

National Institute for Health and Care Excellence

Health Technology Evaluation

**Obinutuzumab for treating active systemic lupus erythematosus [ID6670]
Response to stakeholder organisation comments on the draft remit and draft scope**

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Roche (company)	Yes, the proposed evaluation route is appropriate.	Thank you for your comment. No action.
	GSK (comparator)	Agree that the NICE STA route is appropriate for the appraisal of this technology	Thank you for your comment. No action.
	Lupus UK	Yes, it is appropriate for NICE to appraise the use of obinutuzumab for treating active extra-renal lupus via a single technology appraisal, as proposed.	Thank you for your comment. No action.
Wording	Roche (company)	Extra renal lupus is an outdated phrase and doesn't reflect current clinical language. "Extra-renal lupus" has largely been replaced in modern clinical practice by "systemic lupus". As Systemic Lupus Erythematosus (SLE) is, by definition, a systemic disease, SLE is viewed as a single disease.	'Serologically active extra-renal lupus' replaced by 'active systemic lupus erythematosus' throughout.

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		SLE encompasses both renal and non-renal manifestations of the disease and the ALLEGORY study evaluated the efficacy and safety of obinutuzumab plus standard therapy compared with placebo plus standard therapy in patients with active SLE. So, Roche believe the most appropriate wording is: <i>“Obinutuzumab for treating active systemic lupus erythematosus”</i>	
	GSK (comparator)	Yes [Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider?]	Thank you for your comment. No action.
Timing issues	Roche (company)	<p>Roche considers this appraisal to be urgent.</p> <p>Systemic lupus erythematosus (SLE) is a severe, chronic and potentially life-threatening autoimmune disease affecting ~3.4 million people worldwide, with marked disparities by sex, race, ethnicity, age, geography, and income level, creating a substantial and uneven public health burden across populations (1, 2).</p> <p>SLE is associated with substantial impacts to health-related quality of life. As a systemic disease, SLE causes progressive, irreversible damage to multiple organs (e.g. kidneys, skin, and the cardiovascular, musculoskeletal and central nervous systems) and is associated with a 2.4 to 4.5-fold increased mortality compared to the general population (3, 4). Approximately half of patients develop organ damage within 10 years of diagnosis, most frequently affecting the neuropsychiatric, musculoskeletal, and renal systems, as a result of both ongoing disease activity and the cumulative toxicity of long-term corticosteroid treatment (4-6).</p> <p>SLE imposes a substantial and multidimensional burden on patients' health-related quality of life, driven by both active inflammation and irreversible</p>	Thank you for your comments. No action.

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		<p>organ damage, with the greatest impact on physical function, pain, general health, vitality, and social functioning (7, 8). SLE also imposes a substantial burden on healthcare systems, through high annual healthcare resource use (i.e., high hospitalisations of patients [13.7%], emergency care [25.7%], outpatient care [94.4%]), with costs rising sharply with increased disease severity, resulting in significant economic impact (9).</p> <p>There is currently no cure for SLE and, despite current available treatments, there is high unmet need for more efficacious and convenient treatment options that reduce disease activity, reduce reliance on high-dose corticosteroids, and improve quality of life in moderate to severe SLE patients who have ongoing disease activity despite standard therapy (10, 11). There is a critical need for effective therapies in SLE patients who require treatment escalation to achieve sustained disease control and steroid sparing without cumulative and long-term toxicity (12).</p> <p>Available targeted therapies deliver modest response rates and incomplete corticosteroid sparing, leaving many patients with residual disease activity and ongoing corticosteroid dependence. In addition, standard-of-care therapies (e.g. immunosuppression and corticosteroid treatments) are associated with low response rates coupled with substantial toxicities and persistent disease flares, which have a significant impact on patient health-related quality of life and worse long-term disease outcomes (13, 14). Given the severity of SLE, the limited efficacy of current standard-of-care (SOC), and toxicities associated with current SOC, there remains a high need for new safe, effective and convenient therapies for patients with SLE.</p> <p>Obinutuzumab is a humanised type II anti-CD20 monoclonal antibody that binds to the CD20 antigen, a proven target for CD20+ B cells. Obinutuzumab offers disease-modifying treatment effects in SLE including deep B-cell</p>	

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		<p>depletion, statistically significant improvements in responder rates and disease activity scores, supported by statistically significant corticosteroid tapering and delay to first disease flare. Disease control was sustained throughout the trial period, thus supporting durability of clinical benefit. These outcomes establish obinutuzumab as a viable alternative to current limited treatments. It demonstrates improved clinical response and robust benefits, with the potential to reduce corticosteroid- and flare-related morbidity. Obinutuzumab also has a favourable and well-understood safety profile and convenient bi-annual dosing.</p> <p>Obinutuzumab reduces the societal burden of SLE and related productivity losses by improving sustained disease control, reducing flares, and limiting steroid exposure. This supports stable daily functioning in a population where only 46% participate in daily work, 34% experience work disability, and absenteeism is two to three times higher than in the general population (15-17).</p> <p>There are significant health inequities among patients with SLE. SLE disproportionately affects women of working and child-bearing age, with women approximately 8.5-fold more likely to be affected than men (2, 3). In the UK, in the BILAG Biologics Register of moderate–severe SLE patients requiring biological therapy, almost half of the patients in the registry are from a non-white background, showing how access to advanced therapies is also an equality issue (18).</p>	

Comment 2: the draft scope

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Background information	Roche (company)	<p>As with previous comments on the draft wording, we believe that the remit of the appraisal is incorrect. SLE encompasses both renal and non-renal manifestations. The ALLEGORY study evaluated the efficacy and safety of obinutuzumab plus standard therapy compared with placebo plus standard therapy in patients with active SLE. So, Roche request that the initial limiting text in the background information section is removed to reflect the wider SLE population: <i>“Serologically active extra-renal lupus is a subtype of systemic lupus erythematosus (SLE) characterised by abnormal serological biomarkers (for example, positive anti-double-stranded DNA or low complement levels), indicating disease activity in organs and tissues outside the kidneys.”</i> Roche also request that any other mention of <i>extra-renal lupus</i> in the background information section be removed. For example, <i>“People with extra-renal lupus and SLE have limited treatment options.”</i></p> <p>This also applies in The technology section. Where, <i>“Obinutuzumab (Gazyvaro, Roche) does not currently have a marketing authorisation for serologically active extra-renal lupus.”</i> should read <i>“Obinutuzumab (Gazyvaro, Roche) does not currently have a marketing authorisation for SLE.”</i></p>	‘Serologically active extra-renal lupus’ replaced by ‘active systemic lupus erythematosus’ throughout.
	Lupus UK	<p>The background information mentions that SLE is more common in people with Black African, Caribbean, or Asian backgrounds, however it does not mention or discuss that is more likely to be more severe and include an increased risk of cardiovascular disease and organ involvement in those cases. Alongside differential risk of different ethnic ancestries, some research suggests that ethnicity may impact treatment response, including both treatment outcome and adverse effects. We would recommend this be included, particularly in any Equalities assessment (some references have been included below).</p>	Details on severity added to background section and to equalities assessment (EIA) form.

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		<ul style="list-style-type: none"> - Demkova K, Morris DL, Vyse TJ. Genetics of SLE: does this explain susceptibility and severity across racial groups? <i>Rheumatology (Oxford)</i>. 2023 Mar 29;62(Suppl 1):i15-i21. doi: 10.1093/rheumatology/keac695. PMID: 36583554; PMCID: PMC10050932. - Alarcón, G.S., McGwin Jr, G., Bartolucci, A.A., Roseman, J., Lisse, J., Fessler, B.J., Bastian, H.M., Friedman, A.W. and Reveille, J.D., 2001. Systemic lupus erythematosus in three ethnic groups: IX. Differences in damage accrual. <i>Arthritis & Rheumatism: Official Journal of the American College of Rheumatology</i>, 44(12), pp.2797-2806. - Kallas, R., Li, J., Goldman, D.W., Magder, L.S. and Petri, M., 2022. Trajectory of damage accrual in systemic lupus erythematosus based on ethnicity and socioeconomic factors. <i>The Journal of Rheumatology</i>, 49(11), pp.1229-1235. - Parodis, I., Lanata, C., Nikolopoulos, D., Blazer, A. and Yazdany, J., 2023. Reframing health disparities in SLE: A critical reassessment of racial and ethnic differences in lupus disease outcomes. <i>Best Practice & Research Clinical Rheumatology</i>, p.101894. - Segura, B.T., Bernstein, B.S., McDonnell, T., Wincup, C., M Ripoll, V., Giles, I., Isenberg, D. and Rahman, A., 2020. Damage accrual and mortality over long-term follow-up in 300 patients with systemic lupus erythematosus in a multi-ethnic British cohort. <i>Rheumatology</i>, 59(3), pp.524-533. - Isenberg, D., Appel, G.B., Contreras, G., Dooley, M.A., Ginzler, E.M., Jayne, D., Sanchez-Guerrero, J., Wofsy, D., Yu, X. and Solomons, N., 2010. Influence of race/ethnicity on response to lupus nephritis treatment: the ALMS study. <i>Rheumatology</i>, 49(1), pp.128-140 - Merrill, J.T., Neuwelt, C.M., Wallace, D.J., Shanahan, J.C., Latinis, K.M., Oates, J.C., Utset, T.O., Gordon, C., Isenberg, D.A., Hsieh, H.J. and Zhang, D., 2010. Efficacy and safety of rituximab in moderately-to-severely active systemic lupus erythematosus: the randomized, double-blind, phase II/III systemic lupus erythematosus evaluation of rituximab trial. <i>Arthritis & Rheumatism: Official Journal of the American College of Rheumatology</i>, 62(1), pp.222-233. 	

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Population	Roche (company)	No, as above, the proposed population for obinutuzumab should be for “adults with SLE”	Amended to adults with active SLE.
Subgroups	Roche (company)	<p>There are no subgroups within this population that should be considered separately.</p> <p>Obinutuzumab is an effective treatment across all subgroups. A broad population ensures the value of obinutuzumab is assessed to reduce unmet need for the greatest number of patients and address health inequalities across the system.</p>	Thank you for your comment. No action.
	Lupus UK	<p>The appraisal should consider the whole population, particularly as the trial data is across a broad population and lupus is a flaring condition with unmet need across the whole community.</p> <p>There are some subgroups which could be considered alongside the broad population:</p> <ul style="list-style-type: none"> - Patients with adverse reactions to rituximab or a secondary non-response to rituximab. Clinically significant reactions to rituximab may be more common in SLE than in other conditions (Hennessey et al, 2019), can occur on subsequent doses even where a first dose was successful, and can prevent retreatment. Additionally, around 12% of patients have a secondary non-response to rituximab (Yusof et al, 2017). Obinutuzumab may be a particularly important alternative for these patients. - Patients with poor adherence to oral treatments. There is often a high tablet burden in lupus, and many patients struggle with adherence for a number of reasons including complex regimens, brain fog, or lack of acceptance of their condition. Patients with poor adherence have 	<p>Subgroups may be discussed by the committee if it feels they are appropriate and evidence allows.</p> <p>The committee will not use evidence on health inequality impacts to make optimised recommendations for subgroups based solely on social characteristics.</p> <p>If robust condition- or disease-specific evidence shows that uncertainty or biases in the health inequality</p>

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		<p>worse clinical outcomes, particularly as inadequately treated lupus can lead to the accumulation of damage, including significant organ damage. As an intravenous treatment, obinutuzumab may be particularly beneficial and cost effective for patients who struggle with adherence.</p> <ul style="list-style-type: none"> - Patients with particular ethnic ancestry, particularly those with Black African, Black Caribbean, or Asian ancestry. As discussed in our response to the Background section, SLE is more common and tends to be more severe in these populations. Where research for subgrouping is available, it should be considered whether obinutuzumab is more effective (and/or cost effective) in people with Black or Asian ethnic ancestry as they may have particular unmet need. <p>Hennessey A, Lukawska J, Cambridge G, Isenberg D, Leandro M. Adverse infusion reactions to rituximab in systemic lupus erythematosus: a retrospective analysis. <i>BMC Rheumatol.</i> 2019 Aug 29;3:32. doi: 10.1186/s41927-019-0082-7. PMID: 31485560; PMCID: PMC6714312.</p> <p>Yusof, Md Yuzaiful Md, et al. Predicting and managing primary and secondary non-response to rituximab using B-cell biomarkers in systemic lupus erythematosus. <i>Annals of the rheumatic diseases</i> 76.11 (2017): 1829-1836.</p>	<p>evidence are caused by structural or social barriers to accessing care or participating in research, the committee may accept a higher level of uncertainty in the health inequality evidence and analysis.</p>
Comparators	Roche (company)	<p>Roche agrees that the comparators included in the draft scope are all used in the UK for the treatment of SLE. However, it is important to note that not all are licensed, or would be considered SOC. Specifically, the comparators that do not have a UK marketing authorisation are mycophenolate, azathioprine and rituximab. This information should be included for clarity.</p>	<p>Drugs without a marketing authorisation for the patient population (off-label use) can be included as comparators if they represent current standard treatment in the NHS. It is not</p>

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			standard practice to label these as such in the scoping doc.
	GSK (comparator)	Agree with the selection of comparators	Thank you for your comment. No action.
	Lupus UK	<p>Comparators listed are currently used in NHS.</p> <p>However, it is important to note that, as a heterogenous disease, there is no single 'best' treatment, treatment response can vary considerably between patients, and some cases are refractory to all available treatments. This means it is not possible to describe any of the currently available treatments as 'best alternative care' for all patients as there is no regimen that is effective for all. It also means that, even where there are treatments which have been shown to be effective and have been approved, there is a need for more treatments, particularly for those patients who are refractory.</p> <p>It is worth noting that rituximab is currently not licensed for the treatment of SLE but is available as a treatment option through routine commissioning for refractory SLE in adults and post-pubescent children. It can only be used where the patient has failed to respond, or has had adverse events, to two or more immunosuppressive therapies, has particular disease activity scores, is managed by a specialist centre, and is not eligible for clinical trials or belimumab.</p>	Thank you for your comment. No action.
Outcomes	Roche (company)	The outcomes listed are appropriate and capture important clinical and health-related impacts of SLE.	B cell depletion has been added to the list of potential outcomes.

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		<p>However, Roche feels the scope could go further in considering some key clinical outcomes relating to disease modification. The clinical evidence for obinutuzumab in SLE and lupus nephritis demonstrates that obinutuzumab achieves deep, sustained B-cell depletion, which is an outcome that suggests a potential for disease modification rather than just symptom management.</p> <p>Obinutuzumab has the potential to slow progression to organ damage, which is related to substantially higher NHS costs per year. For example, the NHS spends an estimated £6.4 billion per year on dialysis, which is 3.2% of the NHS budget, and is projected to spend even more on dialysis in the future, potentially rising to £10.9 billion by 2033 (19). Early intervention with obinutuzumab for SLE patients has the potential to substantially reduce this burden alongside other severe SLE organ complications. Given the pressure on healthcare services, it is important to include outcomes relating to not only cost but also capacity savings to the NHS.</p> <p>Roche also feels that the scope is too narrow to holistically consider the impact to patients, their families and the health system. Roche calls for the committee to consider a wider perspective. Obinutuzumab reduces SLE societal burden and related productivity losses by improving sustained disease control and reducing flares and steroid exposure, thereby supporting more stable daily functioning in patients where only about 46% participate in the labour force, around 34% experience work disability, and absenteeism occurs two to three times more often than in the general population (15-17). As SLE predominantly affects people of working age, Roche believes ID6670 could be a candidate for NICE to consider trialling a wider societal perspective. With recent calls from the Department of Health and Social Care relating to the importance of reducing burden on the NHS and getting people back to work, it is becoming increasingly important to consider not only health</p>	<p>Organ damage is listed in the outcome measures.</p> <p>The objective of NICE's evaluations is to offer guidance that represents an efficient use of available NHS and Personal Social Services resources. For these reasons, the reference-case perspective on costs is that of the NHS and</p>

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		impacts but also any impact to society, including lost productivity associated with having a chronic condition such as SLE.	PSS. Productivity costs should not be included.
	GSK (comparator)	Agree with the outcomes listed	Thank you for your comment. No action.
	Lupus UK	Outcomes listed are appropriate and important. Wherever possible, the economic analysis should consider any long-term benefits and cost savings of preventing or reducing flares and reducing reliance on corticosteroids. Flares necessitate increased contact with health services, including appointments and further treatment, as well as potentially increasing irreversible damage from disease activity (leading to poorer HRQoL and potentially further treatments), all of which has a cost implication for the health service. Increased disease activity can also lead to reduced ability to engage in work, education, and social/family life, which also has a cost implication in individual economic activity (including in unpaid caring for dependants). Corticosteroids have well-documented side effects, including osteoporosis. If obinutuzumab can reduce or prevent flares and disease activity, as well as reducing the need for steroids to achieve this, the longer-term cost saving should be carefully considered in any cost-effectiveness analysis, as well as the incremental cost per quality adjusted life year.	The committee will take into account all relevant health effects and associated costs.
Equality	Roche (company)	SLE disproportionately affects women of working and child-bearing age, with women approximately 8.5-fold more likely to be affected than men (2, 3). Disease burden is further amplified by health disparities, with populations of lower socioeconomic status and certain ethnic groups (Black, Hispanic and Asian) experiencing worse disease outcomes, greater organ damage accumulation, and higher mortality (20, 21).	We have noted your comments in the equality impact assessment (EIA) form. This will be considered by the committee.

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		<p>Epidemiological data suggests that individuals from Afro-Caribbean, South Asian and East Asian backgrounds not only develop lupus at a younger age but also experience more rapid disease progression and a higher accrual of organ damage (22, 23). Health inequalities within these populations are well-documented in the UK. Studies indicate that patients from ethnic minority backgrounds often report higher disease activity (increased flare frequency and greater severity of systemic symptoms) and a greater treatment burden (24). These patients also tend to have poorer long-term prognosis, with higher rates of morbidity and mortality compared to the Caucasian population, often exacerbated by socioeconomic factors and delayed access to specialist care (25). Therefore, a uniform approach to diagnosing and treating SLE across the UK is essential to mitigate diagnostic and treatment inequities (26, 27).</p>	
	Lupus UK	<p>As mentioned in our comments under ‘Background Information’ SLE affects people of all ethnic groups but is more prevalent, and has poorer outcomes in, people of African, Caribbean, and Asian ancestry. People of Black African/Caribbean ancestry are also at a higher risk of developing diabetes and hypertension. It should be considered whether steroid-sparing treatments such as obinutuzumab could have additional advantages over standard treatments by reducing some adverse effects and risks of comorbidities – especially considering the high dependence on corticosteroids in current standard therapy.</p> <p>Relatedly, as discussed further in our response to the ‘background information’ section, there may be differences in treatment response related to ethnicity. Alongside the wider issues of SLE as a heterogeneous disease requiring a range of treatment options, the appraisal should consider whether a greater range of available treatments may particularly benefit those from minority ethnic backgrounds who are more likely to develop SLE, more likely</p>	<p>We have noted your comments in the equality impact assessment (EIA) form. This will be considered by the committee.</p>

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		to have an accelerated progression of disease, and are likely to be impacted by the variation in treatment due to health inequalities.	
Questions for consultation	Roche (company)	<p>Where do you consider obinutuzumab will fit into the existing care pathway for serologically active extra-renal lupus?</p> <p>Obinutuzumab will fit into the existing care pathway. Obinutuzumab is administered intravenously every 6 months after the first year. Rheumatology services already administer treatments intravenously, so there are no additional considerations for prescribing obinutuzumab over alternatives.</p> <p>Other treatments for SLE are administered much more frequently. For example, belimumab is administered intravenously every 4 weeks or subcutaneously weekly. Obinutuzumab has the potential to reduce the system, clinical and societal burden, through twice yearly administration (after the first year), thus improving adherence issues and reducing the need for multiple clinical appointments and frequent follow-ups.</p> <p>Roche expects obinutuzumab to be an additional treatment option alongside standard therapy for people with active SLE and an alternative option to belimumab or rituximab add-on therapy.</p> <p>Have all the relevant comparators been included? Which treatments would continue as supportive care, alongside obinutuzumab if it were recommended?</p> <p>Roche believes all relevant comparators have been included. Roche expects obinutuzumab to be an additional treatment option alongside standard therapy for people with active SLE, where standard therapies could include conventional DMARDs (such as hydroxychloroquine), conventional</p>	Thank you for your comments.

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		<p>immunosuppressants (such as MMF) and oral corticosteroids. Roche expects obinutuzumab will provide an alternative treatment option to currently available belimumab or rituximab add-on therapy.</p> <p>To what extent does the patient population covered in NICE technology appraisal guidance 752 (belimumab for autoantibody-positive systemic lupus erythematosus) overlap with the patient population in the proposed appraisal of obinutuzumab for treating serologically active extra-renal lupus?</p> <p>Please select from the following, will obinutuzumab be:</p> <p>A. Prescribed in primary care with routine follow-up in primary care</p> <p>B. Prescribed in secondary care with routine follow-up in primary care</p> <p><u>C. Prescribed in secondary care with routine follow-up in secondary care</u></p> <p>D. Other (please give details):</p> <p>Roche expects that obinutuzumab will be prescribed, administered and routinely followed up in secondary care. Obinutuzumab will be administered in the current care pathway, intravenously in an outpatient hospital setting.</p> <p>Obinutuzumab is already prescribed and administered in secondary care for chronic lymphocytic leukemia and lupus nephritis. Hospital pharmacists already stock, prepare and store obinutuzumab in this setting and we see no additional impact on the service for obinutuzumab for SLE.</p>	

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		<p>For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.</p> <p>Would obinutuzumab be a candidate for managed access?</p> <p>There is limited further data collection planned for the ALLEGORY study and there are no additional studies planned for obinutuzumab specifically for the treatment of SLE, Roche considers it to be unlikely that obinutuzumab would be a candidate for managed access. However, Roche remains open to all routes to patient access.</p> <p>Do you consider that the use of obinutuzumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?</p> <p>Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.</p> <p>Yes, Roche believes that the benefits of obinutuzumab are likely to extend beyond the domains considered within the QALY calculation:</p> <p>Obinutuzumab has the potential to relieve reliance on glucocorticoid treatments, which are associated with substantial impacts on patient quality of life. Chronic use of glucocorticoids is a primary driver of irreversible organ damage in lupus; even low-dose maintenance therapy increases the risk of serious adverse events (28). Furthermore, the immunosuppressive nature of therapy leaves patients highly susceptible to opportunistic infections, which remain a leading cause of hospitalisation and mortality within this patient</p>	

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		<p>population (29). Thus, it is important to capture the positive effects of steroid sparing on patient quality of life.</p> <p>LN is typically diagnosed and treatment is initiated at working age. The impact of SLE can result in many patients regularly missing days of work, and half of patients stop work altogether (30). This can have detrimental impacts on patient quality of life. Similarly, carers of patients with LN have reported the need to take time off work to provide care. This has negative impacts on their financial status and social activity, which in turn impacts carer quality of life (30). Obinutuzumab will be administered twice yearly (after the first year), substantially reducing the administration burden experienced with current treatments. This convenient regimen reduces the need for multiple clinical appointments and frequent follow-ups and thus has the potential to improve adherence and clinical outcomes. Better outcomes improve the chances of patients maintaining the freedom to work, reducing negative impacts to patient and carer quality of life.</p> <p>Many patients with SLE are women of childbearing age. Pregnancy associated with SLE is often a cause for concern among patients, as active disease is associated with poor maternal and foetal outcomes (31). Uncertainty over childbearing is likely to have a substantial impact on the quality of life of women with SLE.</p> <p>As noted in the Equality section, SLE disproportionately affects women of working and child-bearing age, with women approximately 8.5-fold more likely to be affected than men (2, 3). Disease burden is further amplified by health disparities, with populations of lower socioeconomic status and certain ethnic groups (Black, Hispanic and Asian) experiencing worse disease outcomes, greater organ damage accumulation, and higher mortality (20, 21).</p> <p>Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product</p>	

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		<p>Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.</p> <p>NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:</p> <ul style="list-style-type: none"> · could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which obinutuzumab will be licensed; · could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology; · could have any adverse impact on people with a particular disability or disabilities. <p>Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.</p> <p>See response to Equality section.</p>	

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	GSK (comparator)	<p>1) Where do you consider obinutuzumab will fit into the existing care pathway for serologically active extra-renal lupus?</p> <ul style="list-style-type: none"> The proposed positioning in the pathway is for patients with high disease activity/severe disease, plus initial treatment failure. Possibly overlapping with current rituximab use in UK for extra-renal SLE patients. It is also likely to be positioned as an alternative to belimumab in people with high disease activity satisfying the TA752 criteria or where belimumab is contraindicated or not tolerated, or after belimumab for patients with persistent activity or frequent flares despite belimumab. <p>2) To what extent does the patient population covered in NICE technology appraisal guidance 752 (belimumab for autoantibody-positive systemic lupus erythematosus) overlap with the patient population in the proposed appraisal of obinutuzumab for treating serologically active extra-renal lupus?</p> <ul style="list-style-type: none"> Obinutuzumab is likely to be used more often in refractory or biologic-experienced patients e.g. post-rituximab or post-belimumab - where it has been used in patients with at least 1 serological biomarker (positive anti-double-stranded DNA or low complement) and a SELENA SLEDAI score of greater than or equal to 10. <p>3) Setting for the management of the disease with obinutuzumab Option C. Prescribed in secondary care with routine follow-up in secondary care. It will require specialist oversight and infusion facilities. This is the same as the prescribing of the intravenous formulation of belimumab. The subcutaneous formulation of belimumab can be self-administered at home.</p> <p>4) Would obinutuzumab be a candidate for managed access? Yes, managed access could be considered appropriate if there is uncertainty:</p>	Thank you for your comments.

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		<ul style="list-style-type: none"> • in the longer-term benefits and safety of obinutuzumab in patients with extra-renal SLE • as to whether a particular subgroup of patients may demonstrate a greater response to the medicine (and the best time to determine if they are a “responder”) than the broader licensed population. <p>5) Could the remit and scope lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology</p> <p>Immunosuppression and vaccination: Profound B-cell depletion impacts vaccine responses (COVID-19, pneumococcal, HPV), which may be particularly problematic for older adults and those with comorbidities or disabilities. Obinutuzumab is similar to rituximab in mechanism of action and so it is important that evidence is generated that could monitor the impact of B-cell depletion e.g. conducting immunogenicity studies and obtaining registry data for assessing infection incidence and vaccination outcomes in SLE patients receiving anti-CD20 therapy.</p> <p>Formulation: Obinutuzumab is currently delivered via IV infusion only. Patients from rural or deprived areas, or with caring/working responsibilities, may have difficulty attending frequent infusion appointments and covering the cost of travel.</p>	
	Lupus UK	<p>Would obinutuzumab be a candidate for managed access?</p> <p>Yes, obinutuzumab should be considered for managed access if there is insufficient evidence to approve it for use during this appraisal. It could also be considered for managed access for children and/or adolescents, if more evidence is required for this age group, as young people with SLE are more likely to have a severe case and develop organ damage, and there are very few licensed treatments options for children.</p>	Thank you for your comments.

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>It should also not only be appraised on the basis of cost-effectiveness related to comparator treatments. As a heterogenous disease with varied treatment responses, there is an unmet need for patients who are refractory to other available treatments. If obinutuzumab was found to be effective, but not more cost effective than comparators, it should still be made available on the NHS, at the very least, for those patients with no feasible treatment options. This may be particularly important for those patients who develop an adverse reaction or secondary non-response to rituximab.</p> <p>Do you consider that the use of obinutuzumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?</p> <p>The appraisal should consider secondary morbidities such as cardiovascular disease (the leading cause of death of people with SLE) and consider PROMs such as fatigue which may not be fully captured in HRQoL measures but have a significant impact on the QoL of people with lupus.</p> <p>As noted in the Background section, SLE most commonly impacts women of childbearing age. Due to advances in treatment and understanding, many women with SLE are now able to have successful pregnancies, however it is important that lupus activity is well-controlled prior to conception. Reducing disease activity and flares could have a significant impact on people's ability to plan a family and successfully carry a pregnancy.</p> <p>The appraisal should also consider whether the calculation sufficiently accounts for the potential benefits of reducing or preventing the further accumulation of damage, particularly for those who are refractory to other treatments or who are more likely to have an accelerated course of damage.</p>	

Section	Consultee/ Commentator	Comments [sic]	Action
		<p>This may include benefits of preventing the need for additional treatment and urgent interaction with the healthcare system at times of flare, and associated socio-economic costs such as the impact of further disease on ability to work, social life, and family life.</p> <p>Although it is included as an outcome in the scope, it is important that all the impacts of corticosteroid treatment are included in the appraisal. Steroid use has a significant impact on quality of life, including both physical and mental health. Updates to guidelines for the management of SLE, including EULAR, ACR, and the forthcoming BSR guidelines due later this year, emphasise the need to reduce reliance on corticosteroids.</p>	

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

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