

obinutuzumab concentrate for solution for infusion (Gazyvaro®) Roche Products Ltd

4 September 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

obinutuzumab (Gazyvaro®) is accepted for use within NHSScotland.

Indication under review: in combination with mycophenolate mofetil (MMF), for the treatment of adult patients with active Class III or IV, with or without concomitant Class V, lupus nephritis (LN).

In a double-blind phase III study, obinutuzumab was associated with a statistically significant improvement in complete renal response rate at week 76 compared with placebo, with both treatments administered in addition to MMF and a tapered corticosteroid regimen. An indirect comparison suggests no evidence of a difference in clinical outcomes between obinutuzumab and belimumab, voclosporin or rituximab (all used in combination with MMF and corticosteroids).

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.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Obinutuzumab is a recombinant humanised monoclonal antibody that targets CD20 transmembrane antigen on the surface of pre-B and mature B-lymphocytes. It induces direct cell death, mediates antibody dependent cellular cytotoxicity and phagocytosis through immune effector cells and produces some complement dependent cytotoxicity.¹

For the treatment of lupus nephritis, obinutuzumab is administered as a 1,000 mg intravenous infusion given at treatment initiation, week 2, week 24, and week 26, then every 6 months thereafter. It should be used in combination with mycophenolate mofetil (MMF), and treatment continuation should be reviewed based on response at week 76 and beyond. For more information, please see Summary of Product Characteristics (SPC).¹

1.2. Disease background

Systemic Lupus Erythematosus (SLE) is a chronic, relapsing-remitting, multi-system, auto-immune disease, with accumulated damage and increased risk of premature death. It primarily affects women with peak incidence during the childbearing years. The clinical manifestations of acute disease are largely driven by inflammatory processes triggered by immune complex formation. In lupus nephritis (LN), their deposition in the kidneys results in renal inflammation and damage. Lupus nephritis is categorised into classes (I to VI) based on renal lesions. Within 10 years of an initial SLE diagnosis, 5 to 20% of patients with LN progress to end-stage kidney disease, which is associated with a 26-fold increase in mortality compared with the general population.²⁻⁶

1.3. Treatment pathway and relevant comparators

For new or relapsing class III or IV (with or without class V) LN, guidelines recommend individualised induction according to patient and disease characteristics with glucocorticoids (GC, intravenous followed by tapering oral GC), and mycophenolic acid analogues (MPAA) in combination with obinutuzumab or belimumab or calcineurin inhibitors (voclosporin, or tacrolimus). Other options include MPAA alone or combined with rituximab, and cyclophosphamide alone or combined with belimumab.

For patients achieving 12-month treatment targets, maintenance therapy should continue for at least 3 years with the combinations of immunosuppressants. Treatment options for refractory LN include clinical trials, switching to another induction immunosuppressant combinations, and/or re-induction with GC.^{4, 7, 8}

Belimumab has been accepted by SMC for restricted use in active SLE (SMC2477) but, in the absence of a submission, it is not accepted for use in combination with background immunosuppressive therapies for active LN (SMC2483). Voclosporin has been accepted for use in combination with MMF for active class III, IV or V (including mixed class III/V and IV/V) lupus nephritis (SMC2570).

The submitting company considers MMF alone or in combination with voclosporin or rituximab (all with corticosteroids) to be the most relevant comparators.

Clinical experts consulted by SMC consider that obinutuzumab would most likely displace some use of belimumab-, calcineurin inhibitor-, cyclophosphamide- or rituximab-based combination therapies.

1.4. Category for decision-making process

Eligibility for a PACE meeting

Obinutuzumab meets SMC orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of obinutuzumab for the indication under review comes from the REGENCY study as detailed in Table 2.1.

Table 2.1. Overview of relevant study ⁹⁻¹¹

Criteria	REGENCY
Study design	International, randomised, double-blind, phase III study
Eligible patients	• Age 18 to 75 years • Active or active/chronic ISN/RPS 2003 Class III or IV proliferative LN by renal biopsy performed in the 6 months prior to screening or during screening, with or without concomitant Class V disease • SLE according to the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria, which are met by the presence of Class III or IV LN and current or past positive antinuclear antibody • UPCR ≥ 1 g/g on a 24-hour collection at screening • Receipt of at least one dose of pulse methylprednisolone IV or equivalent for treatment of the current episode of active LN during the 6 months prior to screening or during screening, or given on Day 1 prior to the first infusion • A maximum of 3 g methylprednisolone IV or equivalent during the 4 weeks prior to screening or during screening
Treatments	During the blinded treatment period (to week 76), patients were randomised equally to obinutuzumab or placebo, both on top of mycophenolate mofetil and corticosteroids with a tapering schedule. Patients assigned to the obinutuzumab group were again randomly assigned in a 1:1 ratio to receive obinutuzumab as 1,000 mg IV infusions on day 1 and weeks 2, 24, 26, 50 and 52 (2-2-2 regimen) or day 1 and weeks 2, 24, 26 and 52 (2-2-1 regimen). Placebo infusions were administered at matching timepoints to maintain blinding. In cases of worsening or severely active disease, investigators could administer rescue therapy. Non-corticosteroid rescue treatments required discontinuation of study treatment. High-dose corticosteroid rescue from week 64 onwards classified patients as non-responders, although they could continue study treatment.
Randomisation	Randomisation was stratified according to geographic region (United States or Canada, Latin America or the Caribbean, or other) and race (Black or other).
Primary outcome	Proportion of patients who achieve complete renal response, evaluated at week 76, defined by: - a UPCR lower than 0.5 based on a timed 24-hour urine collection, - an eGFR of at least 85% of the baseline value, - no occurrence of an intercurrent event that is rescue therapy, treatment failure, death, or early trial withdrawal. Treatment failure was defined as end-stage kidney disease or the use of long-term dialysis or renal transplantation, receipt of rescue therapy (except for glucocorticoid-only rescue), or clinically significant and

	sustained worsening of the UPCR or eGFR beyond week 24 that led the centre investigator to conclude that the assigned regimen had failed.
Key secondary outcomes	- Proportion of patients who achieve CRR with successful prednisone taper at week 76. - Proteinuric response was defined as achievement of all of the following: UPCR < 0.8 g/g and no occurrence of the following intercurrent events: Rescue therapy, treatment failure, death or early study withdrawal. - Change in eGFR at week 76 - Proportion of patients who experience death or renal-related events through week 76, defined as the proportion of patients with one or more of the following events: death; treatment failure; worsening proteinuria, defined as a confirmed $\geq 50\%$ increase in UPCR to a value ≥ 3; worsening eGFR, defined as a confirmed $\geq 30\%$ decrease in eGFR to a value < 60. - Proportion of patients who achieve an ORR, defined as achievement of either CRR or PRR, evaluated at week 50. PRR was defined as achievement of all of the following: $\geq 50\%$ reduction in UPCR from baseline; UPCR < 1 (or < 3 if the baseline UPCR was ≥ 3); eGFR $\geq 85\%$ of baseline, as calculated using the CKD-EPI equation; no occurrence of the following intercurrent events: rescue therapy, treatment failure, death or early study withdrawal. - Change in FACIT-F at week 76. The FACIT-F Scale is a patient-completed questionnaire consisting of 13 items that assess fatigue. Instrument scoring yields a range from 0 to 52, with higher scores representing better patient status (less fatigue).
Statistical analysis	A fallback multiplicity adjustment approach was used, with the primary outcome (CRR at week 76) tested first and followed sequentially by key secondary endpoints in the above order. Testing proceeded only if statistical significance was achieved at each step, with testing stopping at the first non-significant result. Efficacy analyses were performed in the intention-to-treat population, which included all patients who underwent randomisation, regardless of whether they received study treatment. Analyses were conducted by pooling the dosing schedules and comparing the obinutuzumab group with placebo

Abbreviations: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CI, confidence interval; CRR, complete renal response; eGFR, estimated glomerular filtration rate; FACIT-F, Functional Assessment of Chronic Illness Therapy Fatigue; PRR, partial renal response; SLE, Systemic lupus erythematosus; UPCR, urinary protein-to-creatinine ratio.

Obinutuzumab was associated with a statistically significant improvement in complete renal response (CRR) at week 76 compared with placebo. Key efficacy results are detailed in Table 2.2.

Table 2.2. Key efficacy results for REGENCY (data cut-off: 15 August 2024) ⁹

	Obinutuzumab (n=135)	Placebo (n=136)
Primary outcome: CRR at week 76		
Responders, %	46%	33%
Adjusted difference (95% CI), p-value	13.4% (2.0 to 24.8), 0.02	
Key secondary outcome: CRR with successful prednisone taper at week 76		
Responders, %	43%	31%
Adjusted difference (95% CI), p-value	11.9% (0.6 to 23.2), 0.04	
Key secondary outcome: Proteinuric response at week 76		
Responders, %	56%	42%
Adjusted difference (95% CI), p-value	13.7% (2.0 to 25.4), 0.02	
Key secondary outcome: Change in eGFR at week 76		
Adjusted mean (SE), ml/min/1.73 m ²	2.31 (2.71)	-1.54 (2.71)
Difference in adjusted mean (95% CI), p-value	3.84 (-1.83 to 9.51); 0.1842 (NS)	

Key secondary outcome: Death or renal-related events through week 76		
Patients with events, %	19%	36%
Adjusted difference (95% CI)	-16.8% (-27.42 to -6.23);	
Key secondary outcome: Overall renal response at week 50		
Responders, %	59%	51%
Adjusted difference (95% CI)	8.4% (-3.41 to 20.12)	

Abbreviations: CI, confidence interval; CRR, complete renal response; eGFR, estimated glomerular filtration rate; FACIT F, Functional Assessment of Chronic Illness Therapy Fatigue; NS, not significant; SE, standard error.

The 76-week randomised, double-blind, placebo-controlled treatment period was followed by continued blinded dosing every 6 months for responders or transition to open-label treatment for non-responders, with long-term follow-up thereafter. At the 15 August 2024 data cut-off, 50% (67/135) of patients in the obinutuzumab group remained on blinded treatment beyond week 76, compared with 36% (49/136) of patients in the placebo group.^{9, 12}

At approximately 3 years (week 158), among efficacy-evaluable patients remaining in the post-week 76 blinded treatment period, the proportion of patients in CRR was 70% (33/47) in the obinutuzumab group and 55% (23/42) in the placebo group.⁹

The proportion of patients with LN flares (defined as a >20% decline in estimated glomerular filtration rate [eGFR] [in patients with urinary protein-to-creatinine ratio [UPCR] >1 g/g and/or cellular casts], a protocol-defined increase in UPCR, or the need for rescue therapy [excluding corticosteroid-only rescue]) from Week 24 through week 76 was also numerically lower in the obinutuzumab arm compared to placebo (11% versus 24%, respectively). Median times to LN flare from Week 24 through week 76 were not estimable (HR: 0.44 [95% CI: 0.24 to 0.82]).^{9, 12, 13}

2.2. Health-related quality of life outcomes

Health Related Quality of Life was assessed using the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) Scale and the EQ-5D-5L health status questionnaire.

Results suggest some numerical improvements in FACIT-F score at week 76 with obinutuzumab versus placebo,⁹ however, the clinical meaningfulness of these is unknown.

EQ-5D-5L scores were comparable across groups.¹²

2.3. Supportive studies

The NOBILITY study was a phase II, multicentre, randomised, double-blind, placebo-controlled trial in 125 adults with active or active/chronic class III or IV LN (with or without concomitant class V disease) receiving MMF and corticosteroids.

Patients were randomised 1:1 to receive obinutuzumab 1,000 mg (n=63) or placebo (n=62) intravenous infusions on day 1 and weeks 2, 24 and 26. Patients were followed in a blinded fashion through week 104, and those with persistent B-cell depletion had continued safety and B-cell monitoring.

The primary outcome was CRR at week 52, defined as a UPCR <0.5, normal renal function (serum creatinine ≤ upper limit of normal range without >15% worsening from baseline) and inactive urinary sediment. Complete response rate was achieved by 35% of patients receiving obinutuzumab compared with 23% receiving placebo (difference 12%; 95% CI -3.4% to 28%;

p=0.115, which met the prespecified significance threshold for this proof-of-concept study [alpha=0.20]; this study was not powered to provide confirmatory results).^{9, 14}

2.4. Indirect evidence to support clinical and cost-effectiveness comparisons

There is direct evidence comparing obinutuzumab with MMF plus corticosteroids. In the absence of direct evidence versus other comparators, the submitting company provided an indirect treatment comparison (ITC) in the form of a network meta-analysis (NMA). Response rates from the NMA were used to inform the economic case. A Bucher ITC was also conducted which provided renal flare data in the economic analysis. See Table 2.3 for further details.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Bayesian NMA (random effects model) and Bucher ITC.
Population	Adults with active class III or IV, with or without concomitant class V, LN. Three studies (AURA-LV ¹⁵ , AURORA-1 ¹⁶ and BLISS-LN ¹⁷) also included adults with pure class V LN.
Comparators	Belimumab, voclosporin and rituximab (all used in combination with MMF plus corticosteroids, or standard therapy consisting of either MMF or cyclophosphamide plus azathioprine for belimumab) and MMF plus corticosteroids alone.
Studies included	NMA: AURA-LV ¹⁵ , AURORA-1 ¹⁶ , BLISS-LN ¹⁷ , LUNAR ¹⁸ , NOBILITY ¹⁴ and REGENCY ¹⁰ . Bucher ITC: REGENCY ¹⁰ and AURORA-2 ¹⁹ (for ITC versus voclosporin) and NOBILITY ¹⁴ and BLISS-LN ¹⁷ (for ITC versus belimumab)
Outcomes	NMA: CRR, PRR, change from baseline in eGFR and safety, including grade 3 or higher AEs and serious AEs. Bucher ITC: risk of renal flare
Results	The NMA results suggest that there was generally no evidence of a difference in efficacy or safety between obinutuzumab and the comparators. The Bucher ITC results suggest no evidence of a difference for renal flare rates when obinutuzumab was compared with voclosporin (HR 0.50 [95% CI 0.22 to 1.14) and belimumab (HR 0.86 [95% CI 0.37 to 2.03]).

Abbreviations: AE, adverse event; CI, confidence interval; CRR, complete renal response; eGFR, estimated glomerular filtration rate; HR, hazard ratio; ITC, indirect treatment comparison; LN, lupus nephritis; MMF, mycophenolate mofetil; NMA, network meta-analysis; PRR, partial renal response.

[*Other data were also assessed but remain confidential.**](#)

3. Summary of Safety Evidence

In the REGENCY study, at data cut-off 15 August 2024, during the 76-week blinded period, the median number of infusions received in the obinutuzumab group was 5 (ranging 1 to 6) and median treatment duration was 1 year. In both treatment groups, exposure to MMF and corticosteroids was similar. In the obinutuzumab (n=136) and placebo (n=132) groups respectively, patients reporting a grade 3 or higher adverse events (AEs) were 32% versus 17%, patients with a reported serious AE were 32% versus 18%, no AE led to study withdrawal.^{9, 10}

Through week 76, the most frequently reported serious AEs with an incidence ≥2% in the obinutuzumab group versus the placebo group were: Covid-19–related pneumonia (5.1% versus

0), pneumonia (2.9% versus 2.3%), urinary tract infection (2.9% versus 1.5%), Covid-19 (2.9% versus 0.8%), gastroenteritis (2.2% versus 1.5%), and acute kidney injury (2.2% versus 1.5%).¹⁰

There were four deaths during the 76-week treatment period: three (2.2%) in the obinutuzumab arm (caused by: nephrotic syndrome assessed as unrelated to blinded obinutuzumab, and two Covid-19 pneumonia assessed by the investigator as related to blinded obinutuzumab and MMF) and one (0.8%) in the placebo arm (caused by COVID-19 assessed by the investigator as related to treatment). In addition, there was one patient in the placebo arm with fatal AE onset during the 76-week treatment period, but who died after the week 76 data cut (caused by B-cell lymphoma).^{9, 10}

The main risks associated with obinutuzumab in LN are infusion-related reactions, grade ≥ 3 infections, drug-related neutropenia and drug-related thrombocytopenia (occurred in more patients in the obinutuzumab group than in the placebo group: 15% versus 11%, 15% versus 6.8%, 12% versus 3.8%, and 0.7% versus 0, respectively).¹⁰ This profile is consistent with its established safety profile in the haematological indications.⁹

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- The obinutuzumab-based regimen is supported by a well-conducted double-blind, placebo-controlled phase III study, REGENCY.⁹
- In this study, the primary outcome was met; obinutuzumab was associated with a statistically significant and clinically meaningful improvement in CRR at week 76 compared with placebo, with an adjusted difference in response rates of 13.4%. This composite primary outcome included consideration of direct patient health outcomes including end-stage kidney disease, long term dialysis and renal transplantation.⁹
- This was supported by the key secondary outcomes of CRR with successful prednisolone tapering and proteinuric response at week 76, and longer-term data up to 3 years following treatment initiation suggesting continued benefit with obinutuzumab.⁹

4.2. Key uncertainties

- Clinical experts consulted by SMC considered that obinutuzumab would most likely displace some use of belimumab-, calcineurin inhibitor-, cyclophosphamide- or rituximab-based combination therapies. There are no direct data against any of these potentially relevant comparators.
- The submitting company conducted an NMA which compared obinutuzumab with four comparators (belimumab, voclosporin and rituximab, all in combination with MMF and corticosteroids, and MMF alone). Cyclophosphamide and tacrolimus were also identified as potential comparators; however, they did not connect with other treatments in the network and therefore they could not be included in the NMA. The submitting company concluded there were generally no statistically significant differences between obinutuzumab and the comparators. Overall, the NMA was well conducted however there were some key limitations. There were differences between the studies, most notably in terms of disease class (as three

studies included patients with pure class V LN) and outcome definitions, and sparse data were included in the NMA. Wide credible intervals also indicate uncertainty in the results. A Bucher ITC was also conducted; however, this method is limited as it does not adjust for differences between the populations. Due to these limitations, the results are uncertain.

- Uncertainty remains regarding the long-term effect of obinutuzumab on renal function and the durability of treatment benefit. While many patients achieving CRR at week 76 maintained their response during continued blinded treatment in REGENCY up to 3 years, data beyond this time point are limited, including by small patient numbers and the absence of re-randomisation.⁹

4.3. Clinical expert input

Clinical experts consulted by SMC considered that obinutuzumab addresses an unmet need and represents a therapeutic advancement, demonstrating improved CRR rates in a disease area where several treatment options are available, but remission rates remain suboptimal.

4.4. Service implications

Clinical experts consulted by SMC considered that the introduction of this intravenously administered medicine may have implications for service delivery due to the requirement for day-case infusion facilities. However, one expert noted that, after the first year, obinutuzumab is administered every 6 months, which may be more convenient for some patients than treatments such as belimumab, which requires either four-weekly intravenous infusions or weekly subcutaneous injections. It was also noted that the mechanism of action for obinutuzumab is similar to that of rituximab, both anti-CD20 antibodies, and that infusion services are generally experienced in administering such therapies.

5. Summary of Patient and Carer Involvement

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

- We received patient group submissions from National Kidney Federation and Lupus UK; both organisations are registered charities.
- National Kidney Federation has received 15% pharmaceutical company funding in the past two years, with none from the submitting company. Lupus UK has received 1.8% pharmaceutical company funding in the past two years, with none from the submitting company.
- Lupus nephritis has a substantial impact on people living with the disease and their close family, including impacts on mortality, morbidity, quality of life, mental health, and ability to engage in work and social life. Patients described making sacrifices because of lupus, including retiring early, deciding not to have children, avoiding holidays and social commitments, and adapting their careers around their health.
- There remains a substantial unmet need for more effective treatment options. As lupus is a heterogeneous disease, there is no single treatment that works for everyone, and some people remain refractory to currently available therapies. There is a particular need for treatments which can reduce the reliance on steroids, due to short- and long-term side-

effects and reduce tablet burden. Reducing disease activity, preventing flares, and limiting long-term organ damage are critical treatment priorities for people living with lupus nephritis.

- There are groups who may particularly benefit from more treatment options, particularly those with Black and Asian ancestries, and those adults who developed SLE in childhood, as there is a higher risk of severe disease and of progression to end-stage renal disease.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The submitting company provided an economic case, as described in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost utility analysis.
Time horizon	Lifetime (70 years), based on a starting age of 33 years.
Population	Adult patients with active Class III or IV, with or without concomitant Class V, lupus nephritis (LN).
Comparators	The submitting company highlighted a 'main' comparison between mycophenolate mofetil (MMF) and obinutuzumab + MMF (OBI+MMF) both in combination with corticosteroids. Additional comparator treatments, voclosporin (VOC) + MMF, rituximab (RTX) + MMF and belimumab (BEL) + MMF, all in combination with corticosteroids were included in the submission. Other comparators, such as cyclophosphamide and tacrolimus, were classed as less relevant for this submission by the submitting company. Similarly, although belimumab was included in the analyses, the company did not consider it to be among the most relevant comparators and included it primarily for completeness.
Model description	The analysis is based on a Markov model with states of chronic kidney disease (CKD) 1-3b, CKD4, CKD5, and death. Within CKD1-3b there are substates of active disease (AD), partial (PR) and complete response (CR). Patients transition between these substates based on; the REGENCY study, an ITC (for CR and PR) including a Bucher ITC for renal flares. The company assumed there were no transitions between PR or CR in the CKD4 substate, with patients only having AD. Similarly, patients could not transition 'backwards' in the model, from CKD4 to CKD1-3b. Patients could only progress to CKD5 dialysis prior to receiving a transplant (CKD5 transplant) which were based on data from the literature. Treatment duration was 36 months for all comparators included in the model, as is for obinutuzumab. The model used a 6-month cycle length which aligned with treatment frequency of obinutuzumab. Half-cycle correction was applied in the model.
Clinical data	Most of the clinical data were taken from the REGENCY study ¹⁰ (NCT04221477). The treatments included in the REGENCY study were OBI+MMF versus MMF, while the additional comparators included in the economic analysis were sourced from an ITC of OBI+MMF, VOC+MMF, RTX+MMF and BEL+MMF using randomised controlled trial evidence (Table 2.3). The company submitted an NMA which was used to adjust the transition probabilities associated with CRR and PRR in the model for the included comparators. An additional Bucher ITC was submitted by the company to incorporate the impact of renal flares on disease progression (Table 2.3).
Extrapolation	The model extrapolated treatment effects beyond the follow-up available from the clinical studies. Complete and partial renal response probabilities were estimated using ITC data and extrapolated using a Weibull function over a three-year treatment-effect period before waning to the probabilities in the MMF arm over different periods based on the comparator being considered. Long-term CKD progression, end-stage renal disease and mortality were

	informed by external literature sources, while reductions in renal flares were assumed to reduce progression to advanced CKD, based on Bucher ITC data.
Quality of life	Health related quality of life (HRQoL), using the EQ-5D-5L, was evaluated in the REGENCY study. However, the study derived utilities lacked face validity. Utility values sourced from previous UK cost-effectiveness analyses, considering VOC+MMF for LN. Adverse events used literature sourced utility decrements applied to expected duration of each adverse event and the incidence of adverse events in the population. A disease progression disutility was applied on progression to the CKD 4 health state.
Costs and resource use	Cost included in the model were medicine acquisition costs, healthcare resource use costs, cost of adverse reaction, administration costs, and the costs of subsequent treatments. Other costs include end of life care costs and health state unit costs.
PAS/contract price	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. A PAS discount or National Framework Contract Price was applicable for some of the comparators.

6.2. Results

The base case results are presented in tables 6.2-6.4. SMC would wish to present the with-PAS cost-effectiveness results that were used for decision-making. However, SMC is unable to publish these results due to commercial in confidence concerns regarding the PAS. SMC considered results for decision-making that considered all relevant prices. SMC is unable to present these results due to competition law issues.

Table 6.2 Base case results versus MMF

	Total			Incremental			ICER
	Costs	LYG	QALYs	Costs	LYG	QALYs	
OBI + MMF + MPDL + PDS	CIC	17.78	CIC	CIC	1.13	CIC	CIC
MMF + MPDL + PDS	CIC	16.64	CIC	-	-	-	-

Abbreviations: CIC, commercial in confidence; ICER, incremental cost-effectiveness ratio; LYG, life years gained; MMF, mycophenolate mofetil; MPDL, methylprednisolone; OBI, obinutuzumab; PAS, patient access scheme; PDS, prednisone; QALYs, quality-adjusted life years.

Table 6.3 Base case results versus VOC

	Total			Incremental			ICER
	Costs	LYG	QALYs	Costs	LYG	QALYs	
OBI + MMF + MPDL + PDS	CIC	17.78	CIC	CIC	0.50	CIC	CIC
VOC + MMF + MPDL + PDS	CIC	17.27	CIC	-	-	-	-

Abbreviations: CIC, commercial in confidence; ICER, incremental cost-effectiveness ratio; LYG, life years gained; MMF, mycophenolate mofetil; MPDL, methylprednisolone; OBI, obinutuzumab; PAS, patient access scheme; PDS, prednisone; QALYs, quality-adjusted life years; VOC, voclosporin.

Table 6.4 Base case results versus BEL

	Total			Incremental			ICER
	Costs	LYG	QALYs	Costs	LYG	QALYs	
OBI + MMF + MPDL + PDS	CIC	17.78	CIC	CIC	0.22	CIC	CIC
BEL + MMF + MPDL + PDS	CIC	17.55	CIC	-	-	-	-

Abbreviations: BEL, belimumab; CIC, commercial in confidence; ICER, incremental cost-effectiveness ratio; LYG, life years gained; MMF, mycophenolate mofetil; MPDL, methylprednisolone; OBI, obinutuzumab; PAS, patient access scheme; PDS, prednisone; QALYs, quality-adjusted life years.

Table 6.5 Base case results versus RTX

	Total			Incremental			ICER
	Costs	LYG	QALYs	Costs	LYG	QALYs	
OBI + MMF + MPDL + PDS	CIC	17.78	CIC	CIC	0.83	CIC	CIC
RTX + MMF + MPDL + PDS	CIC	16.95	CIC	-	-	-	-

Abbreviations: CIC, commercial in confidence; ICER, incremental cost-effectiveness ratio; LYG, life years gained; MMF, mycophenolate mofetil; MPDL, methylprednisolone; OBI, obinutuzumab; PAS, patient access scheme; PDS, prednisone; QALYs, quality-adjusted life years; RTX, rituximab.

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in Table 6.6 below. The company conducted one-way sensitivity analysis, probabilistic sensitivity analysis and scenario analysis to explore uncertainty. The analysis suggested that varying parameters such as transition probabilities had the most impact on the results, regardless of which comparator was being considered.

Table 6.6 Scenario Analysis Results

Number #	Parameter	Base case	Scenario
1a	Treatment duration	6 cycles	12
1b			18
5a	Impact of renal flares applied to transition to	CKD Stage 4	No
5b			Response to active disease
5c			Active disease and CKD stage 4
9a	Renal flare surrogacy	100%	0%
9b			50%
10a	HR of reducing renal flare OBI + MMF vs. placebo	0.44 (significant)	0.82
10b			0.24
10c	HR of reducing renal flare VOC + MMF vs. placebo	0.88 (non-significant)	0.49
10d			1.45
10e	HR of reducing renal flare BEL + MMF vs. placebo	0.51 (non-significant)	0.28
10f			0.92
13	CKD1-3b response OR (various)	Various	OR =1
14	Belimumab formulation	Belimumab formulation: IV	Belimumab formulation: SC
15	Rituximab formulation	Rituximab formulation: IV	Rituximab formulation: SC
C1	10a + 5b	HR of reducing renal flare OBI + MMF (0.44) + Impact of renal flares applied to transition to: CKD stage 4	HR of reducing renal flare OBI + MMF (0.82) + Impact of renal flares applied to transition to: Active disease
C2	10a + 5c	HR of reducing renal flare OBI + MMF (0.44) + Impact of renal flares applied to transition to: CKD stage 4	HR of reducing renal flare OBI + MMF (0.82) + Impact of renal flares applied to transition to: Active disease and CKD stage 4

C3	10a + 10c	HR of reducing renal flare OBI + MMF (0.44) + HR of reducing renal flare VOC + MMF (0.88)	HR of reducing renal flare OBI + MMF (0.82) + HR of reducing renal flare VOC + MMF (0.49)
C4	10a + 10e	HR of reducing renal flare OBI + MMF (0.44) + HR of reducing renal flare BEL + MMF (0.51)	HR of reducing renal flare OBI + MMF (0.82) + HR of reducing renal flare BEL + MMF (0.28)
C5	10a + 8b	HR of reducing renal flare OBI + MMF (0.44) + Renal flare surrogacy (100%)	HR of reducing renal flare OBI + MMF (0.910) + Renal flare surrogacy (50%)
C6	13 + 9a	CKD1-3b response OR (various) + Renal flare surrogacy (100%) + AE disutility + treatment waning	CKD1-3b response OR (various) = 1 + Renal flare surrogacy = 0% + no AE disutility + equivalence in response and waning assumptions (CMA)

6.4. Key strengths

- The model structure and overall modelling approach were considered appropriate for the disease area and decision problem. The approach was consistent with previous UK health technology assessments and earlier submissions in the same disease area, providing reassurance regarding its face validity and methodological acceptability.
- Health states were aligned with recognised CKD classifications and reflected disease definitions reported in the literature and Kidney Disease Improving Global Outcomes (KDIGO) guidance.
- Long-term disease progression and survival estimates were informed by established evidence sources.
- The company appropriately explored several key areas of structural uncertainty, including treatment duration, treatment waning, utility sources, discontinuation assumptions, time horizon, discounting, subsequent treatment use and the application of renal flare effects. This provided a clearer understanding of the key drivers of cost effectiveness.

6.5. Key uncertainties

- The comparative effectiveness estimates used to derive complete renal response (CRR) are highly uncertain. Odds ratios generated through the ITC were associated with wide credible intervals that crossed 1 for all relevant treatment comparisons. Consequently, there was no clear statistical evidence of superiority between treatments, yet these estimates form a key component of the transition probabilities used in the economic model. The resulting uncertainty is not fully reflected in the company's analyses and may lead to overestimation of treatment benefits.
- The modelling of renal flares represents a major source of uncertainty and was identified as a key driver of the cost-effectiveness results. Hazard ratios used to link reductions in renal flare rates to slow CKD progression were associated with wide confidence intervals and were derived from multiple sources with differing levels of evidence. Any economic advantage generated through differential flare modelling is highly dependent on modelling assumptions

rather than statistically demonstrated comparative efficacy. Sensitivity analyses demonstrated that altering assumptions relating to renal flare surrogacy, hazard ratios, or the health state within the model where flare effects were applied could substantially change the results and, in some comparisons, alter conclusions.

- The model may double count treatment benefit associated with renal outcomes. Improvements in complete and partial renal response are already captured through transition probabilities and their influence on disease progression. The additional application of renal flare-derived hazard ratios to further reduce progression risks assumes an independent treatment effect beyond response status. This approach may count the benefits of improved disease control twice and may overestimate the long-term effectiveness of obinutuzumab. Although exploratory analyses suggested a limited impact against MMF, larger effects were observed in comparisons with other active treatments.
- The relationship between renal flares and long-term kidney outcomes is simplified. The model assumes a constant treatment-related effect of renal flare reduction over time and does not adequately account for the cumulative impact of repeated flares on subsequent prognosis. Emerging evidence suggests that recurrent renal flares are associated with worsening renal outcomes and reduced likelihood of achieving future response. Failure to account for flare history may oversimplify disease progression and introduce additional uncertainty regarding long-term treatment effects, even with the use of obinutuzumab.
- Assumptions used to extrapolate CRR over time are associated with considerable uncertainty. The company harmonised response outcomes to a 3-year time point and employed Weibull extrapolations despite the most relevant clinical evidence extending to approximately 1.5–2 years. This requires assumptions that short-term response predicts long-term response, that treatment effects remain stable over time and that the selected extrapolation function appropriately reflects disease progression. These assumptions are not directly supported by observed trial evidence and are likely to influence treatment-effect estimates in favour of obinutuzumab.
- Additional combined analyses conducted by the economic assessor identified uncertainties around CRR extrapolation methods, renal flare assumptions, transition probabilities and structural model restrictions that were not comprehensively tested by the company. As a result, the overall uncertainty surrounding the cost-effectiveness estimates may be understated in the submitted base case.

7. Conclusion

After considering all the available evidence, the Committee accepted obinutuzumab for use in NHSScotland.

8. Guidelines and Protocols

In 2018, the British Society for Rheumatology published a guideline for the management of SLE in adults.³ An updated guideline was published in 2026.⁴

In 2023, the European Alliance of Associations for Rheumatology (EULAR) and the European Renal Association–European Dialysis and Transplantation Association (ERA-EDTA) published a joint guideline for the management of SLE.²⁰ An updated guideline for the management of SLE with kidney involvement was published in 2026.⁷

In 2024, the KDIGO group published a guideline for the management of LN.⁸

9. Additional Information

9.1. Product availability date

15 December 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per year (£)
obinutuzumab	1,000 mg intravenous infusion given at baseline, week 2, week 24, and week 26, then every 6 months thereafter	Year 1: £13,248 Subsequent year: £6,624

Costs from BNF online on 03/07/2026. Costs calculated using the full cost of vials assuming wastage. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 1,121 patients eligible for treatment with obinutuzumab in each year 1 and 1,131 patients in year 3, to which confidential uptake rates were applied.

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/contract price discounts associated with comparator medicines.

[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 18 August 2026.

**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 includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS 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. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC 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 PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees 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.