Celsentri is indicated for your treatment-experienced adult patients with CCR5-tropic HIV-1 infection in combination with other ARVs.

Celsentri is a well-tolerated treatment option that has no cross-resistance to other ARV classes.^{1,2}

The image above shows the antiretroviral drug maraviroc (depicted in orange) binding to the CCR5 receptor. CCR5 with bound maraviroc is stabilized in an inactive conformation which prevents HIV from using the receptor for cell entry.^{3,4}

Celsentri® maraviroc 150mg and 300mg tablets

Prescribing Information

See Summary of Product Characteristics (SPC) before prescribing.

Indication: IVI in >18 years as part of combination therapy for treatment-experienced adults with only CCR5-tropic HIV-1. **Dosage and administration:** CCR5 tropism status must be confirmed shortly before starting Celsentri. *Adults:* Orally: Celsentri 150 mg, 300 mg or 600 mg twice daily depending on interactions with co-administered antiretroviral therapy and other medicinal products (see SPC). Celsentri can be taken with or without food. *Elderly:* Limited data in 65+ yrs. *Renal* impairment: Caution and adjust Celsentri dosage interval in patients with creatinine clearance < 80ml/min taking potent CYP3A4 inhibitors (see SPC). Hepatic impairment: Caution due to < 80m//min taking potent CYP3A4 inhibitors (see SPC). Hepatic impairment: Caution due to lack of data. Contraindications: hypersensitivity to any ingredient (including peanut or soya). Warnings and precautions: Risk of severe skin & hypersensitivity reactions. Discontinue Celsentri and other suspect agents immediately if suspected. Not recommended in treatment naïve patients. Adjust Celsentri dose and/or dose interval when co-administered with interacting medication. Risk of dose-related dizziness: caution patients with a history of postural hypotension or receiving medicines known to lower blood pressure. Risks of ostenerosis, immune reactivation syndrome, potential effect on immunity. Use Celsentri with caution in patients with severe cardiovascular disease, severe renal insufficiency, reduced hepatic function, significant underbring liver diserders, hepatitis PLC acid inforting are read-immented to to lave, of data underlying liver disorders, hepatitis B/C co-infection or renal impairment due to lack of data

Consider discontinuation of Celsentri in any patient with signs or symptoms of acute hepatitis. Celsentri contains soya lecithin. **Interactions:** Celsentri is a substrate of (but does not inhibit or induce) CYP3A4. See SPC for dose adjustment guidance when co-administering Celsentri with CYP3A4 inhibitors and/or inducers. Use with fosamprenavir/ritonavir, St John's Wort or two inducers (e.g. rifampicin + efavirenz) not recommended. Caution with dabigatran etexilate. **Pregnancy and lactation:** Not recommended. Avoid breast-feeding. **Side effects:** See SPC for full datalis. Huncen discharge fortune, baddebe addebing in flotupeer cash actbong in prompine incompared. details. Nausea, diarrhoea, fatique, headache, abdominal pain, flatulence, rash, asthenia, insomnia depression, anorexia, anaemia and increased levels of alanine aminotransferase and aspartate. Rarely, neoplasms, blood disorders, cardiac disorders, hepatotoxicity, Stevens Johnson syndrome, toxic epidemal necrolysis, muscle atrophy. **Basic NHS cost**: 150mg: 60 tablets £519.14 EU/1/07/418/003; 300mg : 60 tablets £519.14 EU/1/07/418/008. MA holder: ViiV Healthcare UK Ltd, 980 Great West Road, Brentford, Middlesex TW8 9GS. Further information available from Customer Contact Centre, GlaxoSmithKline UK Ltd, Stockley Park West, Uxbridge, Middlesex UB11 1BT.

POM S1A

Celsentri is a registered trademark of the ViiV Healthcare Group of Companies. Date of Approval: October 2016

Zinc code: UK/MVC/0007/13(3)

ELSENTRI

(maraviroc) tablets

Adverse events should be reported. For the UK, reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to GlaxoSmithKline on 0800 221 441.

Adverse events should be reported. For Ireland, adverse events should be reported directly to the HPRA; Freepost, Pharmacovigilance Section, Health Products Regulatory Authority, Earlsfort Terrace, Dublin 2, Tel: +353 1 676 4971, medsafety@hpra.ie. Adverse events should also be reported to GlaxoSmithKline on 1800 244 255.

References: 1. Gulick RM, Lalezari J, Goodrich J, et al. Maraviroc for previously treated patients with R5 HIV-1 infection. N Engl J Med. 2008;359(14):1429-1441. 2. Dorr P, Westby M, Dobbs S, et al. Maraviroc (UK-427,857), a potent, orally bioavailable, and selective small molecule inhibitor of chemokine receptor CCR5 with broad-spectrum antihuman immunodeficiency virus type 1 activity. Antimicrob Agents Chemother. 2005;49(11):4721-4732. 3. Tan Q, Zhu Y, Li J, et al. Structure of the CCR5 chemokine receptor—HIV entry inhibitor maraviroc complex. Science. 2013;341:1387-1390. 4. The Scripps Research Institute. Molecular structure reveals how HIV infects cells. http://www.scripps.edu/news/press/2013/20130912stevens html. Published September 12, 2013, Accessed January 9, 2017.



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Date of preparation: January 2017 VIIV/MVC/0004/16

PRESCRIBING INFORMATION: Consult the Summary of Product angioedema & puritus. Legal Category: POM. Pack: Bottle of Characteristics (CPC) before prescribing 30 film-coated tablets. Price: UK NHS List Price - 6879.51: Éire/Ireland ricitabine 200mg/ tenofovir alafenamide 10mg or ated tablets

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 Indication: In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults & adolescents (aged 2 years, weighing at least 35 kg). Dose adolescents (aged 2 years, weighing at least 35 kg). Dose tablet, once daily, orally with or without food. The dose of Descoy should be administered according to the third agent in the HIV treatment regimen. Please consult the SPC for further information. *Children (s.12) years, or weighing at 35 kg)*. Safety & efficacy has not been established. Elderly: No dose adjustment is required in adult or adolescent patients (aged ≥ 12 years, weighing at least 35 kg). With estimated creatinine clearance (CrCI) ≥ 30 mL/min during at least 35 kg) with estimated creatinine clearance (CrCI) ≥ 30 mL/min during at least 35 kg) with estimated the patic impairment: not recommended. Should be adjustment required. Severe hepatic impairment: not recommended. Should be adolescents (aged 2 years & older weighing at least 35 kg) with estimated creatinine clearance (CrCI) ≥ 30 mL/min during at least 35 kg) with estimated creatinine clearance (CrCI) ≥ 30 mL/min during at least 35 kg) with estimated creatinine clearance (CrCI) ≥ 30 mL/min during at least 35 kg) with estimated creating at least 35 kg) with estimated creating at least 35 kg) with estimated creating to the commended. Should be adjustment reguired. Severe hepatic impairment: not recommended for any excipients. Warnings & Precautions: Safety & efficacy in HBV/ HBV or olicitations: Hypersensitivity to the active substances or to any excipients. Warnings & Precautions: Safety & efficacy in HBV/ HBV **Indication:** In combination with other antiretroviral agents for the any excipients. Warnings & Precautions: Safety & efficacy in HBV/ HCV co-infected hIV/HBV patients should be closely monitored for at least several months following discontinuation for symptoms of severe acute exacerbations of hepatitis. Descovy should be avoided in antiretroviral patients with HIV-I harbouring the K65R mutation. Risks of mitochondrial dysfunction, immune reactivation syndrome, opportunistic infections, osteonecrosis with CART therapy. Interactions: Co-administration with certain anticonvulsants (eg., carbamazepine, oxcarbazepine, phenobarbital & phenytoin), antimycobacterials (eg., rifampicin, ifabutia, 8; faganetino). Decogravity clappene. ifabutin & rifapentine), boceprevir, telaprevir, St. John's wort and HIV Pls other than atazanavir, lopinavir and darunavir is not recommended. PIs other than atazana'ur, lopinavir and darunavir is not recommended. Should not be administered concomitantly with medicines containing tenofovir disoproxil (as fumarate), lamivudine or adefovir dipivoxil. Co-administration of emtricitabine with medicinal products that are eliminated by active tubular secretion may increase concentrations of entricitabine. Medicinal products that decrease renal function may increase concentrations of emtricitabine. Medicinal products that induce P-glycoprotein (P-gp) are expected to decrease the absorption of tenofovir alafenamide, which may lead to loss of therapeutic effect of Descovy and development of resistance. Co-administration with medicinal products that inhibit P-gp are expected to increase the absorption and plasma concentration of tenofovir alafenamide. Tenofovir alafenamide is a substrate of OATPIBI and OATPIB3 *in vitro*. The distribution of tenofovir alafenamide in the body may be affected The distribution of tenofovir alafenamide in the body may be affected by the activity of OATP1B1 and OATP1B3. **Pregnancy & lactation:** Use by the activity of OATPID and OATPIDS, regulately a treatment of the potential risk to the potential breakfi justifies the potential risk to the foetus. Breast-feeding; not recommended. Side effects: Refer to SPC for full information regarding side effects. Very common ($\frac{1}{2}$ /100); Nausea. Common ($\frac{1}{2}$ /100 to $\frac{1}{100}$; Headache, dizziness, diarrhoea, vomiting, abdominal pain, flatulence, abnormal dreams, rash & fatigue. ngjoedema & pruritus. Legal Category: POM. Pack: Bottle of o film-coated tablets. Price: UK NHS List Price - £355.73; Eire/Ireland €587.98. Marketing Authorisation Number: EU/1/16/1099/001; - 658/395. Marketing Authorisation Number: EU//16/1099/001; EU//16/1099/003, Further information is available from Gilead Sciences Ltd, 280 High Holborn, London, WCIV 7EE, UK; Telephone: +44 (0) 8000 113700, For Ireland: +353 214 825 999. E-mail: Ukmedinfo@gilead.com. Descovy is a trademark. Date of approval: June 2016; FTAF/UK/16-03/MM/1052(1).

▼ This medicinal product is currently subject to additional monitoring. 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. Any suspected adverse reactions to Descovy should ted to Gilead via email to Safety_FC@gilead.com or by telephone +44 (0) 1223 897500.

PRESCRIBING INFORMATION: Consult the Summary of Product

PRESCRIBING INFORMATION: Consult the Summary of Product Characteristics before prescribing. GENVOYA'♥ elvitegravir 150mg/cobicistat 150mg/emtricitabine 200mg/ tenofovir alafenamide 10mg film coated tablets. Indication: Treatment of HIV-1 infection in adults & adolescents (aged 12 years & older weighing at least 35 kg) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir. Dosage: Adults & adolescents (aged ≥ 12 years. weighing at least 35 kg): One tablet, once daily, orally & whole with food. Children (<12 years or weighing <35 kg): Safety & efficacy has not been established. Elderly: No dose adjustment is required. Renal: No dose adjustment is required in adult or adolescent batients Renal: No dose adjustment is required in adult or adolescent patients $aged \ge 12$ years, weighing at least 35 kg) with estimated creatinine clearance (CrCl) \ge 30 mL/min. In patients with CrCl < 30 mL/min: Elearance (CrCl) ≥ 30 mL/min. In patients with CrCl < 30 mL/min. not recommended. Should be discontinued in patients whose CrCl declines to < 30 mL/min during treatment. <u>Hepatic:</u> Mild/moderate nepatic impairment: no dose adjustment required. Severe hepatic mpairment: not recommended. **Contraindications**: Hypersensitivity to the active substances or to any excipients. Co-administration with alfuzosin, amiodarone, quinidine, carbamazepine, phenobarbital, phenytoin, rifampicin, dihydroergotamine, ergometrine, ergotamine, atment of pulmonary arterial hypertension & oral midazolam & am. Warnings & Precautions: Should not be co-administered ther antiretroviral products. Safety & office-ction has explan apride. St. John's wort. Iovastatin. simvastatin. pim triazolam, Warnings & Precautions: Should not be co-administered with other antiretroviral products. Safety & efficacy in HBV/HCV co-infection has not been established. Co-infected HIV/HBV patients should be closely monitored for at least several months following discontinuation for symptoms of severe acute exacerbations of hepatitis. Should not be administered concomitantly with medicines containing tenofovir disoproxil (as fumarate), lamivudine or adefovir for treatment of HBV infection. Patients with galactose intolerance, Lapp lactase deficiency & glucose-galactose malabsorption should not take Genvoya. Women of childbearing potential should use either a hormonal contraceptive containing at least 30 µg ethinylestradiol of contraception. Risks of mitochondrial dysfunction, immune reactivation syndrome, oportunistic infections, osteonecrosis with eactivation syndrome, opportunistic infections, osteonecrosis with iucleoside analogues & CART therapy. Interactions: Co-administration with modicines that induce (15th) CORT with medicines that induce/inhibit CYP3A may affect the exposure of elvitegravir by decreasing its plasma concentrations leading to a reduced therapeutic effect of Genvoya. Cobicistat is an inhibitor OCYP3A & is a CYP3A substrate. Medicines highly dependent on CXP3A metabolism & have high first pass metabolism are most susceptible to large increases in exposure when co-administered with cobicistat. Medicines that inhibit CYP3A may decrease the clearance of cobicistat, resulting in increased plasma concentrations of cobicistat. Co-administration with medicines that are substrates of P-gp. BCRP, OATPIB & OATPIBT any result in increased plasma concentrations of these products. Medicines that decrease renal function may increase concentrations of emtricitabine. **Pregnancy** & lactation: Should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. It should no be used during breast-feeding. Side effects: Refer to SPC for full information regarding side effects. <u>Very common (a1/10)</u>; Nausea. <u>Common (a1/100 to <1/10)</u>; headache, dizziness, diarrhoea, vomiting, abdominal pain, flatulence, abnormal dreams, rash & fatigue. <u>Uncommon (a1/1000 to <1/100</u>): anaemia, depression, dyspepsia, vith medicines that induce/inhibit CYP3A may affect the exposure

alafenamide 25mg film coated tablets. Indication: Treatment of HIV-1 infection in adults & adolescents (aged 12 years & older weighing at least 35 kg) without any known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor class, tenofovir or emtricitabine and with a viral load < 100,000 HIV-1 RNA copies/mL. **Dosage**: Adults & adolescents (aged > 12 years, weighing at least 35 kg): One tablet, once daily, orally with food. Children (< 12 years or weighing < 35 kg): Safety & efficacy has not been established. <u>Eldery</u>: No dose adjustment is required. <u>Benal</u>: No dose adjustment is required in adult or adolescent patients (aged > 12 wars, weighing at least 25 kg): Who setimeted required, <u>kenal</u>, No dose adjustment is required in aduit or addrescent patients (<u>adde 12</u> years, <u>weighing at least 35 ka</u>) with estimated creatinine clearance (CrCl) > 30 mL/min. In patients with CrCl < 30 mL/mir: not recommended. Should be discontinued in patients whose CrCl declines to < 30 mL/min during treatment. <u>Hepatic</u>: Mild/moderate hepatic impairment: no dose adjustment required Use with caution in patients with moderate hepatic impairment Severe hepatic impairment: not recommended. **Contraindications:** Hypersensitivity to the active substances or to any excipients. It should not be co-administered with medicines that can result in significant decreases in rilpivirine plasma concentrations (due to cytochrome P450 [CYP]3A enzyme induction or gastric pH increase), cytochrome P450 [CYP]3A enzyme induction or gastric pH increase), which may result in loss of therapeutic effect of Odefsey including: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampicin, rifapentine, omeprazole, esomeprazole, dexlansoprazole, lansoprazole, pantoprazole, rabeprazole, dexamethasone (oral and parenteral doses), except as a single dose treatment, St. John's parenteral doses), except as a single dose treatment, St. John's wort, Warnings & Precautions: There are insufficient data to justify the use in patients with prior NNRTI failure. Resistance testing and/or historical resistance data should guide the use of Odefsey. At supratherapeutic doses (75 mg once daily and 300 mg once daily), rilpivirine has been associated with prolongation of the QTc interval of the electrocardiogram (ECG). Should be used with caution when co-administered with medicines with a known risk of Torsade de Pointes. Safety & efficacy in HBV or HCV co-infection has not been established. Co-infected HIV/HBV patients should be closely monitored with both clinical and laboratory follow up for at least several months following discontinuation for sevents. several months following discontinuation for symptoms of severe acute exacerbations of hepatitis. The safety and efficacy of Odefsey acute exacerbations of hepatitis. The safety and efficacy of Odefsey in patients with significant underlying liver disorders have not been established. Risks of mitochondrial dysfunction, immune reactivation syndrome, opportunistic infections, osteonecrosis with CART therapy. Should not be co-administered with other antiretroviral medicines or with other medicines containing tenofovir alafenamide, lamivudine, tenofovir disoproxil (as fumarate) or adefovir dipivoxil. Interactions: Co-administration of emtricitabine with medicines that are eliminated by active tubular secretion may increase concentrations of emtricitabine and/or the co-administered Much medicines that are eminimated by active (ubduar secretion insteaded increase concentrations of emtricitabine and/or the co-administered medicines. Medicines that induce or inhibit CYP3A may thus affect the clearance of ripivirine. Medicines that induce P-glycoprotein (P-gp) are expected to decrease the absorption of tenofovir alafenamide, resulting in decreased plasma concentration of tenofovir alafenamide, which may lead to loss of therapeutic effect of Odefsey and development of resistance. Co-administration with medicines that inhibit P-gp are expected to increase the absorption and plasma concentration of tenofovir alafenamide. Tenofovir alafenamide is a substrate of OATPIB1 and OATPIB3 *in vitro*. The distribution of tenofovir alafenamide in the body may be affected by the activity of OATPIB1 and OATPIB3. **Pregnancy & lactation:** Use in pregnancy only if potential benefit justifies the potential risk to the foetus. Breast-feeding; not recommended. **Side effects**: Refer to SPC for full information regarding side effects. <u>Very common</u> <u>>1/10):</u> increased total cholesterol (fasted), increased LDL cholesterol (a)/(D); increased total cholesterol (fasted), increased DL cholesterol (fasted), insomnia, headache, dizziness, nausea, increased pancreatic amalyse, increased transaminases (AST and/or ALT). <u>Common (a)/(00</u> to c1/(0); decreased white blood cell count, decreased haemoglobin, decreased platelet count, decreased appetite, increased triglycerides (fasted), depression, abnormal dreams, sleep disorders, depressed mood, somolence, abdominal pain, vomiting, increased lipase, abdominal discomfort, dry mouth, flatulence, diarrhoea, increased bilirubin, rash, fatigue. <u>Uncommon (a)/(000 to c1/(00);</u> anaemia, immune reactivation syndrome, dyspepsia, sever skin reactions with systemic symptoms, angioedema, pruritus, arthralgia. Lega Lategory: POM **Pacit:** Bottle of 30 film-coated tablets. **Price:** UK with systemic symptoms, angioedema, pruritus, arthralgia. Legal Category: POM. Pack: Bottle of 30 film-coated tablets. Price: UK NHS List Price - £525.95; Eire/Ireland - TBC. Marketing Authorisation Number: EU/1/16/1112/001; EU/1/16/1112/002. Further information is available from Gilead Sciences Ltd, 280 High Holborn, London, WCIV 7EE, UK; Telephone: +44 (0) 8000 113700, For Ireland: +353 214 825 999. E-mail: <u>ukmedinfo@gilead.com</u>. Odefsy is a trademark. Date of approval: June 2016; ODE/UK/16-05/MM/1015.

30 film-coated tablets. Price: 0K NHS LISt Price - £873.51, Elify Ireland - €1266.00. Marketing Authorisation Number: EU/1/15/1061/001 Further information is available from Gilead Sciences Ltd, 280 High Holborn, London, WCIV 7EE, UK; Telephone: +44 (0) 8000 113700.

▼ This medicinal product is currently subject to additional monitoring. 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. Any suspected adverse reactions to Odefsey should be reported to Gilead via email to Safety_FC@gilead.com or by telephone +44 (0) 1223 897500.

PRESCRIBING INFORMATION Consult the Summary of Product

PRESCRIBING INFORMATION Consult the Summary of Product Characteristics before prescribing. TRUVADA' emtricitabine 200mg/tenofovir disoproxil (as fumarate) film coated tablets. Indications: In antiretroviral combination therapy for treatment of HIV-1 infected adults. In combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in adults at high risk. Dosage: Adults: One tablet once daily. Paediatric population (<18 vears); Safety & efficacy has not yet been established. Elderly: No dose adjustment required. Renal impairment; exposure to emtricitabine and tenofovir increases in individuals with renal dysfunction, refer to SPC for dosing recommendations. Contraindications: Hypersensitivity to entricitabine, tenofovir disoproxil fumarate (TDF), or any of the excipients. Use of Truvada for PrEP in individuals with unknown or positive HIV-1 status. Warnings and Precautions: *Transmission* of HIV; While effective viral suppression with antiretroviral therapy 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 national guidelines. Truvada is not always effective in preve the acquisition of HIV-1. The time to onset of protection commencing Truvada is unknown. Truvada should only be for PrEP as part of an overall HIV-1 infection prevention stra including the use of other HIV-1 prevention measures (e.c. consistent and correct condom use, knowledge of HIV-1 status regular testing for other sexually transmitted Infections). <u>Risk of</u> <u>resistance with undetected HIV-1 infection</u>; Truvada should only be used to reduce the risk of acquiring HIV-1 in individuals confirmed to be HIV negative. Individuals should be re-confirmed to be HIV-negative at frequent intervals (e.g. at least every 3 months) using a combined antigen/antibody test while taking Truvada for pre-exposure prophylaxis. <u>Adherence</u>; HIV-1 uninfected individuals should be counselled to strictly adhere to the recommended dosing schedule. The effectiveness of Truvada in reducing the risk of acquiring HIV-1 is strongly correlated with adherence as demonstrated by measurable drug levels in blood. <u>Renal</u>; Renal failure and impairment, elevated creatinine, hypophosphatemia and proximal tubulopathy (including Fanconi syndrome) have been reported with use of TDF in clinical practice. It is recommended thereal crCl is calculated in all patients prior to therapy initiation and renal regular testing for other sexually transmitted infections). Risk of CrCl is calculated in all platients practice, it is recommended unitariant crCl is calculated in all platients prior to therapy initiation and renal function monitored after 2 to 4 weeks of treatment, after 3 months of treatment and every 3 to 6 months thereafter. In patients at risk of renal impairment, a more frequent monitoring of renal function is required. Truvada for PrEP has not been studied in HIV-1 uninfected individuals with creatinine clearance < 60 mL/min and is therefore not recommended for use in this population. Risk-benefit assessment and monitoring of renal function is needed when Truvac s used for treatment of HIV-1 in patients with CrCl <60ml/mi is used for treatment of HIV-1 in patients with CrCl <60ml/min. Monitor for signs of toxicity and changes in viral load following introduction of Truvada at prolonged dosing intervals. If CrCl is decreased to <50ml/min (for HIV-1 infected patients) or < 60ml/min (use as PFE) or serum phosphate is decreased to <1.5mg/dl, renal function should be re-evaluated within one week. Consideration bould also be given b interventing treatment with in individuals function should be re-evaluated within one week. Consideration should also be given to interrupting treatment with in individuals with CrCl decreased to < 50 ml/min (for HIV-1 infected patients) or <60ml/min (use as PrEP) or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l). Interrupting treatment should also be considered in case of progressive decline of renal function when no other cause has been identified. Avoid with concurrent or recent use of nephrotoxic medicinal product. If concomitant use with nephrotoxic agents is unavoidable, monitor renal function weekly. If co-administered with a NSAID, renal function should be monitored adequately. A binder risk of renal impairment has heen monitored adequately. A higher risk of renal impairment has been reported in patients receiving TDF in combination with a ritonavir 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. <u>HBV or HCV co-infection</u>, patients should be closely monitored for at least several months following discontinuation of Truvada for symptoms of exacerbation of hepatitis. The safety and efficacy of Truvada for PrEP in patients with HBV/HCV co-infection has not been established. <u>Use with</u> <u>HCV antivirals</u>; Co-administration of TDF with ledipasir/sofosbuvir has been shown to increase plasma concentrations of tenofovir, especially when used together with an HIV regimen containing TDF and a pharmacchinetic enhancer (ritonavir or robicitat). The safety and a pharmacokinetic enhancer (ritonavir or cobicistat). The safety of TDF in this setting has not been established. Assess potential of TDF in this setting has not been established. Assess potential risks and benefits of use particularly in patients at increased risk of renal dysfunction. Patients should be monitored for adverse reactions related to TDF. <u>Hegatic</u>, Patients with pre-existing liver dysfunction should be monitored interruption or discontinuation of treatment must be considered if evidence of worsening liver disease. Qther, Weight and levels of blood lipids and glucose may increase during antiretroviral therapy. Monitor blood lipids & glucose as per HIV treatment guidelines. Manage lipid disorders as clinically appropriate. Rare hereditary galactose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption. Mitochondrial dysfunction (*in utero* exposure). Immune Reactivation Syndrome. Osteonecrosis. Decreased bone mineral density and bone abnormalities. Avoid in antiretroviral experienced density and bone abnormalities. Avoid in antiretroviral experienced patients with strains harbouring K65R mutation. Consult the SPC before prescribing. **Interactions:** As a fixed combination, Truvada before prescribing, interactions: As a fixed combination, iruvada should not be administered concomitantly with medicinal products containing emtricitabine, TDF tenofovir alafenamide, cytidine analogues such as lamivudine or adefovir dipivoxil. Low potential for CYP450 mediated interactions with other medicinal products. Co-administration 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. For a complete list of interactions refer to CPC presence a lattice in the complete list of interactions refer to administered product. For a complete list of interactions refer to SPC. **Pregnancy & lactation:** May be considered during pregnancy. Breast-feeding: not recommended. **Side effects:** <u>HIV-1 infection:</u> <u>Very common (sI/IO)</u>; hypophosphataemia, dizziness, headache, diarrhoea, nausea, vomiting, rash, elevated creatine kinase, asthenia. <u>Common (sI/IO)</u>; neutropenia, allergic reaction, <u>buecctricuscridonemia</u>, <u>buecctricuscridonemia</u>, <u>albergenia</u> Asuferial <u>control reprove</u> (2010), <u>control reprove</u> and <u>control</u> and <u>control</u> above dreams, flatulence, dyspepsia, abdominal pain, elevated serum lipase, elevated amylase including elevated pancreatic amylase, abdominal distention, hyperbilirubinaemia, increased transaminases, elevated serum aspartate aminotransferase &/or elevated serum alanine aminotransferase, pruritus, maculopapular rash, urticaria, vesiculobullous rash, pustular rash and skin discolouration (increased elevated) activity additiona elevated activity and alanine aminotransferase and skin discolouration (increased elevated) activity addition accession activity addition activity and alanine aminotransferase activity and and and alanine addition activity addition accession activity and alanine addition activity addition accession activity and alanine addition activity addition accession activity and alanine addition accession activity addition activity addition accession activity addition accession activity addition accession accession activity addition accession accession activity addition accession accession accession activity addition accession accession accession activity addition accession acc pigmentation), pain. In addition, anaemia was common and ski pignentation, pair, in addition, anaemia was common and som discoloration very common when emtricitabine was administered to paediatric patients. *PrEP*: No new adverse reactions to Truvada were paediatric patients. *PrEP*: No new adverse reactions to Truvada were identified from two randomised placebo-controlled studies. Refer to SPC for full information regarding side effects. **Legal Category:** POM. **Pack**: Bottle of 30 film-coated tablets. **Price**: UK NHS £355.73; Erre €691.74. **Marketing Authorisation Number**: EU/1/04/305/001-2. Further information is available from the local representative of the marketing authorisation holder: Gilead Sciences Ltd, 280 High Holborn, London, WCIV 7EE, UK; Telephone: +44 (0) 8000 113700. For Ireland: +353 214 825 999. E-mail: <u>ukmedinfo@gilead.com</u>. Truvada is a trademark. **Date of approval**: September 2016. Truvada is a trademark. Date of approval: 164/UK/16-08/MM/1079.

Any suspected adverse reactions to Truvada should be reported to Gilead via email to Safety_FC@gilead.com or by telephone +44 (0) 1223 897500.

Adverse events should be reported. For the UK, reporting forms and information can be found at www.mhra.gov.uk/vellowcard.

For Ireland, suspected adverse reactions should be reported to the HPRA Pharmacovigilance using a Yellow Card obtained For ireland, suspected adverse reactions should be reported to the HPRA Pharmacovigilance using a Vellow Card obtained either from the HPRA, or electronically via the website at <u>www.hpra.ie</u>. Adverse reactions can also be reported to the HPRA by calling +35316764971.

