

elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, tenofovir disoproxil (as fumarate) 245mg film coated tablet (Stribild®)

SMC No. (887/13)

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## Gilead Sciences Ltd

05 July 2013

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 Scotland. The advice is summarised as follows:

**ADVICE:** following a full submission

**elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil (as fumarate) film coated tablet (Stribild®)** is accepted for use within NHS Scotland.

**Indication under review:** treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral treatment-naïve or are infected with HIV-1 without known mutations associated with resistance to the three antiretroviral agents in Stribild®.

Stribild® was at least as effective as two other recommended antiretroviral regimens in treatment-naïve HIV-1 infected patients.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of Stribild®. This SMC 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

Treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over who are antiretroviral treatment-naïve or are infected with HIV-1 without known mutations associated with resistance to the three antiretroviral agents in Stribild®.

## Dosing Information

One tablet taken once daily with food. Therapy should be initiated by a physician experienced in the management of HIV infection.

## Product availability date

03 June 2013

## Summary of evidence on comparative efficacy

Stribild® is a fixed dose combination of four drugs (three antiretrovirals and a booster):

- elvitegravir (150mg) is a new integrase strand transfer inhibitor
- emtricitabine (200mg) is a nucleoside reverse transcriptase inhibitor (NRTI)
- tenofovir disoproxil (245mg) (as fumarate) is a NRTI
- cobicistat (150mg) is a new booster. It is a derivative of ritonavir and is a CYP3A inhibitor which has no antiviral activity but boosts the plasma levels of elvitegravir.

Stribild® is the first combination tablet containing elvitegravir and cobicistat, together with a preferred NRTI backbone, emtricitabine and tenofovir. Elvitegravir and cobicistat (as single agents) are anticipated to receive individual marketing authorisation later in 2013.

The evidence to support the efficacy of Stribild® comes from the results of two similar pivotal double-blind, randomised, phase III studies.<sup>1,2</sup> Eligible patients were men and women aged ≥18 years, with HIV-1 infection and plasma HIV-1 RNA ≥5,000 copies/mL who had not received previous treatment with antiretroviral drugs. Patients were also required to have an estimated glomerular filtration rate of ≥70mL/min and be susceptible to efavirenz or atazanavir, emtricitabine and tenofovir. In the first study, patients were randomised to receive (Stribild®) taken once daily with food or efavirenz 600mg/emtricitabine 200mg/tenofovir disoproxil fumarate 300mg (Atripla®) taken on an empty stomach at bedtime.<sup>1</sup> Each combination was taken as a co-formulated single tablet and patients also received matching placebo tablets of the alternative treatment to maintain double-blinding. In the second study, patients were randomised to receive (Stribild®) taken once daily with food or atazanavir 300mg/ritonavir 100mg/emtricitabine 200mg/tenofovir disoproxil fumarate 300mg (ATV/RTV+FTC/TDF) taken once daily with food, with each combination taken as four tablets (active and placebo) per day.<sup>2</sup> Study treatment was continued for 96 weeks, but after the primary endpoint was reached, this was extended to 192 weeks. In both studies, randomisation was stratified by HIV RNA concentration at screening (≤100,000 copies/mL and >100,000 copies/mL).

The studies tested the non-inferiority of Stribild® versus comparator using a margin of 12% and a one-sided significance of 0.025. The primary endpoint was the proportion of patients with viral suppression (defined as HIV RNA <50 copies/mL) at week 48. This analysis was performed in the intention-to-treat (ITT) snapshot analysis population which included patients with viral suppression during the week 48 window (between days 309 and 378). The secondary endpoint

of time to loss of virological response (percentage of patients achieving and maintaining HIV RNA <50copies/mL at week 48) was analysed in the ITT population. Key results for both studies are detailed in the table below, and demonstrate the non-inferiority of Stribild® versus comparators. Non-inferiority was confirmed in the per protocol population.

**Table: virological suppression (HIV RNA < 50 copies/mL) in ITT snapshot analysis (primary endpoint) and at week 48 and key secondary endpoint (TLOVR).<sup>1,2</sup>**

	Study 1		Study 2	
	Stribild®	Atripla®	Stribild®	ATV/RTV+FTC/TDF
Primary endpoint				
Virological suppression, % (n/N)	88% (305/348)	84% (296/352)	90% (316/353)	87% (308/355)
Difference (95% CI)	3.6% (-1.6 to 8.8)		3.0% (-1.9 to 7.8)	
Secondary endpoint				
TLOVR, % (n/N)	86% (299/348)	83% (293/352)	86% (304/353)	85% (301/355)
Difference (95% CI)	2.7% (-2.6 to 8.1)		1.6% (-3.6 to 6.8)	

ATV/RTV+FTC/TDF= atazanavir 300mg/ritonavir 100mg/emtricitabine 200mg/tenofovir disoproxil fumarate 300mg

CI= confidence interval

TLOVR= time to loss of virological response

In both studies, the proportion of patients with virological suppression was higher in the Stribild® than comparator group at visits up to week 12-16, after which they appear similar.<sup>1,2</sup> Subgroup analyses according to age (<40 years and ≥40 years), sex, race (white and non-white), baseline HIV RNA concentration (≤100,000 copies/mL and >100,000 copies/mL), baseline CD4 cell count (≤350 cells/mm<sup>3</sup> and >350 cells/mm<sup>3</sup>) and adherence to study drug (<95% and ≥95%) found the relative treatment effect to be similar and consistent in both studies.<sup>1,2</sup>

Virologic failure (defined as patients with HIV RNA ≥50 copies/mL at week 48, patients who discontinued early due to lack or loss of efficacy, or for reasons other than adverse event, death or lack or loss of efficacy and had a viral load of ≥50 copies/mL at the time of discontinuing) was reported in 7% of patients in each group in the first study and 5% of patients in each group in the second study.<sup>3</sup>

In both studies, the changes from baseline in CD4 cell counts were similar in each treatment groups at most time-points. At week 48, the mean increase was significantly higher in the Stribild® than Atripla® group (239 cells/mm<sup>3</sup> versus 206 cells/mm<sup>3</sup>, p=0.009) in study 1, and similar in the Stribild® and ATV/RTV+FTC/TDF group in study 2 (207 cells/mm<sup>3</sup> and 211 cells/mm<sup>3</sup>, respectively).<sup>1,2</sup>

In a randomised, double-blind phase II study, 71 treatment-naïve adults with HIV-1 infection were randomised, in a ratio of 2:1, with stratification by HIV RNA ≤100,000 copies/mL or >100,000 copies/mL, to receive Stribild® once daily with food or Atripla® at bedtime for 48 weeks.<sup>4</sup> The primary endpoint of viral suppression (HIV RNA <50 copies/mL at week 24) in the ITT population was achieved in 90% (43/48) of Stribild® and 83% (19/23) of Atripla® patients. The study was not powered to detect a treatment difference but an *a priori* planned analysis included a point estimate difference: 5.0% (95% CI: -11% to 21%). The secondary endpoint of

viral suppression at 48 weeks was achieved in 90% and 83% of patients respectively: difference 8.4% (95% CI: -8.8% to 26%).

The company's submission included results of a pre-planned integrated analysis of the two pivotal phase III studies plus the phase II study described above which have been presented as a conference poster.<sup>5</sup> The analysis showed a significant benefit with Stribild® over Atripla® in viral suppression at 48 weeks (89% versus 84%: difference of 5.1% [95% CI: 0.7 to 9.4],  $p=0.016$ ) and similar effects between Stribild® and ATV/RTV+FTC/TDF (89% versus 87%: difference 1.9% [95% CI: -2.3% to 6.1%]).

An abstract report of an open-label study in 48 HIV infected patients indicated that switching treatment from raltegravir/emtricitabine/tenofvir disoproxil fumarate to Stribild® did not result in loss of virologic suppression. All 48 patients maintained HIV RNA <50 copies/mL at week 12.<sup>6</sup>

## Summary of evidence on comparative safety

In the first phase III study, non-serious adverse events were reported by 74% (258/348) of Stribild® and 80% (282/352) of Atripla® patients, and serious adverse events by 12% (41/348) and 6.8% (24/352) of patients respectively.<sup>1</sup> The proportions of patients discontinuing treatment due to adverse events were similar in both groups: 3.7% (13/348) and 5.1% (18/352) patients respectively. Five Stribild® treated patients had renal adverse events which led to discontinuation (two with increased serum creatinine, two with renal failure and one with Fanconi syndrome). Four of these patients had evidence of renal impairment before starting study drug, although they met the inclusion criterion (estimated glomerular filtration rate  $\geq 70$  mL/min). The most frequently reported adverse events, occurring in  $\geq 10\%$  of patients in either the Stribild® or Atripla® group respectively, were diarrhoea (23% versus 19%), nausea (21% versus 14%), fatigue (11% versus 13%), upper respiratory infection (14% versus 11%), dizziness (6.6% versus 24%), headache (14% versus 10%), abnormal dreams (15% versus 27%), insomnia (8.6% versus 14%), depression (9.5% versus 11%) and rash (6.3% versus 12%). Nausea was significantly more common in Stribild® than Atripla® treated patients ( $p=0.016$ ) but similar proportions of patients had moderate to severe nausea (2.9% versus 2.6%, respectively). Dizziness, abnormal dreams, insomnia and rash were significantly more common in Atripla® than Stribild® treated patients ( $p<0.001$ ,  $p<0.001$ ,  $p=0.031$  and  $p=0.009$  respectively). By week 48, serum creatinine increased more and estimated glomerular filtration rate decreased more in Stribild® than Atripla® patients. Median fasting total cholesterol, LDL and HDL cholesterol increased significantly less from baseline in Stribild® than Atripla® patients.

In the second phase III study, non-serious adverse events were reported by 71% (252/353) of Stribild® and 77% (272/355) of ATV/RTV+FTC/TDF patients, and serious adverse events by 7.4% (26/353) and 8.7% (31/355) of patients respectively.<sup>2</sup> Similar proportions of patients discontinued study treatment due to adverse events: 3.7% (13/353) and 5.1% (18/355) patients respectively. Renal adverse events lead to discontinuation in one patient from each treatment group. The most frequently reported adverse events, occurring in  $\geq 10\%$  of patients in the Stribild® or ATV/RTV+FTC/TDF groups respectively were diarrhoea (22% versus 27%), nausea (20% versus 19%), upper respiratory infection (15% versus 16%), headache (15% versus 12%), fatigue (14% versus 13%) and ocular icterus (0.6% versus 14%). Ocular icterus occurred in significantly more ATV/RTV+FTC/TDF than Stribild® patients ( $p<0.001$ ). Nausea and diarrhoea were generally mild and self-limiting, occurring early in treatment. By week 48, serum creatinine increased significantly more and estimated glomerular filtration rate decreased significantly

more in Stribild® than ATV/RTV+FTC/TDF patients. There were no significant differences between the treatment groups in median changes in fasting total cholesterol, LDL and HDL cholesterol. Patients in the Stribild® group experienced significantly fewer total bilirubin abnormalities than patients in the ATV/RTV+FTC/TDF group.

## Summary of clinical effectiveness issues

Evidence from the two phase III studies demonstrated non-inferiority of Stribild® compared with two relevant comparators which are recommended by current guidelines. However, although Atripla® is recommended in current guidelines, it is not licensed for treatment-naïve patients but for patients with virologic suppression to HIV-1 RNA levels of <50 copies/mL on their current combination antiretroviral therapy for more than three months. An integrated analysis of these studies plus the phase II study suggested superiority over Atripla® but results are currently limited to a conference poster presentation.<sup>5</sup>

Although the study populations comprised patients with treatment-naïve HIV infection, the licence includes both treatment-naïve patients and patients infected with HIV-1 without known mutations associated with resistance to the three antiretroviral agents in Stribild®. Data to support the latter group of patients are limited to the small switch study described above.

Antiretroviral therapy is usually started in treatment-naïve HIV infected patients when the CD4 cell count is  $\leq 350$  cells/mm<sup>3</sup>.<sup>7</sup> In the phase III studies, there was no CD4 cell count requirement for entry. The baseline CD4 cell counts were  $>350$  cells/mm<sup>3</sup> in more than half of patients in each study suggesting that treatment may have been initiated slightly earlier than in clinical practice in some patients.<sup>1,2</sup>

Both phase III studies required patients to have an estimated glomerular filtration rate of at least 70mL/min.<sup>1,2</sup> Therefore, the draft summary of product characteristics recommends that Stribild® should not be initiated in patients with creatinine clearance below 70mL/min and that it should be discontinued in patients whose creatinine clearance falls below 50mL/min since this requires dosage adjustment of emtricitabine and tenofovir.<sup>3</sup> In both phase III studies, there were low proportions of female patients (8 to 12%). Further studies are planned to address these limitations of the data.<sup>1,2</sup>

By week 48, treatment-emergent resistance had developed in eight and five patients in the Stribild® groups of the first and second studies respectively.<sup>1,2</sup> Longer-term efficacy data and information on resistance are awaited as well as longer-term safety data. There are currently inadequate data to determine whether co-administration of tenofovir disoproxil fumarate and cobicistat is associated with a greater risk of renal adverse reactions compared with regimens that include tenofovir disoproxil fumarate without cobicistat.

The introduction of this fixed combination product may be useful in patients in whom a simplified regimen is required and, therefore, it may have advantages over the single drug components and the NNRTI plus dual combination NRTI tablet option. A simpler regimen may improve adherence which may reduce the likelihood of treatment failure and drug resistance.<sup>8</sup> However, this formulation is not suitable for patients who require adjustment in dosing of any of the components. Stribild® is the first fixed combination product to include an integrase inhibitor and is a once daily medicine. The alternative integrase inhibitor, raltegravir, requires twice daily

dosing. Elvitegravir and cobicistat are not included in current HIV treatment guidelines as the guidelines predate their availability.<sup>7</sup>

## Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis comparing Stribild® with two different combinations of treatments:

- (i) atazanavir, ritonavir, emtricitabine and tenofovir (referred to as ATV/RTV+FTC/TDF)
- (ii) efavirenz, emtricitabine, tenofovir (referred to as Atripla®)

To estimate costs and benefits over the lifetime of a cohort of patients, a Markov model was constructed taking account of three sets of factors:

- Virological response to treatment (2 levels, whether viral load suppressed based on threshold of 50 copies/mL)
- CD4 cell count (6 levels)
- Line of treatment (4 levels – 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, non-suppressive)

Data on transition rates between these states with different treatments were taken from the main clinical studies for Stribild®. Where extrapolation was required to go beyond the end of the follow-up period of the clinical studies, methods included projection of trends in the clinical study period and the use of trends from other clinical studies of HIV treatment.

Quality of life data came from a published study of utility values by CD4 grouping, and these have been used in previous health technology assessment submissions. Mortality rates in the model were based on Scottish population figures adjusted for the excess mortality associated with HIV/AIDS.

Costs were considered from an NHS and social care perspective and included the costs of medicines, the costs of changing patients from one medicine to another, and the on-going costs of care for HIV. A patient access scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable to NHS Scotland. Under the PAS a confidential discount is given on the list price of the medicine.

Without the PAS, the results were as follows:

- Compared to Atripla®, Stribild® cost an additional £30,192 over the lifetime of the patient and a gain of 0.02 quality adjusted life years (QALYs). The added cost per QALY gained was £1,332,746.
- Compared to ATV/RTV+FTC/TDF, Stribild® cost an extra £22,558 for an additional 0.01 QALYs. The added cost per QALY gained was £2,818,023.

With the PAS, the results indicated that Stribild® was the dominant (cheaper, more effective) treatment.

One-way and probabilistic sensitivity analyses were carried out. Important features identified included the virological response rate and the assumption about long-term rates of change in CD4.

Weaknesses of the submission were as follows:

- In the base case, numerical differences between treatments were used even though they were not statistically significant in the clinical study.
- In extrapolating the clinical data, values were selected from the literature for key variables but it was not clear how these values were selected (e.g. was the literature search systematic?) and it was not clear how relevant the figures were (e.g. were they in patients receiving the same line of treatment?). However, if it is accepted Stribild® is non-inferior, then these data inputs would be the same for each treatment.
- The utility values were from published studies and are quite high, especially in more advanced disease. Again, if Stribild® is non-inferior then the similar level of effectiveness means this is not important in driving results.
- Some of the resource use data were quite old and more recent figures would have been preferable; once again, non-inferiority means this is less important in this case.

Despite these issues, the economic case was considered demonstrated when the PAS was incorporated into the analysis.

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

## Summary of patient and public involvement

A Patient Interest Group Submission was not made.

## Additional information: guidelines and protocols

The British HIV Association (BHIVA) issued “Guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy” in 2012.<sup>7</sup> The primary aim of antiretroviral therapy (ART) is the prevention of the mortality and morbidity associated with chronic HIV infection at low cost of drug toxicity. Treatment should improve the physical and psychological well-being of people living with HIV infection.

The following recommendations with respect to treatment are included:

- Patients with chronic HIV infection start ART if the CD4 cell count is  $\leq 350$  cells/mm<sup>3</sup>. In patients with an AIDS diagnosis, HIV-related co-morbidity, co-infection with hepatitis B or C and non-AIDS-defining malignancy, ART may be started sooner. Refer to, guideline for details.
- Therapy-naïve patients start ART with two NRTIs plus one of the following: a ritonavir-boosted protease inhibitor, an NNRTI or an integrase inhibitor
- A NRTI backbone of tenofovir and emtricitabine is the preferred option in treatment-naïve patients with abacavir and lamivudine as acceptable alternatives (only in HLA-B\*57:01 negative patients and if baseline viral load is  $< 100,000$  copies/mL).
- The preferred third agent is efavirenz or one of the following: atazanavir/ritonavir; darunavir/ritonavir; or raltegravir in treatment-naïve patients. Acceptable alternatives include lopinavir/ritonavir; fosamprenavir/ritonavir; nevirapine or rilpivirine.
- PI monotherapy is not recommended for initial therapy for treatment-naïve patients. The use of PI-based dual therapy with a single NRTI, NNRTI or integrase inhibitor is not recommended for initial therapy for treatment-naïve patients.

The guidelines predate the availability of Stribild®.

## Additional information: comparators

Emtricitabine plus tenofovir disoproxil in combination with efavirenz (or atazanavir/ritonavir or darunavir/ritonavir or raltegravir or rilpivirine). These may be given as individual components or as combination preparations. Some of these treatments are not included in current guidelines.

Refer to summary of product characteristics for licensed indications, as there is some variation between drugs e.g. Atripla® is licensed for patients with virologic suppression on their current combination antiretroviral therapy for more than three months.

## Cost of relevant comparators

Drug	Dose Regimen	Cost per year (£)
<b>Stribild®</b>	<b>One tablet once daily</b>	<b>12,555</b>
Raltegravir plus Truvada®	400mg twice daily plus one tablet once daily	11,433
Raltegravir plus emtricitabine plus tenofovir disoproxil	400mg twice daily plus 200mg once daily plus 245mg once daily	11,257
Darunavir plus ritonavir plus Truvada®	800mg once daily plus 100mg once daily plus one tablet once daily	8,927
Darunavir plus ritonavir plus emtricitabine plus tenofovir disoproxil	800mg once daily plus 100mg once daily plus 200mg once daily plus 245mg once daily	8,751
Atazanavir plus ritonavir plus Truvada®	300mg once daily plus 100mg once daily plus one tablet once daily	8,995
Atazanavir plus ritonavir plus emtricitabine plus tenofovir disoproxil	300mg once daily plus 100mg once daily plus 200mg once daily plus 245mg once daily	8,818
Atripla®	One tablet once daily	7,606
Efavirenz plus Truvada®	600mg once daily plus one tablet once daily	7,508
Efavirenz plus emtricitabine plus tenofovir disoproxil	600mg once daily plus 200mg once daily plus 245mg once daily	7,331
Eviplera®	One tablet once daily	7,508
Rilpivirine plus Truvada®	25mg once daily plus one tablet once daily	7,508
Rilpivirine plus	25mg once daily plus	7,331

emtricitabine plus tenofovir disoproxil	200mg once daily plus 245mg once daily	
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Doses are for general comparison and do not imply therapeutic equivalence. Costs from eMIMs 25 April 2013 with the exception of Stribild® which is from the company submission.

## **Additional information: budget impact**

The submitting company estimated the population eligible for treatment to be 362 in year 1 rising to 436 in year 5. The budget impact submitted was based on an estimated uptake of 10% in year 1 and 20% in year 5.

Without PAS: The gross impact on the medicines budget was estimated to be £439k in year 1 and £1.057m in year 5. As other drugs were assumed to be displaced, the net medicines budget impact is expected to be £165k in year 1 and £397k in year 5.

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

## References

The undernoted references were supplied with the submission. The reference shaded in grey is additional to those supplied with the submission.

1. Sax PE, DeJesus E, Mills A et al. Co-formulated elvitegravir, cobicistat, emtricitabine and tenofovir versus co-formulated efavirenz, emtricitabine and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks. *Lancet* 2012;379:2439-48.
2. DeJesus E, Rockstroh JK, Henry K et al. Co-formulated elvitegravir, cobicistat, emtricitabine and tenofovir disoproxil fumarate versus ritonavir-boosted atazanavir plus co-formulated emtricitabine and tenofovir disoproxil fumarate for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3, non-inferiority trial. *Lancet* 2012;379:2429-38.
3. Gilead Sciences Ltd. Draft summary of product characteristics for Stribild®.
4. Cohen C, Elion R, Ruane P et al. Randomised, phase 2 evaluation of two single-tablet regimens elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate for the initial treatment of HIV infection. *AIDS* 2011;25:F7-F12.
5. Fisher M, Ward D, Crofoot G et al. Efficacy and safety of elvitegravir/cobicistat/emtricitabine/tenofovir DF from an integrated analysis of phase 2 and 3 clinical trials. Poster presented at the 19<sup>th</sup> Annual Conference of the British HIV association (BHIVA) 16-19 April 2013, Manchester, UK.
6. Mills A, Croffot G, Ortiz R et al. Safety and tolerability of switching from twice daily Raltegravir plus Truvada to STRIBILD in virologically suppressed HIV -1 infected subjects. HIV DART 2012. Frontiers in drug development for antiviral therapies, San Diego, California, December 4-7,2012
7. BHIVA. British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2012. *HIV Medicine* 2012;13 (Suppl.2):1-85.
8. Schrijvers R, Debyser Z. Quad's in it for antiretroviral therapy? *Lancet* 2012;379:2403-05.

This assessment is based on data submitted by the applicant company up to and including 12 June 2013.

*\*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](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. These have been confirmed from the eVadis drug database. 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.*