Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2477

belimumab 120mg and 400mg powder for concentrate for solution for infusion (Benlysta®)

GlaxoSmithKline UK Ltd

07 October 2022

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 NHSScotland. The advice is summarised as follows:

ADVICE: following a second resubmission

belimumab (Benlysta®) is accepted for restricted use within NHSScotland.

Indication under review: Add-on therapy in patients aged 5 years and older with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy.

SMC restriction: in adults with evidence for at least one marker of serological disease activity (low complement, positive anti-dsDNA) and a Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score ≥10.

Belimumab, in addition to standard therapy, modestly improved disease control in patients with SLE in two phase III studies.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chairman
Scottish Medicines Consortium

Indication

Add-on therapy in patients aged 5 years and older with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy. [1, 2]

Dosing Information

The recommended dose regimen is 10mg/kg by intravenous infusion over 1 hour on days 0, 14 and 28 and at 4-week intervals thereafter. The patient's condition should be evaluated continuously. Discontinuation of treatment should be considered if there is no improvement in disease control after 6 months of treatment. [1, 2]

Treatment should be initiated and supervised by a qualified physician experienced in the diagnosis and treatment of SLE. Infusions should be administered by a qualified healthcare professional trained to give infusion therapy. Administration of belimumab may result in severe or life-threatening hypersensitivity reactions and infusion reactions. Patients have been reported to develop symptoms of acute hypersensitivity several hours after the infusion has been administered. Recurrence of clinically significant reactions after initial appropriate treatment of symptoms has also been observed. Therefore, it should be administered in an environment where resources for managing such reactions are immediately available. Patients should remain under clinical supervision for a prolonged period of time (for several hours), following at least the first two infusions, taking into account the possibility of a late onset reaction. Premedication including an antihistamine, with or without an antipyretic, may be administered before the infusion of belimumab. [1, 2]

Product availability date

19 September 2011

Summary of evidence on comparative efficacy

Belimumab is a human IgG1λ monoclonal antibody specific for soluble human B Lymphocyte Stimulator protein (BLyS). Belimumab binds to BLyS and inhibits the survival of B cells. Levels of BLyS are elevated in patients with SLE and there is an association between plasma BLyS levels and SLE disease activity. [1]

The submitting company has requested that SMC considers belimumab when positioned for use in adults with evidence for at least one marker of serological disease activity (low complement, positive anti-dsDNA) and a Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score ≥10. The SELENA-SLEDAI index ranges from 0 to 105, with a score of 0 indicating no disease activity, scores >10 indicating high activity and ≥20, indicating very high activity. [3, 4]

Evidence comes from two similar phase III multi-centre, randomised, double-blind, placebo-controlled studies, BLISS-76 and BLISS-52, that evaluated the efficacy and safety of belimumab with standard therapy versus standard therapy alone in patients with SLE. [5, 6] Eligible patients were aged at least 18 years with an SLE diagnosis according to the American College of Rheumatology criteria, active disease (SELENA-SLEDAI ≥6) at screening, sero-positivity and a treatment regimen that was stable for at least 30 days. Patients with severe active lupus nephritis or severe active central nervous system lupus were excluded from the studies. [5, 6]

Patients were centrally stratified according to SELENA-SLEDAI score, proteinuria and race, then randomised equally to receive belimumab 10mg/kg, 1mg/kg or placebo by intravenous infusion over 1 hour on days 0, 14 and 28 and every 28 days through to week 72 in BLISS-76, and to week 48 in BLISS-52. All study medication was administered with standard of care, a stable treatment regimen, which could include prednisone (or equivalent) up to 40mg daily with antimalarials, non-steroidal anti-inflammatory drugs (NSAIDs), and/or immunosuppressants. Initiation of immunosuppressants was prohibited during the study but addition of a new antimalarial drug and dosage increases of concomitant immunosuppressive or antimalarial drugs were permitted until week 16. After week 16, the maximum dose of immunosuppressive or antimalarial drug could not be increased above the baseline or the week 16 dose, whichever was greater. [5, 6]

In both studies, the primary efficacy outcome was response rate at week 52, evaluated using the SLE Responder Index (SRI). This is a composite measure, combining three validated tools for estimating SLE activity: SELENA-SLEDAI, Physician's Global Assessment (PGA) and the British Isles Lupus Assessment Group (BILAG) index. Response was defined as a reduction of ≥4 points in the SELENA-SLEDAI score and no new BILAG A organ domain score or no more than one new BILAG B organ domain score and no worsening in PGA score (increase <0.3) at week 52 compared with baseline. Analyses were performed on the modified intention to treat population, all randomised patients who received at least one dose of study agent. The results for the belimumab 10mg/kg, the licensed dose of belimumab, and placebo are presented. [5, 6]

In BLISS-76, SRI response at week 52 was 43% (118/273) and 34% (93/275) for patients in the belimumab 10mg/kg and placebo groups respectively, odds ratio 1.52 (95% confidence interval [CI]: 1.07 to 2.15), p=0.021.[4, 5]

Not all the secondary outcomes were met. SRI response at week 76 was not statistically different between the treatment groups: 38% (105/273) and 32% (89/275) in the belimumab 10mg/kg and placebo groups respectively. There was no significant difference in steroid-sparing in patients taking at least 7.5mg prednisolone daily at baseline; the proportion of patients with an average reduction in prednisolone dose of ≥25% to ≤7.5mg daily during weeks 40 to 52 was 18% (21/120) versus 13% (16/126) for 10mg/kg versus placebo.[4, 5]

In BLISS-52, the primary outcome, SRI response rate at week 52, was significantly higher in the belimumab 10mg/kg group compared with placebo: 58% (167/290) versus 44% (125/287) respectively, odds ratio (OR) 1.83 (95% CI: 1.30 to 2.59) p=0.0006. [4, 6]

In both studies, patient reported outcomes included the short form 36 version 2 (SF-36v2) physical component summary, the Functional Assessment of Chronic Illness Therapy fatigue score and the EQ-5D index scores and EQ-5D$_{vas.}$ There was generally no significant differences between belimumab 10mg/kg and placebo. [5, 7, 6, 8]

The submitting company presented evidence to support the use of belimumab in the target population within the proposed positioning, using data pooled from both studies. SRI response rate at week 52 in this target population (that is adults with evidence for at least one marker of serological disease activity (low complement or positive anti-dsDNA) and a SELENA-SLEDAI score ≥10) was reported as 63% (166/262) in the belimumab 10mg/kg group and 43% (117/270) in the placebo group corresponding to an odds ratio of 2.29 (95% CI: 1.61, 3.26).[9]

There are some long-term data supporting sustained benefit. BLISS-76 US long-term extension (LTE) was a US multicentre LTE study to assess long-term safety and efficacy of belimumab in patients with SLE who completed BLISS-76 study. Patients received standard therapy plus belimumab. Organ damage was assessed using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI). The primary efficacy assessment was the SRI response rate. Of 268 patients, 140 completed the study. Concerning organ damage, the mean ± SD SDI score at baseline was 1.2 ± 1.5 and at study year 7 it increased by 0.4 ± 0.7 from its value at baseline. An SRI response was achieved by 42% (96/229) and 76% (90/119) of patients at the study year 1 and study year 7 midpoints, respectively. [10]

BLISS-52/76 non-US LTE was a multicentre, LTE study in non-US patients of BLISS-52 and BLISS-76 studies. Patients received standard therapy plus belimumab; 738 patients entered the extension study and 735 received one dose of belimumab. The mean (± SD) SDI was 0.6 (1) at baseline and it increased by only 0.2 (0.5) at study year 8. [11]

The submitting company summarised a propensity score matching (PSM) analysis that was performed to match patients treated with belimumab (plus standard therapy) in the BLISS-76 US LTE study with patients from the Toronto Lupus Cohort (TLC) treated with standard therapy, to compare long-term effectiveness of both treatments. It was used in the economic analysis to generate a calibration factor that is used to adjust the modelling of organ damage. The primary outcome was the difference in change in SDI score from baseline to 5 years. For the 5-year analysis, of the 195 patients from BLISS-76 US LTE and 372 from the TLC, 99 from each cohort were 1:1 propensity score matched. Change in SDI score at year 5 was lower for patients treated with belimumab compared with standard therapy (−0.434; 95% CI –0.667 to –0.201; p<0.001). Authors concluded propensity score-matched patients receiving belimumab had significantly less organ damage progression compared with patients receiving standard therapy. [12]

Summary of evidence on comparative safety

In a pooled safety analysis of all belimumab studies, the incidence of adverse events (AEs) was similar between the belimumab and placebo treatment groups. At least one treatment-emergent AE was experienced by the majority of patients. The most frequently reported AEs were headache, upper respiratory tract infections, arthralgia, nausea, urinary tract infections, diarrhoea, fatigue and pyrexia. [4]

The main AE of special interest were infections, infusion reactions and malignancy. The incidence of infections across the studies was 70% and 67% in the belimumab 10mg/kg and placebo groups respectively. Severe infections occurred in 3.3% and 3.7% of patients respectively. Most infusion-related reactions occurred during either the first or second infusion and the incidence declined over subsequent infusions. Serious infusion or hypersensitivity reactions occurred in 0.9% and 0.4% of belimumab and placebo treated patients respectively. Belimumab is an immunomodulator so the potential risk for malignancy may be a concern. The malignancy rate reported during the relatively short duration of the studies was similar to the background rate for SLE patients.

Progressive multifocal leukoencephalopathy has been reported with belimumab treatment for SLE.[1, 2]

Summary of clinical effectiveness issues

SLE is a chronic, autoimmune, multisystem disorder with a relapsing-remitting clinical course.[4, 13] It is associated with a high risk of permanent organ damage and a significant impact on mortality. The disease mainly affects young women who often require treatment over many years. The current standard of care includes the use of antimalarials, NSAIDs, corticosteroids and immunosuppressants. There is some off-label use of rituximab despite a lack of robust evidence in the treatment of SLE. Belimumab is the first biological agent to show benefit in patients with SLE. It has been developed as a targeted therapy for a specific aspect of SLE pathology associated with immune response in SLE, the BLyS pathway. [4] Clinical experts consulted by SMC considered that belimumab fills an unmet need in this therapeutic area due to the limited number of treatments currently available.

The submitting company has requested that SMC considers belimumab when positioned for use in adults with evidence for at least one marker of serological disease activity (low complement, positive anti-dsDNA) and a SELENA-SLEDAI score ≥10. Clinical experts consulted by SMC felt that the proposed positioning was appropriate.

In the two pivotal studies, belimumab demonstrated a modest benefit in the treatment of SLE as measured by the SRI response rate. This was primarily assessed at week 52 and longer term controlled data are limited. Many of the secondary endpoints in BLISS-76 were not met, including the SRI response rate measured at week 76. While there was no significant difference in quality of

life between the treatment groups, regulators noted that data for belimumab suggests a beneficial effect on fatigue. The improvement in fatigue scores was more pronounced in the subgroups of patients with higher disease activity. The BLISS-52 study, with patients recruited mainly from Latin America and Asia-Pacific and only 11% from Eastern Europe had more positive results but the results may be less generalisable to the Scottish population than those from BLISS-76, which recruited patients mainly from USA/Canada and Europe/Israel.[4-6] A more stringent endpoint, requiring a reduction of at least six points, or a score less than two on the SLEDAI component, found a greater benefit associated with belimumab. Additional analyses also suggested that patients with higher disease activity (SELENA-SLEDAI ≥10) responded better to belimumab. The treatment effect of belimumab in addition to standard therapy was considered clinically relevant in patients with high disease activity. [4]

The studies had a number of limitations. The duration was short for this chronic disease and may have been inadequate to measure clinically detectable organ damage. Patients with central nervous system manifestations and lupus nephritis were excluded from the clinical studies. The baseline SELENA-SLEDAI score in BLISS-76 and BLISS-52 was ≥10 for 52% of patients. Prednisone (or equivalent) was taken daily by 96% of patients; 67% to 71% of patients were taking more than 7.5mg daily at baseline. Less than half of the patients studied were taking an immunosuppressant, such as azathioprine, methotrexate or mycophenolate mofetil. Antimalarials were used by 64% to 70% of patients. There seems to be no clear consensus on maximal treatment measures in practice but it remains unclear if patients had been optimally treated.[5, 6] The target population corresponds to only 32% (532/1684) of the pooled BLISS-76 and BLISS-52 study population (patients with positive anti-dsDNA or low complement, and SELENA-SLEDAI of ≥10 who received placebo or the licensed belimumab regimen [10mg/kg IV]). In addition, analyses in this subgroup relevant to the proposed positioning were not powered and should be interpreted with caution.

In the belimumab LTE studies, organ damage accrual was low when compared with prospective SLE inception cohorts measuring damage accrual; however authors noted BLISS studies excluded patients with severe lupus nephritis and central nervous system disease and these exclusions could account, in part, for the reported lower rates of organ damage.[10, 11].

The submitting company considers standard therapy as the relevant comparator which includes, either alone or in combination, the use of antimalarials (for example, hydroxychloroquine), NSAIDs, corticosteroids and immunosuppressants (such as azathioprine, methotrexate and mycophenolate mofetil); many of these medicines are unlicensed for SLE. Rituximab may also be used in a small number of patients, but standard therapy seems to be the most relevant comparator.

Because the only available long-term data were non-comparative, the submitting company presented a PSM analysis that indirectly compared long-term effectiveness of belimumab (plus standard therapy) versus standard therapy. There were a number of limitations (including some acknowledged by the authors[12] and some identified by previous HTA body review[14]) that affected the validity of this analysis. TLC was the unique source of data for standard therapy; TLC data were from North American patients and from an older time period and changes in medical care may

influence organ damage development. It is uncertain whether using only BLISS-76 US LTE data was more appropriate than using all BLISS LTE studies. It is unknown how many of the compared patients had at least one marker of serological disease activity (low complement, positive anti-dsDNA) and a SELENA-SLEDAI score ≥10. Overall, it is uncertain how generalisable the results are to the Scottish population that might be eligible to belimumab in practice. One of the key limitations however is the differences in the study designs between BLISS-76 US LTE and TLC; there are no specific requirements for patients to remain in the TLC for 5 years, whereas in order to continue follow-up in BLISS-76 US LTE patients must (a) have successfully completed 76 weeks of follow-up in the original BLISS-76 study (in order to then enrol in BLISS-76 US LTE) while maintaining adequate response to treatment, and (b) continue to receive belimumab for at least 5 years in total. The PSM analysis is considered potentially biased in favour of the belimumab arm. Therefore, the results of the PSM analysis are highly uncertain and should be interpreted cautiously.

Clinical experts consulted by SMC considered that belimumab is a therapeutic advancement. They considered that its place in therapy would be as per licensed indication, as an add-on when standard therapy has not been sufficient, and that the proposed positioning was appropriate. With regard to service implications, hypersensitivity reactions can occur with belimumab so facilities and staff to manage these are required. Patients should remain under clinical supervision for a prolonged period of time (for several hours), following at least the first two infusions. [1, 2]

Summary of comparative health economic evidence

The company submitted a cost-utility analysis covering the proposed positioning. This was for belimumab to be used as an add-on therapy in adult patients with active, autoantibody-positive SLE, evidence for at least one marker of serological disease activity (e.g. low complement or positive anti-double stranded DNA) and a SELENA-SLEDAI score ≥10. As a result, there was no active comparator and patients were either assumed to receive belimumab in addition to standard therapy, or standard therapy alone. Patients could receive belimumab for the duration of their lifetimes, but only subject to response being achieved at 24 weeks (defined as a decrease in SELENA-SLEDAI score of ≥4 points).

The company presented a patient level simulation, which followed individual patients throughout the duration of their lifetime. The model traced changes in disease activity (as measured by SELENA-SLEDAI score) and changes in organ damage across 12 systems (cardiovascular, diabetes, gastrointestinal, malignancy, musculoskeletal, neuropsychiatric, ocular, peripheral vascular, premature gonadal failure, pulmonary, renal and skin). The impact of belimumab on the level of steroid use was also captured.

Short-term effects of belimumab on disease activity were estimated from the pooled data of the BLISS-52[6] and BLISS-76[5] studies. Long-term outcomes for disease activity, organ damage, steroid use and mortality were projected using an American cohort – the Johns Hopkins Lupus Cohort. However, the company felt that the estimates of disease activity and organ damage over time lacked clinical plausibility, and so these were subject to further adjustment. The constant in the

regression model used to predict SELENA-SLEDAI over time was increased to slow the reduction in projected disease activity as a patient aged. Further, the results of the PSM analysis were used to estimate a calibration factor that reduced the level of organ damage experienced by belimumab patients.

Health related quality of life information was collected from participants of the BLISS-52 and BLISS-76 studies. These were used to estimate patient and disease activity specific utility values, assuming no organ damage. Additional disutilities were extracted from the literature to capture the effects of organ damage. These were included multiplicatively, with only the most impactful disutility included in the event of multiple systems being damaged. No AEs disutilities were included, as the company reported limited differences between the two arms of the BLISS-52 and BLISS-76 studies.

Medicine costs covered the acquisition and administration of belimumab. Standard therapy costs and AE costs were excluded, having been assumed equal across model arms. Resource use for those with SLE were projected using 86 UK patients from the Systematic Lupus Erythematosus Cost of Care in Europe (LUCIE) study.[15] The LUCIE study collected data on laboratory tests, biopsies and imaging tests, medical treatments, visits to specialists, hospitalisation and rehabilitation stays. This database was used to model the relationship between SELENA-SLEDAI score and costs. Additional organ damage costs were extracted from the literature.

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 NHSScotland. Under the PAS, a discount was offered on the list price. The results presented below are inclusive of that PAS discount.

Use of belimumab in combination with standard therapy was projected to increase NHS costs, but also generate better health care outcomes than standard therapy alone. Based on the submitted model, the incremental cost-effectiveness ratio (ICER) was estimated as £11,624.

In addition to the base case results, the submitting company also provided a range of scenarios exploring areas of uncertainty. A selection of these are outlined in Table 1.

Table 1. Scenario analysis, inclusive of the PAS discount on belimumab

#	Description of scenario	Description of base case	ICER
1	Belimumab treatment duration and effect restricted to 10 years	Belimumab treatment duration and effect is maintained for patient lifetime	£4,595
2	Belimumab treatment duration and effect restricted to 6 years		Dominant
3	Constant in disease activity regression unadjusted	Constant in disease activity regression adjusted upward	£11,568
4	Exclusion of the calibration factor on the organ damage risk model	Inclusion of the calibration factor on the organ damage risk model	£28,216
5	Organ damage calibration factor applied to both the belimumab and standard therapy arms for 6 years	Organ damage calibration factor applied to the belimumab arm only, for 6 years	£5,934

#	Description of scenario	Description of base case	ICER
6	Organ damage calibration factor applied to belimumab only, for patients lifetime		£7,139
7	Organ damage calibration factor based on data from belimumab responders (at 24 weeks) only	Organ damage calibration factor based on data all belimumab patients (responders and non-responders at 24 weeks)	£13,013
8	Maximum patient age 88 years	Life time horizon (all patients dead by 98)	£11,624
9	Maximum patient age 78 years		£11,625

From the scenario analysis, it was clear that duration of belimumab treatment (scenarios 1 and 2 of Table 1) as well as the adjustments made to the organ damage projection model (scenarios 4 to 7) were major determinants of the cost effectiveness.

The strengths of the analysis were identified as being:

- The comparator used in the economic modelling was appropriate.
- The model structure, methodological approach and inputs shared a high degree of commonality with a previously accepted belimumab submission in a slightly narrower patient population (SMC775/12). However, this also means that there were some weaknesses identified at that point, which were not addressed.
- The presentation of results and exploration of uncertainty was adequate to allow robust decision making.

The weaknesses of the analysis were identified as being:

- The duration of the central clinical studies (BLISS-52 and BLISS-76) was relatively short for a life-long treatment. The company relied on an American lupus cohort to estimate the long-term outcomes. That cohort had generalisability issues to the participants of the BLISS studies, having generally less severe SLE, and further, may not adequately represent outcomes expected in a Scottish population.
- Uncertainty on the appropriateness of the long-term projections was highlighted by the subsequent adjustments that the company felt necessary to apply to the disease activity and organ damage estimates. In particular, the calibration factor applied to the organ damage estimates was shown in scenario analysis to be large drivers of results (again, see Scenarios 4 to 7 in Table 1) and was regarded as uncertain. This calibration factor was based on PSM analysis, which suffered from several weaknesses and may have lead to the introduction of bias. This could have contributed towards an artificially low cost-effectiveness estimate.
- The model appeared to show a degree of non-linearity, with deterministic base case results being slightly lower than the mean results from stochastic estimation (ICER =£13,859). The stochastic results may have been more representative of the expected outcomes than the deterministic results.

Despite these limitations, the economic case was considered to have been made.

Summary of patient and carer involvement

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

- We received a patient group submission from Lupus UK, which is a registered charity.
- Lupus UK has received 2.64% pharmaceutical company funding in the past two years, including from the submitting company.
- SLE often has a substantial impact on the lives of people with the disease and their family. It also represents a risk of early mortality. People living with the condition describe the most challenging aspects of living with it as, the symptoms (particularly fatigue and joint/muscle pain), the impact on their ability to work, and their mental wellbeing. Many find maintaining employment difficult. In addition to the caring requirements, the unpredictable nature of lupus can often disrupt social activities and reduce quality of life for the person as well as their family and friends.
- Standard therapy isn't always effective in controlling symptoms and may not be tolerated well by all patients. In recent decades, the percentage of patients progressing into end stage renal disease (ESRD) remains steady despite improvements in therapeutic strategies. This pattern suggests limitations in the effectiveness of, or access to, current treatments. Standard therapy is over-reliant on glucocorticoids as induction and maintenance therapy. This has a negative impact on patients through both short and long term side-effects.
- Belimumab offers an additional treatment option, representing hope for those with active disease who do not respond to standard therapy. For those patients who do not respond sufficiently well to standard therapy alone, belimumab may assist them in reducing their steroid dose over time, helping to reduce the risk of side-effects and future comorbidities. If patients experience a substantial improvement in the management of their condition because of belimumab, it may reduce the number of hospital visits and admissions they have which would be a positive change for them and their family/carers.

Additional information: guidelines and protocols

The British Society for Rheumatology updated their guideline for the management of SLE in adults in October 2017. It states that rituximab or belimumab may be considered for the management of moderate SLE that is refractory to other drugs. It notes that rituximab can be prescribed and reimbursed in England according to the NHS England 2013 interim clinical commissioning policy statement for rituximab in adult SLE patients. For severe SLE, rituximab or belimumab may be

considered on a case by case basis where patients have failed on other immunosuppressive drugs because of inefficacy or intolerance. [16]

The European League against Rheumatism (EULAR) task force updated their recommendations for the management of SLE in March 2019 based on evidence and expert consensus. It states that for moderate disease, patients who have had an inadequate response to standard of care (combinations of hydroxychloroquine and glucocorticoids with or without immunosuppressive agents), defined as residual disease activity not allowing tapering of glutocosteroids and/or frequent relapses, add-on treatment with belimumab should be considered. In addition, patients with persistent disease may benefit from belimumab; more likely to respond are patients with high disease activity (such as SLEDAI >10), prednisone dose >7.5mg/day and serological activity (low C3/C4, high antidsDNA titres), with cutaneous, musculoskeletal and serological manifestations responding the most. It was noted that because of the negative results of randomised controlled trials, rituximab is currently only used off-label, in patients with severe renal or extrarenal (mainly haematological and neuropsychiatric) disease refractory to other immunosuppressive agents and/or belimumab, or in patients with contraindications to these drugs. Cyclophosphamide can be used for severe organ-threatening or life-threatening SLE as well as 'rescue' therapy in patients not responding to other immunosuppressive agents. [17]

Additional information: comparators

Standard of care includes the use of antimalarials, NSAIDs, corticosteroids and immunosuppressants.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per year (£)
Belimumab	**By intravenous infusion, 10mg/kg on day 0, 14 and 28 and at 4 week intervals thereafter**	**In first year: £11,542.** **Subsequent years: £10,004.**

Costs from BNF online on 05/08/2022. Costs calculated with an adult weight of 70kg. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 770 patients eligible for treatment with belimumab in year 1 rising to 942 in year 5. Those values represented the patients currently eligible for belimumab treatment under SMC775/12 as well as those covered by the new positioning. Based on the populations within the BLISS-52 and BLISS-76 studies only 25.6% of eligible patients would be additional. Therefore, the submitting company estimated there would be 197 additional patients eligible for treatment with belimumab in year 1 rising to 241 in year 5. The uptake rate was estimated to be 10% in year 1 (20 additional patients) and 58% in year 5 (140 additional patients). Accounting for failure to respond and discontinuation, the company predicted that there would be 5 additional patients actively receiving treatment in year 1 rising to 18 additional patients in year 5.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

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

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This assessment is based on data submitted by the applicant company up to and including 20 September 2022.

**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:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine 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 medicine 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 NHSScotland 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 NHSScotland 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.