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

**golimumab (Simponi®)** is not recommended for use within NHS Scotland.

**Indication under review:** treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies.

In a study of adults with moderately to severely active ulcerative colitis who had inadequate response or intolerance to conventional therapy, a greater proportion of patients given golimumab induction therapy achieved a clinical response compared with placebo. In patients who had a clinical response to golimumab induction, golimumab maintenance treatment was associated with a greater clinical response rate over 54 weeks, compared with placebo.

The company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

Overleaf is the detailed advice on this product.

**Chairman,**
**Scottish Medicines Consortium**
**Indication**
Treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies.

**Dosing Information**
To be administered by subcutaneous injection.

Patients with body weight less than 80kg: initial dose of 200mg, followed by 100mg at week 2, then 50mg every 4 weeks thereafter.

Patients with body weight greater than or equal to 80kg: initial dose of 200mg, followed by 100mg at week 2, then 100mg every 4 weeks thereafter.

During maintenance treatment, corticosteroids may be tapered in accordance with clinical practice guidelines. Available data suggest that clinical response is usually achieved within 12 to 14 weeks of treatment (after 4 doses). Continued therapy should be reconsidered in patients who show no evidence of therapeutic benefit within this time period.

Treatment is to be initiated and supervised by qualified physicians experienced in the diagnosis and treatment of ulcerative colitis. Patients should be given the Patient Alert Card.

**Summary of evidence on comparative efficacy**

Ulcerative colitis (UC) is a chronic inflammatory disorder of the rectum and colon characterised by mucosal ulceration, rectal bleeding, diarrhoea, and abdominal pain. Golimumab is a human monoclonal antibody that binds to tumour necrosis factor alpha (TNFα), inhibiting its inflammatory effects.1 TNFα is considered to be an important inflammatory mediator contributing to the pathophysiology of UC.2

Evidence for golimumab in UC is from two multicentre, randomised, double-blind, phase III studies: PURSUIT-SC induction and PURSUIT-Maintenance.3,4

PURSUIT-SC induction comprised two parts: a dose-finding, phase II study and a confirmatory phase III study. Following analysis of the phase II data, two induction regimens were selected for further study in the phase III part of the study in which 774 patients participated.3 The study recruited patients with established UC and moderate-to-severe disease activity (defined as a Mayo score 6 to 12 and an endoscopic sub-score $\geq 2$). The Mayo score consists of four sub-scores: stool frequency, rectal bleeding, endoscopic findings and a physician’s global assessment. Each sub-score range from 0 to 3, with higher scores indicating more severe disease, thus the total score ranges from 0 to 12. Patients were either corticosteroid-dependent or had an intolerance or inadequate response to at least one of the conventional therapies: oral 5-aminosalicylates, oral corticosteroids, or thiopurines (azathioprine or mercaptopurine). Concurrent UC treatment was required to be stable and maintained for the duration of the study.3

Product availability date
19 September 2013
Induction regimens consisted of subcutaneous injections at week 0 and 2. In phase III, patients were randomised to placebo (n=258), golimumab 200/100mg (n=258), or golimumab 400/200mg (n=258). The primary endpoint in the phase III part of the study was clinical response at week 6, analysed in the intention-to-treat (ITT) population which included all randomised patients regardless of whether they had received study medication. Clinical response was defined as a decrease from baseline in the Mayo score by $\geq 30\%$ and $\geq 3$ points, with either a decrease in rectal bleeding sub-score of at least 1 point, or a rectal bleeding sub-score of 0 or 1. Patients who had changes in their concomitant UC medication, discontinued due to lack of efficacy or had a colectomy or colostomy before week 6 were considered to have failed treatment. Fixed-sequence testing (high to low-dose) was employed to control the type 1 error (significance level of 0.05). At week 6, significantly greater proportions of patients achieved a clinical response in the golimumab licensed-dose group (200/100mg) compared with placebo (51% versus 30%, p<0.0001).

Results of the major secondary endpoints were also significant in favour of golimumab. The proportion of patients in clinical remission (Mayo score $\leq 2$, with no individual sub-score $>1$) in the golimumab 200/100mg group was 18% compared with the placebo group, 6.4% (p<0.0001). Mucosal healing (endoscopy sub-score of 0 or 1) was evident in a greater proportion of golimumab 200/100mg patients compared with placebo (42% versus 29%, p=0.0014).

Health-related quality of life was measured using the 32-item Inflammatory Bowel Disease Questionnaire (IBDQ). Each question was rated from 1 (very severe problem) to 7 (no problem at all), with total scores from 32 to 224. The higher the IBDQ score the better the quality of life. Golimumab 200/100mg was associated with statistically significant increase in IBDQ score from baseline compared with placebo (mean change: 27.0 and 14.8, respectively). A 20-point improvement in IBDQ score is considered to be consistent with a clinical response.

The PURSUIT-Maintenance study had a placebo-controlled randomised-withdrawal study design, conducted over 54 weeks, and enrolled patients completing the induction studies PURSUIT-SC and PURSUIT-IV (a golimumab induction study in which an intravenous dosage regimen was employed). Patients who had a clinical response to golimumab induction therapy (n=464) were randomly assigned maintenance treatment with subcutaneous golimumab 50mg (n=154), 100mg (n=154) or placebo (n=156) every four weeks. Randomisation was based on: investigation site, previous induction therapy (dose and route of golimumab administration) and remission status coupled with corticosteroid use at baseline.

Concomitant UC medications were to remain stable for the duration of the study, with the exception of corticosteroids which were to be tapered from week 0 (5mg/week for doses $>20$mg prednisolone equivalent/day and 2.5mg/week for doses $\leq 20$mg). Treatment was modified if patients lost clinical response.

Partial Mayo scores (all sub-scores except for endoscopy) were recorded every four weeks. Endoscopy was conducted at weeks 30 and 54 and when partial Mayo scores suggested loss of clinical response. The primary endpoint was maintenance of clinical response through week 54 analysed in the randomised ITT population. The results of the primary outcome and the major secondary outcomes presented in the fixed-sequence for significance testing are tabulated below.
Golimumab

<table>
<thead>
<tr>
<th></th>
<th>100mg</th>
<th>50mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients maintaining clinical response through week 54</td>
<td>50% (p&lt;0.001)</td>
<td>47% (p=0.01)</td>
<td>31%</td>
</tr>
<tr>
<td><strong>Major Secondary Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients in clinical remission at both weeks 30 and 54</td>
<td>28% (p=0.004)</td>
<td>23% (NS)</td>
<td>16%</td>
</tr>
<tr>
<td>Proportion of patients with mucosal healing at both weeks 30 and 54</td>
<td>42% (p=0.002)</td>
<td>42%*</td>
<td>27%</td>
</tr>
<tr>
<td>No. of patients in clinical remission at baseline</td>
<td>n=54</td>
<td>n=52</td>
<td>n=54</td>
</tr>
<tr>
<td>Proportion of patients in clinical remission at baseline who were in remission at both weeks 30 and 54</td>
<td>39% (NS)</td>
<td>36%*</td>
<td>24%</td>
</tr>
<tr>
<td>No. of patients receiving corticosteroids at baseline</td>
<td>n=82</td>
<td>n=78</td>
<td>n=87</td>
</tr>
<tr>
<td>Proportion of patients with corticosteroid-free remission at week 54 among patients receiving corticosteroids at baseline</td>
<td>23%*</td>
<td>28%*</td>
<td>18%</td>
</tr>
</tbody>
</table>

Table: Primary and major secondary endpoints in the PURSUIT-Maintenance study. NS = not significant. *Significance could not be formally tested due to failure to demonstrate significance for the previous endpoint in the fixed-sequence testing procedure.

Colectomy was undertaken in 1.3%, 2.6% and 1.9% of golimumab 100mg, 50mg and placebo patients through to week 54. Dosage modification was required in 37% of patients in the primary analysis population: 28%, 34% and 49% of golimumab 100mg, 50mg and placebo patients respectively. Antibodies to golimumab were identified in 2.9% (32/1,103) of all patients tested (randomised and non-randomised) up to week 54.

An extension to the PURSUIT-Maintenance is ongoing with the aim of following patients up to week 228.

Summary of evidence on comparative safety

No comparative safety data are available. Refer to the summary of product characteristics for details of adverse effects.

**Induction**

Across all parts of PURSUIT-SC induction, 330 patients had placebo and 331 patients received the licensed dose of golimumab (200/100mg). Similar proportions of patients had at least one adverse event in these treatment groups: 38% and 38%, respectively. Discontinuation due to adverse event was low: 0.9% and 0.3% respectively. The most common adverse events were infection (12% in both groups), headache (5.2% versus 3.0%), nasopharyngitis (3.3% in both groups), UC (3.9% versus 2.1%) and injection-site reaction (1.5% versus 3.3%). A small proportion of patients had serious adverse events: 6.1% of placebo patients and 2.7% of golimumab 200/100mg patients. Serious infection was reported in six placebo patients and in one patient in the golimumab 200/100mg group.

**Maintenance**

Amongst all treated patients, adverse events were experienced by 64%, 73% and 74% of patients who received placebo, golimumab 50mg and 100mg respectively. These were similar proportions to the randomised patients’ groups: 66%, 73% and 73% respectively. Discontinuation from the randomised
groups due to adverse events was 6.4% for placebo and 5.2% and 9.1% for golimumab 50mg and 100mg. Frequently experienced adverse events (% patients randomised to placebo, golimumab 50mg, golimumab 100mg) included: infection (28%, 39%, 39%), UC (19%, 18%, 16%), nasopharyngitis (7.1%, 9.1%, 14%), abdominal pain (2.6%, 7.1%, 7.1%) and injection-site reactions (1.9%, 1.9%, 7.1%).

There were four cases of tuberculosis reported up to week 54: one patient on placebo maintenance following golimumab induction, and three patients on 100mg maintenance following golimumab induction. All patients were taking concurrent corticosteroid upon study entry. Two patients developed serious opportunistic infections: cytomegalovirus (golimumab induction and placebo maintenance), and *Staphylococcus aureus* and *Nocardia* cultured from a brain abscess (golimumab induction and 100mg maintenance).

The European Medicines Agency (EMA) considered the safety profile of golimumab when used in patients with UC was similar to the profile for the other licensed indications.

### Summary of clinical effectiveness issues

Golimumab is the third TNFα inhibitor to be granted a marketing authorisation for use in adults with moderate to severe UC who have had inadequate response or are intolerant to conventional UC therapy. However neither infliximab nor adalimumab has been accepted by SMC for use in NHS Scotland. Clinical guidelines recommend treatment choices that take into account the severity and location of the disease and patient preference. Long-term maintenance therapy is recommended to address symptoms, maintain remission and improve quality of life. Thiopurines are used when aminosalicylates provide inadequate response or in patients who require oral corticosteroid to maintain remission. The most recently published guidelines from the European Crohn’s and Colitis Association recommended that in:

- Patients with moderately active UC despite corticosteroid treatment - TNFα inhibitors, tacrolimus or admission for parenteral corticosteroids or surgery are options.
- Patients with moderately active UC refractory to thiopurines - TNFα inhibitors, tacrolimus or surgery are options.

In the PURSUIT studies, the primary outcome was clinical response as measured using the Mayo score, which assesses symptoms and signs of UC of importance to patients. Patients achieving a clinical response may still have measurable disease activity although in the context of inadequate response or intolerance to conventional therapy, this is still a relevant outcome. A significantly greater proportion of patients given golimumab for induction achieved a clinical response compared with placebo. In patients who had responded to golimumab induction, maintenance with golimumab 50mg or 100mg every four weeks was associated with greater response rates over 54 weeks, compared with placebo. For the patient group investigated in the studies, the treatment effect over placebo was considered by the EMA to be of clinical significance. The EMA was unconvinced by any major difference in clinical response or remission between the golimumab maintenance doses in patients <80kg, but additional data presented by the company supported an additional benefit of the 100mg dose in heavier patients. European guidelines consider corticosteroid-free remission to be the therapeutic goal for patients with UC.

In both studies, patients who had an inadequate response or intolerance only to 5-aminosalicylate could be included (19% in PURSUIT-SC induction and 17% in PURSUIT-Maintenance). These patients are not necessarily eligible for golimumab under its licensed indication. The EMA noted that exclusion of these patients from the analyses did not make a major difference to the results of the studies.
PURSUIT-Maintenance employed an enriched enrolment, randomising patients who had responded to golimumab induction after six weeks. The summary of product characteristics (SPC) for golimumab notes that “clinical response is usually achieved within 12 to 14 weeks (4 doses)”, recommending a review of patients who do not benefit within this time. Maintenance data is only available for patients who responded after two doses. The study used fixed-dosing unrelated to body weight. It is unclear what the treatment effect is when used as per the recommendations in the SPC.

Induction with golimumab was associated with an improvement in health-related quality of life as measured with the IBDQ.

Rates of colectomy in all groups were low in the maintenance study. This may reflect the exclusion criterion in the PURSUIT Induction study i.e. patients at risk of colectomy.

### Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis over a 10-year time horizon comparing golimumab with colectomy for the treatment of moderately to severely active UC in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-MP or AZA, or who are intolerant to or have medical contraindications for such therapies. Colectomy was selected as the comparator on the basis that SMC had not accepted any other TNFα inhibitor for use in the same place in the treatment pathway. The exclusion of intravenous corticosteroids as a comparator was justified by the company on the basis that they are unsuitable for long-term use.

The economic model was divided in two parts: a decision tree part (consisting of an induction phase only), and a Markov model part (that consisted of a pre-colectomy maintenance phase, a relapse management phase, and colectomy). Each of the aforementioned models contained health states within them. Patients in the golimumab arm entered the induction phase and, if the treatment failed, progressed into the relapse management phase; otherwise, they moved into the maintenance phase. In relation to the relapse management phase, patients could move into this health state from a treatment failure in the induction phase and from a treatment failure before the week 16 of the maintenance phase. If the intravenous steroid treatment in the relapse management phase failed, patients then moved to colectomy. Patients in the colectomy arm started in the colectomy phase and remained in the health states within that phase for the rest of the model time horizon.

The clinical data for the golimumab arm in the economic model were primarily taken from the pivotal trials and from a published systematic review of steroid use in patients with UC. These studies provided the data for the pre-colectomy phase only. Transitions between health states in the pre-colectomy phase were dependent on Mayo scores. For colectomy (which includes the whole comparator arm and the post-colectomy phase of the golimumab arm), the clinical data were primarily taken from the UK Inflammatory Bowel Disease Audit 2010 and from another published study.

Utility values for the pre-colectomy maintenance phase were based on EQ-5D data collected in the pivotal studies. The relapse management and colectomy health states’ utilities were derived from supportive studies. Drug costs (intervention and concomitant treatment), serious adverse events, hospitalisations and resource use were included.

In the base analysis, the submitting company estimated a cost per quality-adjusted life-year (QALY) of £38,011 based on an incremental cost of £19,252 and a QALY gain of 0.51. 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. As SMC has not
recommended use of the medicine, however, the PAS cannot be implemented in NHS Scotland. Under the PAS, the list price of the 100mg dose of golimumab is provided at the same price as the 50mg dose. With the PAS the incremental cost was reduced to £13,775 and the cost per QALY was reduced to £27,197.

Deterministic sensitivity analyses and probabilistic sensitivity analysis were undertaken. The most important drivers are related to the utilities and to the probabilities and odds ratios that define the efficacy of the treatments.

A number of uncertainties were identified as follows:

- Based on initial feedback from SMC clinical experts, the treatment pathway has not been fully described and the comparator may be inappropriate. The submission suggests that the only options in the licensed position are intravenous steroids and surgery, excluding other treatment options. However SMC clinical experts have indicated there may be some use of infliximab in these patients in practice.

- There may be some bias in the model structure which is linked to the bullet point above. In the golimumab arm, non-responders to induction treatment were assumed to move to the relapse management phase of the model where they could be treated with up to two courses of intravenous steroids. Only once these options have failed do patients move to receive colectomy. However, in the comparator arm, colectomy is the only treatment option. If the target population is patients who are considering surgery following failure of other treatment options, it seems unlikely that patients would receive further intravenous steroid treatment after golimumab treatment has failed. It should be noted the results were sensitive to changes in the model parameters in the relapse management phase of the model. The company subsequently provided an analysis which removed the relapse management phase of the model and this increased the cost per QALY with the PAS to £32k.

- There is a lack of clinical data to support the model prediction that response to golimumab treatment will delay or avoid the need for colectomy. The delay or avoidance of colectomy was not an endpoint measured in the clinical studies and, as noted in the clinical effectiveness section above, patients at imminent risk of colectomy were excluded from the induction study.

- The utility value for patients who received colectomy was 0.595 and this was applied to all patients post-colectomy for the duration of the model, regardless of whether patients experienced any complications. Other published utility values suggest this value may be too low, particularly as it is applied for the duration of the 10-year time horizon. When the utility value for patients who do not experience any complications post-colectomy was increased to 0.65, the cost per QALY increased to £43k.

- The approach used to identify the data sources for the model was not systematic. The submission combined data from clinical efficacy studies of golimumab with data from a single published source on the safety of surgery. While the challenges of conducting a more formal indirect comparison with colectomy are fully acknowledged, the minimum requirement would be a more systematic approach to identification of relevant data sources to estimate the efficacy and safety of colectomy. In response to this, the company subsequently provided sensitivity analysis to show the rate of complications associated with colectomy was not a key driver in the model.

Due to the limitations outlined above, the economic case has not been demonstrated.
Summary of patient and public involvement

A Patient Interest Group Submission was not made.

Additional information: guidelines and protocols

The National Institute for Health and Care Excellence published clinical guideline 166 on the management of UC in 2013. UC is categorised as mild, moderate or severe which in adults is based on the Truelove and Witts’ severity index. This considers factors such as: number of bowel movements per day, presence of blood in stools, pyrexia, heart rate, anaemia, and erythrocyte sedimentation rate. Management options consider the category of UC, the part of the colon and rectum affected, and patient preference. Different formulations of aminosalicylates and corticosteroids are recommended to induce remission of UC, with intravenous ciclosporin, infliximab or surgery considered for acute severe attacks in patients who have had little or no improvement with intravenous corticosteroids, or whose symptoms worsen at any time. Aminosalicylate therapy is the first choice for the maintenance of remission, but oral azathioprine or mercaptopurine should be considered when remission is not maintained by aminosalicylates, there have been at least two exacerbations in the previous year requiring systemic corticosteroids, or if the patient has had an acute severe UC episode. No recommendations are given for the use of biologic agents in the maintenance of UC.

The British Society of Gastroenterology updated its guidelines for the management of inflammatory bowel disease in adults in 2011. Long-term maintenance therapies to reduce the risk of relapse are recommended in all patients: aminosalicylates, azathioprine or mercaptopurine. Long-term treatment with corticosteroids is considered unacceptable. Options for patients with steroid-dependent UC include azathioprine, mercaptopurine, or surgery. Steroid-free remission is the goal, however in the event of failure of immunosuppressive therapy alternative approaches need to be discussed with the patient, which may include surgery. The guideline does not recommend the use of biologic agents in the maintenance of UC.

The European Crohn’s and Colitis Organisation published consensus guidance in 2012. Recommendations are given in relation to various scenarios, including:

- Patients with moderately active UC despite corticosteroid treatment - TNFα inhibitors, tacrolimus or admission for parenteral corticosteroids or surgery.
- Patients with active, corticosteroid-dependent UC - thiopurines (azathioprine or 6-mercaptopurine).
- Patients with moderately active UC refractory to thiopurines - TNFα inhibitors, tacrolimus or surgery.

Without a clear clinical benefit, continued medical therapy is not recommended. No recommendation is given for the duration of treatment with TNFα inhibitors due to limited evidence. In patients with active UC, a large therapeutic gap exists despite positive placebo-controlled studies for both infliximab and adalimumab. Infliximab achieves steroid-free remission in 21% and 26% of patients after 7 and 12 months respectively. After 12 months, adalimumab achieved steroid-free remission in 13% of patients. The guidance concludes that “further studies are needed to define the appropriate patient population, the benefits of concomitant medication and any difference in efficacy for the available anti-TNF therapies”.

All guidelines predate the award of the marketing authorisation for golimumab in Europe.
**Additional information: comparators**

Other biologic agents with marketing authorisations for the treatment of UC in patients with intolerance or refractory to conventional therapy include the TNFα inhibitors infliximab and adalimumab. In NHS Scotland, SMC has not recommended these agents for use in adults.

**Cost of relevant comparators**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose Regimen</th>
<th>Cost per year (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Year 1</td>
</tr>
<tr>
<td>Golimumab</td>
<td>Subcutaneous injection</td>
<td>13,733</td>
</tr>
<tr>
<td></td>
<td>In patients less than 80kg:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Initial dose of 200mg, then 100mg at week 2, then 50mg every 4 weeks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>thereafter.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>In patients ≥80kg:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Initial dose of 200mg, then 100mg at week 2, then</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100mg every 4 weeks thereafter.</td>
<td></td>
</tr>
<tr>
<td>Infliximab</td>
<td>Intravenous infusion of 5mg/kg at week 0, 2 and 6.</td>
<td>13,428</td>
</tr>
<tr>
<td></td>
<td>Further doses every 8 weeks thereafter.</td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Subcutaneous injection</td>
<td>10,916</td>
</tr>
<tr>
<td></td>
<td>Initial dose of 160mg, then 80mg at week 2, followed by</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40mg dose every 2 weeks thereafter.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>The dose can be increased to 40mg every week in patients who</td>
<td></td>
</tr>
<tr>
<td></td>
<td>experience a decrease in response.</td>
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</tbody>
</table>

Doses are for general comparison and do not imply therapeutic equivalence. Costs from [www.mims.co.uk](http://www.mims.co.uk) on 02 June 2014 and based on body weight of 70kg. Infliximab and adalimumab have not been recommended for use in NHS Scotland for ulcerative colitis in adults.

**Additional information: budget impact**

The submitting company estimated there to be 193 patients eligible for treatment with golimumab in year 1 and 198 patients in year 5, with an estimated uptake rate of 33% in each year.

Without the PAS, the submitting company estimated the gross medicines budget impact to be £3.21m in year 1 and £2.58 in year 5. As it was assumed no medicines would be displaced, the net budget impact is the same as the gross. With the PAS, the gross medicines budget impact was estimated to be £2.21m in year 1 and £1.96m in year 5. As it was assumed no medicines would be displaced, the net budget impact is the same as the gross.

The higher cost estimated in year 1, despite lower patient numbers, is due to patients receiving additional doses of golimumab in the induction phase.
References

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


This assessment is based on data submitted by the applicant company up to and including 11 July 2014.

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.