Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
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elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, tenofovir alafenamide 10mg film-coated tablet (Genvoya®) SMC No. (1142/16)

Gilead Sciences Ltd.

08 April 2016

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission

elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide film-coated tablet (Genvoya®) is accepted for use within NHS Scotland.

Indication under review: the treatment of adults and adolescents (aged 12 years and older with body weight at least 35kg) infected with human immunodeficiency virus-1 (HIV-1) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

In two phase III, randomised, double-blind studies (in treatment-naïve adults with HIV-1), and one phase III, randomised, open-label study (in treatment-experienced adults with HIV-1), Genvoya® was non-inferior to alternative antiretroviral regimens at achieving/maintaining a high rate of viral suppression (plasma HIV-1 RNA <50 copies/mL) at week 48.

This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of Genvoya®. This advice is contingent upon the continuing availability of the patient access scheme in NHS Scotland or a list price that is equivalent or lower.

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Indication

The treatment of adults and adolescents (aged 12 years and older with body weight at least 35kg) infected with human immunodeficiency virus-1 (HIV-1) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir.

Dosing Information

One tablet, taken orally, once daily with food. The film-coated tablet should not be chewed, crushed, or split. Therapy should be initiated by a physician experienced in the management of HIV infection.

Product availability date

19 November 2015

Summary of evidence on comparative efficacy

The human immunodeficiency virus (HIV) infects and destroys cells of the immune system, most notably the CD4 T-lymphocytes. HIV-1 is highly virulent and the predominant type affecting the UK.[1] Current guidelines recommend antiretroviral therapy for treatment-naïve patients using a combination of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor, a non-nucleoside reverse transcriptase inhibitor (NNRTI) or an integrase inhibitor.[2,3] Genvoya® is a single-tablet combination comprising two NRTIs plus an integrase inhibitor and a pharmacokinetic enhancer (tenofovir alafenamide 10mg, emtricitabine 200mg, elvitegravir 150mg and cobicistat 150mg).[4] Tenofovir alafenamide is a novel prodrug of tenofovir which is administered at a lower dose than the existing prodrug, tenofovir disoproxil fumarate.[5] Tenofovir disoproxil fumarate is a component of Stribild® (tenofovir disoproxil fumarate 300mg, emtricitabine 200mg, elvitegravir 150mg and cobicistat 150mg), which has previously been accepted for use by SMC.

Clinical evidence derives from four key studies. Studies GS-US-292-0104 and GS-US-292-0111 were phase III, randomised, multicentre, double-blind, non-inferiority studies comparing the efficacy and safety of Genvoya® tablets versus Stribild® tablets. The studies recruited HIV-1-infected, treatment-naïve adults with an estimated creatinine clearance of ≥50mL/minute, an HIV-1 ribonucleic acid (RNA) concentration of ≥1000 copies/mL, and HIV-1 genotype sensitivity to elvitegravir, emtricitabine and tenofovir. Patients were randomised equally to treatment with Genvoya® (n=866) or Stribild® (n=867), taken orally once daily with matching placebo for 96 weeks. Randomisation was stratified by HIV-1 RNA concentration, CD4 cell count and region.[5]

The primary outcome was the proportion of patients with viral suppression (plasma HIV-1 RNA <50 copies/mL) at week 48, as defined by the US Food and Drug Administration (FDA) snapshot algorithm. Assessment of non-inferiority was performed in the full analysis set (FAS), comprising all randomised patients who received at least one dose of study drug. Non-inferiority was demonstrated if the lower bound of the two-sided 95% confidence interval (CI) for the treatment difference was greater than -12%. The studies were combined for a pre-specified pooled efficacy and safety analysis, and non-inferiority was achieved (Table 1).[5,6]

Table 1: Efficacy analyses at week 48 from studies GS-US-292-0104 and GS-US-292-0111[5,6]

Proportion of patients with plasma HIV-1 RNA <50 copies/mL (primary efficacy outcome)			
	GS-US-292-0104	**GS-US-292-0111**	**Pooled analysis**
Genvoya® % (n/N)	93% (405/435)	92% (395/431)	92% (800/866)
Stribild® % (n/N)	92% (399/432)	89% (385/435)	90% (784/867)
Adjusted difference	1.0%	3.1%	2.0%
95% confidence interval	-2.6% to 4.5%	-1.0% to 7.1%	-0.7% to 4.7%
p-value	0.58	0.13	Not reported
Proportion of patients with plasma HIV-1 RNA <20 copies/mL (secondary efficacy outcome)			
Genvoya® % (n/N)	86% (376/435)	82% (355/431)	84% (731/866)
Stribild® % (n/N)	87% (377/432)	81% (351/435)	84% (728/867)
Adjusted difference	-0.6%	1.4%	0.4%
95% confidence interval	-5.1% to 3.8%	-3.7 to 6.5%	-3.0% to 3.8%
p-value	0.78	0.6	0.83

HIV-1 RNA levels reduced rapidly in the first two weeks of treatment, then stabilised from week 8 to 48. In a pre-specified, per-protocol, pooled analysis (performed in those patients who did not discontinue treatment, have missing data or poor adherence in the FAS), viral suppression was also high in both groups: 98% (781/801) in the Genvoya® group and 97% (763/789) in the Stribild® group; adjusted difference 0.8% (95% CI: -1.0% to 2.5%). Virological failure in the pooled analysis was reported in 3.6% (31/866) and 4.0% (35/867) of patients in the Genvoya® and Stribild® groups respectively, and a small proportion of patients in both groups developed primary genotypic resistance to treatment; 0.8% (7/866) and 0.6% (5/867) in the respective groups. The mean (standard deviation) change in CD4 cell count from baseline to week 48, assessed as a secondary efficacy outcome, increased in both groups with a significantly greater increase occurring in the Genvoya® group (230 [177.3] cells/µL) compared with the Stribild® group (211 [170.7] cells/µL); difference in least squares mean 19 cells/µL (95% CI: 3.0 to 36 cells/µL), p=0.024 (pooled analysis).[5,6]

Study GS-US-292-0106 is an ongoing, phase II/III, multicentre, open-label, single-arm study of Genvoya® in HIV-1-infected, treatment-naïve adolescents. The 48-week study is conducted in two parts, of which efficacy is assessed as a secondary objective in Part B. The study recruited adolescents aged 12 to <18 years weighing ≥35kg with plasma HIV-1 RNA levels of ≥1,000 copies/mL, CD4 cell count >100 cells/µL and estimated glomerular filtration rate ≥90mL/minute/1.73m^2 at screening. Patients were required to have no prior use of any anti-HIV-1 treatment and demonstrate genotype sensitivity to elvitegravir, emtricitabine and tenofovir. All patients in Part B of the study received treatment with once-daily Genvoya® (n=50). The primary efficacy outcome is the proportion of patients with viral suppression (plasma HIV-1 RNA <50 copies/mL) at weeks 24 and 48 (defined by the US FDA snapshot algorithm). Interim results at week 24 show this was achieved by 90% (45/50) of patients. Virological failure at week 24 was reported in 8.0% (4/50) of patients. No evidence of virological resistance has been reported.[6,7]

Study GS-US-292-0109 was a phase III, randomised, multicentre, open-label study which evaluated non-inferiority of switching to Genvoya® relative to maintaining a tenofovir disoproxil fumarate regimen in treatment-experienced, HIV-1-infected adults. The study recruited patients who had completed a protocol-defined previous study and were receiving treatment that commenced at least six consecutive months prior to the final visit of the previous study with either: Stribild® tablets once daily; Atripla® tablets (tenofovir disoproxil fumarate 300mg, emtricitabine 200mg, efavirenz 600mg) once daily; ritonavir-boosted atazanavir tablets (100mg/300mg) plus Truvada® tablets (tenofovir disoproxil fumarate 300mg, emtricitabine 200mg) once daily; or cobicistat-boosted atazanavir tablets (150mg/300mg) plus Truvada® tablets once daily. Patients were required to have plasma HIV-1 RNA concentrations at undetectable levels for at least six consecutive months prior to screening, HIV-1 RNA <50 copies/mL at screening, and creatinine clearance ≥50mL/minute.[8] Patients were randomly

allocated in a 2:1 ratio to switch to Genvoya® (n=959) or remain on existing treatment (n=477) for 96 weeks. Randomisation was stratified by prior treatment regimen.[6]

The primary efficacy outcome was the proportion of patients with viral suppression (plasma HIV-1 RNA <50 copies/mL) at week 48, as defined by the US FDA snapshot algorithm.[6,8] Viral suppression was maintained by 97% (932/959) of the Genvoya® group and 93% (444/477) of the existing treatment group; adjusted difference 4.1% (95% CI: 1.6% to 6.7%). Non-inferiority was demonstrated (as the lower bound of the two-sided 95% CI for the treatment difference was greater than -12%), as was subsequent statistical superiority of Genvoya® compared with the existing treatment (p<0.001). Virological failure at week 48 was reported in a small proportion of patients in both groups; 1.0% (10/959) in the Genvoya® group and 1.3% (6/477) in the existing treatment group.[6]

A phase III, multicentre, open-label, single-arm study (GS-US-292-0112) conducted in adults with HIV-1 and mild to moderate renal impairment (creatinine clearance 30 to 69mL/minute) established that, at week 48, viral suppression (plasma HIV-1 RNA <50 copies/mL) was maintained by 92% (222/242) of treatment-experienced patients switched to Genvoya®, and achieved by 100% (6/6) of treatment-naïve patients initiated on Genvoya®, without any dose adjustment.[6,9]

Summary of evidence on comparative safety

The safety profiles of Genvoya® and Stribild® are considered similar.[6] In the pooled results of studies GS-US-292-0104 and GS-US-292-0111, any drug-related adverse event was reported in 40% (342/866) and 42% (364/867) of patients in the Genvoya® and Stribild® groups, respectively, in which 1.4% (12/866) and 1.0% (9/867) were considered to be severe. Any serious drug-related adverse events were reported in 0.4% (3/866) and 0.2% (2/867) of patients. Treatment discontinuation as a result of any adverse events occurred less frequently in the Genvoya® group (0.9% [8/866]) compared with the Stribild® group (1.5% [13/867]). No patients in the Genvoya® group discontinued due to renal adverse events compared with four patients in the Stribild® group (renal adverse events were considered related to study drug). The most commonly reported adverse events in the Genvoya® group were diarrhoea (17% [147/866], versus 19% [164/867] in the Stribild® group), nausea (15% [132/866] versus 17% [151/867]), and headache (14% [124/866] versus 13% [108/867]). At week 48, there were small but greater increases from baseline in the Genvoya® than Stribild® group in total cholesterol, low density lipoprotein, high density lipoprotein and triglycerides; the total cholesterol to high density lipoprotein ratio was the same in both groups. Similar proportions of patients started lipid lowering treatment (3.6% and 2.9% respectively).[5,6]

Changes in pre-specified renal and bone parameters from baseline to week 48 included percentage change in hip and spine bone mineral density, mean change in serum creatinine and median percentage change in treatment-emergent proteinuria. At 48 weeks, patients treated with Genvoya®, compared with Stribild®, demonstrated significantly smaller decreases in bone mineral density of the spine (mean change: -1.30% versus -2.86%; p<0.0001) and the hip (-0.66% versus -2.95%; p<0.0001); significantly smaller mean increases in serum creatinine (0.08mg/dL versus 0.12mg/dL; p<0.0001); and significantly less proteinuria (median change: -3.0% versus 20%; p<0.0001). There were low rates of fractures in both groups and they were considered to be due to trauma and not study drug.[5,6]

In study GS-US-292-0109, a smaller proportion of drug-related adverse events were reported in the treatment groups; 21% (204/959) for Genvoya and 16% (76/477) for the existing treatment group, of which 0.4% (4/959) and 1.9% (9/477) were severe. Treatment discontinuation due to adverse events occurred in 0.9% (9/959) and 2.5% (12/477) of patients in the respective groups. Upper respiratory

tract infection was the most common adverse event in both groups, reported in 16% (151/959) and 11% (54/477) in the Genvoya® and existing treatment groups, respectively.[10]

Summary of clinical effectiveness issues

Patients with HIV-1 are currently prescribed antiretroviral therapy according to the recommendations of the British HIV Association (BHIVA) and the Paediatric European Network for Treatment of AIDS (PENTA).[2,3] Genvoya® is a single-tablet combination comprised of two NRTIs plus an integrase inhibitor and a pharmacokinetic enhancer (tenofovir alafenamide 10mg, emtricitabine 200mg, elvitegravir 150mg and cobicistat 150mg). It is the second fixed-dose, four-drug combination tablet, after Stribild®.

Prior to the launch of Genvoya®, tenofovir was only available as the prodrug, tenofovir disoproxil fumarate, a formulation associated with toxic renal effects and reductions in bone mineral density as a result of high plasma concentrations of tenofovir. Genvoya® includes tenofovir alafenamide (a novel tenofovir prodrug) which reduces plasma concentrations of tenofovir by 90% thereby potentially improving renal and bone safety.[5] It is more efficient than tenofovir disoproxil fumarate at concentrating tenofovir in peripheral blood mononuclear cells and macrophages, where HIV-1 replicates, due to increased plasma stability and intracellular activation through hydrolysis by cathepsin A.[4] Clinical experts consulted by SMC consider Genvoya® is a therapeutic advancement as a result of reduced renal and bone toxicity, and provides an option for patients with renal dysfunction or with risk factors for osteoporosis/fractures.

The European Public Assessment Report (EPAR) concluded that, as a result of lower plasma tenofovir levels, tenofovir alafenamide has a better renal safety profile then tenofovir disoproxil fumarate. Various biomarkers for effects on bone also suggested a benefit for Genvoya® over Stribild®. Tenofovir has lipid-lowering effects and hence the reduced plasma levels of tenofovir associated with Genvoya® resulted in a higher rate of abnormal fasting lipids compared with Stribild®, however, the total cholesterol to high density lipoprotein ratio was the same as in patients treated with Stribild®. The overall the benefits from renal and bone effects were considered to outweigh any concerns with the effects on the lipid profile.[6]

Studies GS-US-292-0104 and GS-US-292-0111 demonstrated Genvoya® was non-inferior to Stribild® at achieving plasma HIV-1 RNA <50 copies/mL at week 48 in treatment-naïve, HIV-1-infected adults, with both treatments achieving a high rate of viral suppression (in 92% and 90% of patients in the pooled analysis, respectively). Significantly greater increases in CD4 cell count were also demonstrated for Genvoya® at week 48. Genvoya® had improved laboratory markers of renal and bone safety compared with Stribild®, although the long-term clinical significance of the findings is currently unknown.[5] Chronic exposure to low levels of tenofovir carries a potential risk of nephrotoxicity, and Genvoya® should not be initiated in patients with estimated creatinine clearance <30mL/minute.[4] The studies were limited by the inclusion of only a small proportion of female patients and those with advanced disease. A similarly high rate of viral suppression (90%) was demonstrated in the interim results for treatment-naïve, HIV-1-infected adolescents receiving Genvoya® in study GS-US-292-0106. The study is, however, limited by its open-label, single-arm design, inclusion of only a small proportion of patients with advanced disease, and absence of data in treatment-experienced adolescents.

In treatment-experienced, HIV-1-infected adults, switching to Genvoya® was concluded to be non-inferior (and also statistically superior) to remaining on existing treatment at maintaining viral suppression (plasma HIV-1 RNA <50 copies/mL) at week 48 in study GS-US-292-0109, with both treatment groups achieving a high rate of viral suppression. The study was limited by inclusion of only a small proportion of female patients.

Inclusion of Stribild® as the active comparator in studies GS-US-292-0104 and GS-US-292-0111 enabled comparison of a single component variable (tenofovir alafenamide versus tenofovir disoproxil fumarate). Study GS-US-292-0109 included comparisons with three alternative treatment regimens in addition to Stribild®. A Bayesian network meta-analysis (NMA), comprising 41 studies, compared Genvoya® with a number of emtricitabine/tenofovir disoproxil fumarate- and lamivudine/abacavir-based regimens in treatment-naïve adults and adolescents aged 12 years or older with HIV-1. The outcomes reported were virological response and all-cause discontinuation. In line with the direct evidence, the NMA demonstrated no difference between Genvoya® and Stribild® for virological response (HIV-1 RNA <50 copies/mL) at week 48. There was also no difference for this outcome between Genvoya® and the alternative comparators considered relevant to the submission, including: emtricitabine/tenofovir disoproxil fumarate (Truvada®) plus dolutegravir; lamivudine/abacavir/dolutegravir (Triumeq®); Truvada® plus raltegravir; lamivudine/abacavir (Kivexa®) plus raltegravir; emtricitabine/tenofovir disoproxil fumarate/rilviripine (Eviplera®); and emtricitabine/tenofovir disoproxil fumarate/efavirenz (Atripla®). Sensitivity analyses also demonstrated no difference between treatments. For all-cause discontinuation at week 48, the results favoured Genvoya® over Stribild® and Atripla®; however, there was no difference between the other comparators considered relevant to the submission. Overall, the analysis was limited by wide networks (with many connections only populated by a single study) and a lack of sufficient data to include treatment-experienced patients and change in CD4 cell count as an outcome. Heterogeneity was apparent across the studies for baseline characteristics, definitions used for virological response and outcomes between the common control arms.

Genvoya® provides an alternative fixed-dose, four-drug combination, with similar antiviral efficacy to Stribild®, but with lower exposure to tenofovir and therefore potentially reduced toxic renal and bone effects. It is also licensed for use in adolescents aged 12 years and older with body weight ≥35kg and is suitable for patients with an estimated creatinine clearance of ≥30mL/minute, which Stribild® is not.

Summary of comparative health economic evidence

The company submitted a cost-minimisation analysis comparing Genvoya® to Stribild® for the treatment of adults and adolescents (aged 12 years and older with bodyweight at least 35kg) infected with HIV-1 without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir. The time horizon was 1 year. Based on SMC expert responses, Stribild® appears to be the comparator most likely to be displaced in Scotland.

The clinical data used in the economic analysis was derived from three clinical studies: GS-US-292-0104 (treatment-naive patients), GS-US-292-0111 (treatment-naive patients) and GS-US-292-0109 (treatment-experienced patients). The primary outcome for all studies was HIV-1 RNA <50 copies/mL at week 48. Based on the results of the analyses, Genvoya® was associated with a numerically higher proportion of patients having HIV-1 RNA <50 copies/mL at week 48, and was considered non-inferior to Stribild®. As such, comparable efficacy was considered to have been demonstrated and no differences in outcomes were assumed between the treatment strategies.

Only drug costs were included in the analysis. As treatment is administered orally, there were no administration costs. Adverse event costs were not included in the analysis.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHS Scotland. Under the PAS, a simple discount was offered which reduced the list price of Genvoya®. It should be noted that a PAS is in place for the comparator Stribild® and this is incorporated in the results. With the PAS, Genvoya® is a cost-effective treatment option versus Stribild®.

The company provided sensitivity analysis comparing Genvoya® to secondary comparators of Truvada® (emtricitabine/tenofovir disoproxil fumarate) plus dolutegravir and Triumeq® (dolutegravir/abacavir/lamivudine). A weighted average comparison versus these comparators was also provided.

There were no major weaknesses in the analysis and the economic case has been demonstrated.

*Other data were also assessed but remain commercially confidential.**

Summary of patient and public involvement

The following information reflects the views of the specified Patient Group.

- A submission was received from Waverley Care, which is a registered charity.
- The patient group has received 1% pharmaceutical company funding in the past two years, including from the submitting company.
- People are living much longer with HIV due to effective HIV treatment, but they are disproportionately impacted by high levels of stigma and discrimination in daily life, combined with high rates of chronic health conditions, including: heart attacks, bone fractures, kidney disease and certain cancers. This impacts their ability to participate in daily life and places increasing burden on work, study and social engagement.
- This new medicine is a welcome option which, compared with current treatment, may reduce the impact on renal and bone toxicity. This is particularly significant for older patients and for those with reduced renal or bone function, and is especially important as the population living with HIV ages in Scotland and shows increasing levels of frailty associated with HIV.

Additional information: guidelines and protocols

The British HIV Association (BHIVA) guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy published in 2015 recommend that all individuals with suspected or diagnosed primary HIV are reviewed promptly by an HIV specialist and offered immediate antiretroviral therapy (ART).[2] For individuals who are therapy-naïve it is recommended that they start ART containing two NRTIs plus one of the following: ritonavir-boosted protease inhibitor (PI/r), NNRTI or integrase inhibitor (INI).

With regards choice of NRTIs, it is recommended that:

- Therapy-naïve individuals start combination ART containing tenofovir and emtricitabine as the preferred NRTI backbone.
- Abacavir and lamivudine is an acceptable alternative NRTI backbone in therapy-naïve individuals. In those with a baseline viral load >100,000 copies/mL, it should be used with caution if there are clinical reasons to prefer over tenofovir and emtricitabine.

- The caution regarding baseline viral load does not apply if abacavir/lamivudine is used with dolutegravir.
- Abacavir must not be used in individuals who are HLA-B*57:01-positive.

In terms of a third agent, the guidelines recommend:

- Therapy-naïve individuals start combination ART containing atazanavir/ritonavir, darunavir/ritonavir, dolutegravir, elvitegravir/cobicistat, raltegravir or rilpivirine.
- For therapy-naïve individuals, efavirenz is an acceptable alternative third agent.

The guidelines also state that the use of PI monotherapy as initial therapy for treatment-naïve patients is not recommended, and advises against the use of the use of PI-based dual ART with a single NNRTI, NRTI or C-C chemokine receptor type 5 (CCR5) antagonist for treatment-naïve patients. Where there is a need to avoid abacavir and tenofovir, a darunavir/ritonavir-based dual ART regimen with raltegravir can be used in treatment naïve patients with CD4 count >200 cells/µL and viral load <100,000 copies/mL.

The Paediatric European Network for Treatment of AIDS (PENTA) published guidelines for treatment of paediatric HIV-1 infection 2015: optimizing health in preparation for adult life.[3] The guideline recommends that in terms of first-line treatment with antiretroviral therapy, effective (at least three drugs) ART should be started, usually consisting of a dual or triple NRTI backbone together with either a ritonavir-boosted PI or an NNRTI. The guideline also recommends that children exposed to nevirapine (NVP) during failed prevention of mother to child transmission (or in whom perinatal NVP exposure cannot be excluded) should be started on a boosted PI-containing regimen, as transmitted resistance may lead to failure of NVP containing ART. Choice may be influenced by factors such as availability of age-appropriate formulations, palatability, dosing frequency and adherence. The guidelines recommend that ritonavir-boosted atazanavir (ATV/r) is the preferred PI in children aged 6 to 12 years and in children aged >12 years it is ATV/r or ritonavir-boosted darunavuir (DRV/r). For those aged <12 years, the guidelines recommend that the preferred first-line NRTIs is abacavir plus lamivudine (ABC/3TC). For those aged >12 years, tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or ABC/3TC (if viral load <100,000 copies/mL) is recommended. When choosing a first-line regimen, it is advised that age, HLA-B*57:01 genotype, previous drug exposure, resistance profile, co-infections, available formulations and likely adherence be taken into account.

Both of these guidelines predate the availability of Genvoya®.

Additional information: comparators

The relevant comparators are considered to be those antiretroviral regimes incorporating the preferred NRTI backbone of emtricitabine plus tenofovir disoproxil fumarate (or lamivudine plus abacavir) in combination with an integrase inhibitor (i.e. elvitegravir, dolutegravir or raltegravir). Stribild® is considered the primary comparator. Truvada® plus dolutegravir and Triumeq® are considered secondary comparators in the economic case. Additional comparators considered relevant by clinical experts consulted by SMC include Atripla® and Eviplera®.

Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
Genvoya®	**One tablet orally once daily**	**10,671**
Stribild®	One tablet orally once daily	10,671
Truvada® and Dolutegravir	One tablet orally once daily 50mg orally once daily	10,368
Triumeq®	One tablet orally once daily	9,684
Atripla®	One tablet orally once daily	6,465
Eviplera®	One tablet orally once daily	6,382

Doses are for general comparison and do not imply therapeutic equivalence. Doses stated are for adults. Costs from eVadis on 03 February 2016. Costs do not take any patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there to be 3,740 patients eligible for treatment in all years.

SMC is unable to publish the with PAS budget impact as the submitting company has stated that this is commercial in confidence. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

*Other data were also assessed but remain commercially confidential.**

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.

1. National Institute for Health and Care Excellence (NICE). Clinical knowledge summaries. HIV infection and AIDS. Last revised September 2015. http://cks.nice.org.uk/

2. British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2015. September 2015.

3. Bamford A, Turkova A, Lyall H *et al.* Paediatric European Network for Treatment of AIDS (PENTA) guidelines for treatment of paediatric HIV-1 infection 2015: optimizing health in preparation for adult life. *HIV Med* 2015.

4. Gilead Sciences Ltd. Genvoya® 150mg/150mg/200mg/10mg film-coated tablets. Summary of product characteristics. Date of revision of the text 11/2015.

5. Sax PE, Wohl D, Yin MT, Post F, DeJesus E, Saag M, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials (including supplement). Lancet. 2015 Jun 27;385(9987):2606-15.

6. European Medicines Agency. European public assessment report for Genvoya (elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide). EMA/688326/2015. 24 September 2015. http://www.ema.europa.eu/ema/

7. **Commercial in Confidence*

8. NCT01815736. Open-label study to evaluate switching from a TDF-containing combination regimen to a TAF-containing combination single tablet regimen (STR) in virologically-suppressed, HIV-1 positive subjects. www.clinicaltrials.gov (accessed 07/01/16).

9. NCT01818596. Open-label safety study of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide single-tablet regimen in HIV-1 positive patients with mild to moderate renal impairment. www.clinicaltrials.gov (accessed 07/01/16).

10. Mills A, Arribas JR, Andrade-Villanueva J, et al. Switching from tenofovir disproxil fumarate to tenofovir alafenamide in antiretroviral regimens for virologically suppressed adults with HIV-1 infection: a randomised, active-controlled, multi-centre, open-label, phase 3, non-inferiority study. Lancet infect Dis. 2016;16:43-52. .

This assessment is based on data submitted by the applicant company up to and including 11 March 2016.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy_statements/Policy_Statements*

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed

Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a drug and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG, established under the auspices of NHS National Services Scotland reviews and advises NHS Scotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.