

# **Clinical Commissioning Policy Proposition:**

**Rituximab for refractory Systemic  
Lupus Erythematosus (SLE) in adults  
and post-pubescent children**

Reference: NHS England 1853



**Prepared by NHS England Specialised Services Clinical Reference Group for  
Specialised Rheumatology**

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# 1 Executive Summary

## Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

## Plain Language Summary

### About Systemic Lupus Erythematosus (SLE)

Systemic lupus erythematosus (SLE, also known as lupus) is a long term autoimmune condition (a condition where your immune system attacks your body) that causes swelling, soreness and inflammation in the body. It affects the whole body including the skin, joints and internal organs and results in long-term ill health. In 2012, SLE affected approximately 1 in 1000 people in the UK. It is more common in people of African-Caribbean and South Asian backgrounds and more common in women than men. SLE in children is more severe and active than in adults. In particular, there are higher numbers of children who have renal (kidney) and central nervous system (brain and spinal) problems.

SLE can cause different symptoms in different people. Patients are prone to flares of their disease. SLE can cause arthritis, kidney inflammation, heart and lung inflammation, central nervous system abnormalities and blood disorders. Renal (kidney) disease occurs in up to 40% of people with SLE and significantly contributes to long-term ill health, including kidney failure and death in some lupus patients.

Inadequately treated active disease causes damage of the affected systems thus increasing complications, morbidity and can lead to an early death. The aim of treatment is to suppress disease activity, prevent organ damage and improve quality of life.

For this policy, patients with refractory SLE are defined as those who have used 2 or more disease modifying anti-rheumatic drugs (DMARDs), (one of which must be EITHER mycophenolate or cyclophosphamide, unless contraindicated), and patients still either have: 1) ongoing moderate to severe active disease OR 2) require excessive use of glucocorticoids (over 7.5mg prednisolone per day) to maintain lower levels of disease activity.

### **About current treatments**

Disease severity can be classified into mild, moderate and severe. Three drugs are currently licensed for use in adults with SLE: hydroxychloroquine (anti-malarial), prednisolone (steroid), and belimumab (biological DMARD).

For mild disease, standard therapy is usually a combination of non-steroidal anti-inflammatory drugs (NSAIDs), hydroxychloroquine and low dose steroids. For moderate and severe disease steroids, hydroxychloroquine and an unlicensed stronger immunosuppressant, such as methotrexate, azathioprine, mycophenolate, cyclophosphamide, leflunomide, ciclosporin or intravenous immunoglobulins are used. These immunosuppressants are associated with side effects and toxicity.

### **About the new treatment**

Rituximab is a biological medicine that selectively targets B cells, cells that are part of the body's immune system that act to reduce the inflammatory response. It is usually given as two intravenous infusions two weeks apart. Rituximab is currently not licensed for the treatment of SLE (BNF 2018).

### **What we have decided**

NHS England has carefully reviewed the evidence to treat refractory SLE with rituximab in adults and post-pubescent children. We have concluded that there is enough evidence to consider making the treatment available.

## 2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to routinely commission rituximab.

This document also describes the proposed criteria for commissioning, proposed governance arrangements and proposed funding mechanisms.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether rituximab for refractory SLE will be routinely commissioned will be made by NHS England following a recommendation from the Clinical Priorities Advisory Group.

## 3 Proposed Intervention and Clinical Indication

### Background

SLE is a chronic complex autoimmune multi-system condition that causes inflammation in the body's tissues which is associated with significant morbidity and mortality. It can affect any organ system either sequentially or at the same time. Patients may have persistent disease activity or experience flares. SLE and the medications to manage the disease affect all aspects of daily life including the ability to work, have children and psychological well-being. It can result in chronic debilitating ill health (Alshaiki et al 2018, Duxbury et al 2013). The cause of SLE is unknown though combinations of genetic, environmental and hormonal factors are thought to play a role.

SLE can cause signs and symptoms such as inflammatory arthritis, myositis, mucocutaneous manifestations such as rashes and mouth ulcers, glomerulonephritis (lupus nephritis) which can lead to kidney failure, heart and lung inflammation such as pericarditis and pleurisy, central nervous system abnormalities such as cerebral vasculitis and epilepsy and blood disorders such as haemolytic anaemia, profound thrombocytopenia and neutropenia. Long-term

damage builds up due to inadequately treated disease activity and the cumulative effects of glucocorticoid treatment (NICE 2014).

#### Existing Treatment

Three drugs are currently licensed for use in adults with SLE: hydroxychloroquine, prednisolone, and belimumab. The treatment regime varies depending on disease severity which can be mild, moderate or severe.<sup>1</sup>

For severe SLE, patients are given high dose immunosuppressive therapies with significant toxicity profiles. One example is intravenous cyclophosphamide. This drug predisposes patients to infections, bone marrow suppression, infertility, premature menopause, bladder cancer and is contraindicated in pregnancy and in those who are trying to get pregnant as it is teratogenic. Glucocorticoids are associated with side-effects such as infection, systemic hypertension, ischaemic heart disease, type 2 diabetes mellitus, cataracts, osteoporosis and fragility fractures. High doses are generally used to treat moderate and severe disease flares and are often required long-term to suppress inflammation (Oon et al 2018).

#### Proposed intervention

Rituximab is a chimeric monoclonal antibody that selectively targets CD20-positive B cells, thereby mediating transient B-cell depletion: B cells having critical roles in the pathogenesis of SLE (Merrill et al 2010), (Mahmoud et al 2017). It is licensed for use in rheumatoid arthritis, ANCA-associated vasculitis and lymphoma and it is used in many other autoimmune conditions as an off-label treatment. Rituximab has been used as an off-label treatment in the UK to treat refractory SLE since the mid-2000s. Access to the drug was previously variable. NHS England published an interim clinical commissioning policy statement for the use of rituximab for the treatment of SLE in adults in August 2013 (A13/PS/a). Over 800 patients with SLE, who are living in the UK, have received rituximab and been registered on the BILAG-BR.

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<sup>1</sup> Classification of severity of disease are available in the British Society for Rheumatology guideline (Gordon et al, 2018).



Biosimilars for rituximab, as well as the rituximab originator, are now available. As part of medicines optimisation, many providers have switched to the cheaper biosimilars.

## 4 Definitions

British Isles Lupus Assessment Group (BILAG) - This is a network of UK Rheumatologists with a specific clinical and research interest in lupus.

The British Isles Lupus Assessment Group -2004 (BILAG-2004) disease activity index evaluates SLE disease activity over the preceding 28 days and can be used to assess flare and response to treatment using 97 items in 9 organ systems. A graded (letter) score can be calculated. The letter score (A to E) indicates the severity of disease activity ranging from A being severe disease activity to E being no disease activity ever in an organ system.

Biologics Register (BILAG-BR) - This is a registry that was established by BILAG to investigate and record the response to and safety of biologic treatments in SLE compared with standard therapy. (McCarthy et al, 2018)

Biosimilars - This refers to biological medicines that are highly similar to rituximab ("reference medicine") in terms of structure, biological activity and efficacy, safety and immunogenicity profile (European Medicines Agency, 2017).

Disease modifying anti-rheumatic drugs (DMARDs) – These are drugs that dampen down the immune system. There are conventional DMARDs e.g. mycophenolate mofetil, cyclophosphamide and biological DMARDs e.g. rituximab and belimumab.

End stage renal disease (ESRD) - The last stage of chronic kidney disease. This means that the kidneys cannot remove waste and fluids from the body effectively and patients require high cost renal replacement therapy e.g. long term haemodialysis, peritoneal dialysis or a kidney transplant.

Post-pubescent children – This policy refers to post-pubescent children in line with the considerations outlined in the Commissioning Medicines for Children in Specialised Services policy. (NHS England 170001/P, 2017).

Lupus Glomerulonephritis/Nephritis - SLE that affects the kidneys, leading to kidney inflammation and potentially long - term renal disease and renal failure that may require renal replacement therapy.

Immunosuppressive therapies - This refers to a group of drugs that suppress the immune system. In this document this term includes anti-malarial agents, glucocorticoids and DMARDs.

Number Needed to Treat (NNT) – This refers to the number of patients you need to treat to prevent one additional adverse outcome (e.g. flare, death). For example, “adjunctive rituximab appears to be better at preventing flares, it has a number needed to treat of 7.” This means 7 people need to be treated with rituximab to prevent 1 additional flare.

Refractory systemic lupus erythematosus (SLE) – Patients with refractory SLE are defined as those who have used 2 or more DMARDs (one of which must be EITHER mycophenolate or cyclophosphamide, unless contraindicated), and patients still either have: 1) ongoing moderate to severe active disease OR 2) require excessive use of glucocorticoids (over 7.5mg prednisolone per day) to maintain lower levels of disease activity.

Relative risk - This is the ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group.

SLE Disease Activity Index 2000 (SLEDAI-2K) - A global numerical scoring system that evaluates SLE disease activity over the preceding 10 or 28 days using 24 items. A score of 6 or more is consistent with significant disease activity (and requiring initiation or escalation of immunosuppressive therapy).

Primary definition of response – This is defined as the loss of all A and B BILAG scores to  $\leq$  1B score with no new A or B scores in other organ domains at 6 months. This is a clinically meaningful response. This is the most commonly used definition of response in clinical practice.

Major clinical response – This is defined in BILAG - BR as BILAG-2004 C, D and Es in all systems with SLEDAI-2K  $\leq$  4 and daily oral prednisolone dose  $\leq$  7.5mg at 6 months. This can equate to clinical remission (McCarthy et al 2018).

## 5 Aims and Objectives

This policy proposition considered:

Rituximab for the treatment of refractory SLE in adults and post-pubescent children.

The objectives were to:

- Ensure evidence based commissioning in the use of rituximab in adults and children with SLE with refractory disease.
- Assess the efficacy, safety, toxicity profile, cost-effectiveness of rituximab.
- Evaluate whether additional rituximab achieved improved outcomes in comparison with standard conventional immunosuppressive treatments only.

## 6 Epidemiology and Needs Assessment

SLE is a multisystem, autoimmune disease that can present at any age. It affected nearly one in 1000 of the population in the UK in 2012 (NICE 2014, Gordon et al 2018). SLE most commonly presents in women in the reproductive age group, and is significantly more common in women than men; a ratio of 9 to 1 (Gordon et al 2018). In the U.K, the highest incidence and prevalence are seen in those of African-Caribbean descent. It is also more prevalent in people of South Asian and Chinese descent compared with people of northern European descent.

The incidence of paediatric SLE (pSLE) is 0.3-0.9/100 000 children per year, with a prevalence of 3.3-8.8/100 000 children. Paediatric SLE is associated with more severe and active disease compared with SLE in adults. In particular, there is a higher incidence of renal and central nervous system involvement (Mahmoud et al 2017).

Over 90% of people with SLE develop problems with their joints and muscles such as inflammatory arthritis and myositis. Up to 40% of SLE patients in the UK develop lupus nephritis (LN) which can lead to ESRD requiring renal replacement therapy such as long term haemodialysis or renal transplantation. LN significantly contributes to morbidity and mortality (NICE 2014). In a UK lupus cohort study followed up for a maximum of 21 years (range of duration of follow up: 1 - 21 years, mean: 7.7 years), 10% mortality was reported with a mean age at death of 53.7 years (Yee et al 2015).

Death from active lupus is rare in the UK; the leading causes of death are due to infection and co-morbidities e.g. atherosclerosis.

The indications for rituximab include failing 2 or more DMARDs (one of which must be EITHER mycophenolate or cyclophosphamide, unless contraindicated), and patients still either have: 1) ongoing moderate to severe active disease OR 2) require excessive use of glucocorticoids (over 7.5mg prednisolone per day) to maintain lower levels of disease activity. The BILAG-BR data records around 6 - 9 new patients with SLE are started on rituximab per month, this adds up to 72 - 108 patients per year (McCarthy et al 2018).

## 7 Evidence Base

NHS England has concluded that there is sufficient evidence to support a proposal for the routine commissioning of this treatment for the indication.

Further details of the evidence are provided below:

Two systematic reviews with meta-analyses and a report of an analysis of the UK British Isles Lupus Assessment Group biologics register (BILAG-BR) fulfilling the PICO criteria for inclusion were found. One systematic review (Alshaiki et al 2018) included 31 studies (two RCTs and 29 observational studies, N=1,112) and the second systematic review (Shamliyan et al 2017) included three RCTs of adult patients (N=420). The BILAG-BR analysis (McCarthy et al 2018) reported on 178 out of a total of 261 patients over five years old treated with rituximab. Individual studies were excluded if they were already included in systematic reviews. Systematic reviews were excluded if more recent systematic review publications included the same primary studies.

The review did not identify any studies assessing the cost effectiveness of rituximab plus standard treatment compared with standard treatment alone for adult and/or children with refractory SLE.

### **Clinical effectiveness**

Major clinical response in 18.4% (33 patients) was reported at six months follow-up in UK patients with SLE in the BILAG-BR analysis (McCarthy et al 2018). However, no comparative results were reported.

There was no difference in any clinical response outcome measures between immunosuppressive agents plus adjunctive rituximab versus immunosuppressive agents alone in adult patients from North America with SLE at 52 weeks follow-up in the RCT (n=257) included in the systematic review by Shamliyan et al (2017). However, this study population did not meet the UK definition of refractory SLE.

On the other hand, global response rates [73% (95% CI 67% to 78%), N=206], complete response rates [46% (95% CI 38% to 55%), N=773] and partial response rates [34% (95% CI 28% to 40%), N=928] improved after rituximab therapy in refractory SLE patients in open label studies. This was also the case in patients with refractory LN with global response rates (N=57) of 70% (95% CI 55% to 81%), complete response rates (N=223) of 51% (95% CI 34% to 68%) and partial response rates of 27% (95% CI 18% to 39%) reported (N=928 for SLE and LN).

This is based on the meta-analysis by Alshaiki et al (2018). However, no comparative results were reported as the results are based mainly on non-comparative studies.

Statistically significant improvements were reported in both BILAG and SLEDAI scores (number of patients was not reported) after rituximab therapy in patient with refractory SLE with or without LN ( $p < 0.001$  for all) in the meta-analysis by Alshaiki et al (2018). However, these were not relative to any comparators as they are based on pooled results from non-comparative studies. The BILAG-BR analysis reported that 49% of patients ( $n=88$ ) had a response in terms of BILAG score [median (IQR) reduced from 15 (10 to 23) at baseline to 3 (2 to 12);  $p < 0.001$  at 6 months]. A reduction in SLEDAI-2K of greater than one point at six months follow-up was also reported in 71.9% of BILAG-BR patients ( $n=128$ ) [median (IQR) reduced from 8 (5 to 12) at baseline to 4 (0 to 7)  $p < 0.001$ ] (McCarthy et al 2018). Again these were not comparative results. In contrast, the RCT Explorer trial showed no difference in disease activity scores between immunosuppressive agents plus adjunctive rituximab versus immunosuppressive agents alone in adult North American patients with SLE at 52 weeks follow-up. Although adjunctive rituximab appears to be better at preventing flares [RR 1.41 (95% CI 1.01 to 1.95) numbers needed to treat (NNT=7)]. This is based on one low quality RCT ( $n=257$ ) included in the systematic review by Shamliyan et al (2017).

Adjunctive rituximab plus immunosuppressive agents increased the rates of partial renal response [RR 2.00 (95% CI 1.05 to 3.82) NNT = 7] but not complete renal response [RR 0.9 (95% CI 0.5 to 1.5)] compared with immunosuppressive agents alone in patients with refractory LN at 52 weeks follow-up. This is based on one low quality RCT ( $n=144$ ) included in the systematic review by Shamliyan et al (2017).

There were significant renal BILAG domain improvements (NNT=5) with immunosuppressive agents plus adjunctive rituximab compared with immunosuppressive agents alone in adult patients with refractory LN at 52 weeks

follow-up. This is based on one low quality RCT (n=144) included in the systematic review by Shamliyan et al (2017).

There was a significant reduction in prednisolone dose (mg/d) from baseline in both LN [mean difference -12.50 (95% CI -6.36 to -18.64),  $p<0.001$ ] and SLE [mean difference -22.93 (95% CI -0.01 to -45.88),  $p<0.001$ ] patients after rituximab therapy. This is based on pooled results from five non-comparative studies (number of patients was not reported) by Alshaiki et al (2018). The BILAG-BR analysis also reported a reduction from baseline in prednisolone dose at six months follow-up (n=149). The median dose reduced from 11.25mg (8.375 to 20 mg) to 7.5mg (5 to 12 mg),  $p<0.001$  (McCarthy et al 2018).

Proteinuria (g/d) was insignificantly decreased in LN patients [mean difference -2.52 (95% CI 0.22 to -5.27),  $p=0.07$ ]. The decline in proteinuria was significant in SLE patients [mean difference -2.40 (95% CI -1.39 to -3.42),  $p<0.001$ ]. These results were based on pooled results from four non-comparative studies (number of patients was not reported) included in Alshaiki et al (2018).

In patients with refractory LN who have had an inadequate response to immunosuppressive agents, adjunctive rituximab reduced urine protein to creatinine (UPC) ratio by  $\geq 50\%$  compared with immunosuppressive agents alone at 78 weeks follow-up (NNT = 6). This is based on one low quality RCT included in the systematic review by Shamliyan et al (2018)

All the above results should be interpreted with caution as they are from non-comparative studies as well as low quality RCTs of rituximab when used in addition to conventional treatment in refractory SLE with or without LN.

### **Safety**

The most common adverse reactions associated with rituximab reported in the systematic review by Alshaiki et al (2018) were infection (urinary or respiratory), acute or delayed infusion reactions, sepsis-like syndrome, thrombocytopenia and serum sickness-like reaction. The authors reported two deaths one from varicella

and the other from septicaemia. The BILAG-BR analysis reported 185 infectious episodes in 82 patients during a nine-month period. Fifty-four patients suffered multiple infections and 29 serious infections occurred in 26 patients (McCarthy et al 2018).

No difference in all-cause mortality or adverse events was reported between immunosuppressive agents plus adjunctive rituximab versus immunosuppressive agents alone in adult patients with refractory SLE including those with LN. This is based on one low quality RCT included in the systematic review by Shamliyan et al (2017).

### **Cost effectiveness**

No studies that evaluated the cost effectiveness of rituximab plus standard treatment compared to standard treatment alone for the treatment of refractory SLE in adults or children were found.

## **8 Proposed Criteria for Commissioning**

Eligibility criteria:

Rituximab should be considered for adults and post-pubescent children with moderate or severe refractory SLE with active disease, who have failed to respond or have had adverse events to 2 or more immunosuppressive therapies (one of which must be either mycophenolate or cyclophosphamide, unless contraindicated) and have:

EITHER

- a) Disease activity with at least one BILAG A and/or two B scores or a SLEDAI-2K score  $\geq 6$

Or

- b) Requiring unacceptably high levels of oral glucocorticoids e.g. more than 7.5mg prednisolone in an adult per day, to maintain a lower disease activity state



AND

- c) been assessed as not eligible for clinical trials or belimumab
- In addition, patients must be managed at, or in shared collaboration, with a recognised centre commissioned to provide specialised rheumatology services that has expertise in the assessment and management of SLE. Ratification of treatment should be at the specialised MDT/multi-speciality meeting. Rituximab can be given at nonspecialised centres (with reimbursement of those centres) if the appropriate use of rituximab has been ratified at a specialised centre.
  - All patients receiving rituximab for SLE must be registered with the National BILAG Biologics Register or UK Juvenile SLE (JSLE) Cohort Study until their transition to the adult service.
  - When prescribing for post-pubescent children, clinicians need to refer to the criteria outlined in the Commissioning Medicines for Children in Specialised Services policy. (NHS England 170001/P, 2017).

Intervention regime:

Usual dosing for adults (and post-pubescent children): IV rituximab 1000 mg on days 1 and 15 of an infusion cycle (with pre-med as per local guidelines e.g. 100mg methylprednisolone, with or without low dose cyclophosphamide). After this, patients are re-treated if they develop a further flare of disease and if they have been deemed to be a “responder”.

Definition of response:

For non-renal disease, a clinically meaningful response by 6 months will be defined as: loss of all A and B BILAG scores to  $\leq 1$  B score with no new A or B scores in other organ domains at 6 months or SLEDAI-2K reduced by 4 or more points from baseline.

For renal disease, a response will be assessed at 6 and 12 months, and by 12 months a response will be defined as:

- 50% improvement in proteinuria and normalisation or stabilisation of eGFR from baseline values.

Any response should also occur in the context of either a stable or reduced glucocorticoid dose requirement compared to baseline, especially in the 8 weeks prior to the 6-month clinical assessment.

Criteria for repeat treatment:

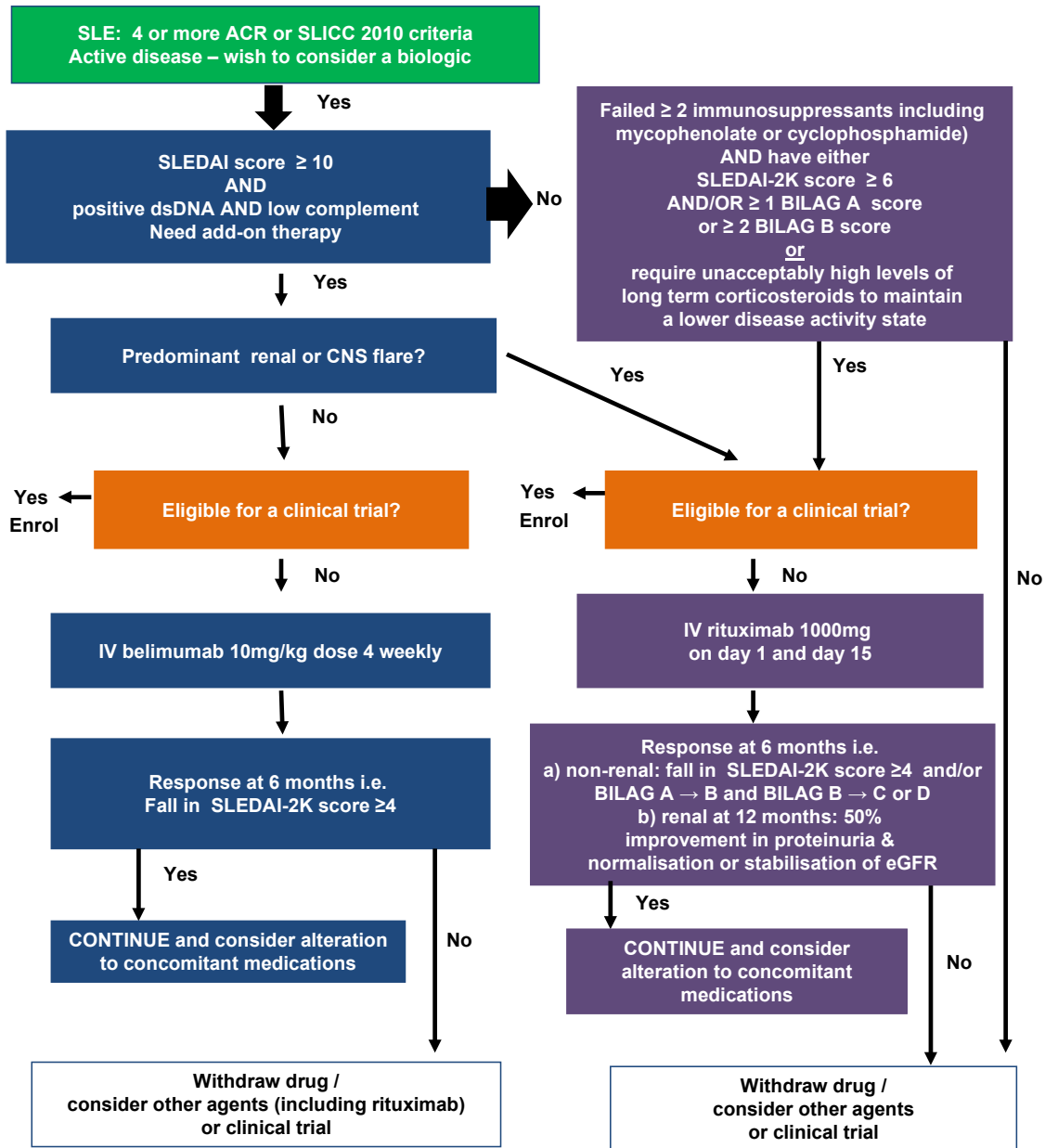
Re-treatment is permitted if the clinical assessment suggests that some improvement in scores has occurred but response is incomplete or a flare is now beginning e.g. the recurrence or persistence of one or more BILAG B scores without waiting for recurrence or development of a BILAG A score or another B score. In patients with severe organ threatening disease, the clinician should follow patients carefully with clinical and serological markers, monitor for signs of an impending flare, e.g. rising anti-dsDNA antibodies, returning B cells/CD19 count, and use their clinical judgement and knowledge of the patient's history to inform the timing and dose of any repeat infusion. Severe flares carry a risk of further organ damage for the patient, and the risk of this needs to be avoided.

The re-treatment interval varies from person to person but should not be more frequent than every 6 months.

## 9 Proposed Patient Pathway

Rituximab should be considered for adults and post-pubescent children as described in the access criteria above. Post-pubescent children must have input from a paediatrician with expertise in specialised rheumatology. The pathway for patients is described below:

NHSE and NICE Guidance for the use of belimumab and rituximab (RTX) in patients with SLE:  
**NB** 1) licensed and NICE approved agent i.e. belimumab to be considered **first**;  
 2) **all** patients receiving either drug must be enrolled in BILAG-BR and be managed at or in collaboration with a specialised centre



ACR- American College of Rheumatology  
 SLICC – Systemic Lupus International Collaborating Clinics

## 10 Proposed Governance Arrangements

As rituximab is unlicensed in the treatment of refractory SLE, any provider organisation treating patients with this intervention will be required to assure themselves that the internal governance arrangements have been completed

before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics committee (or similar) and NHS England may ask for assurance of this process.

Provider organisations will be expected to follow Trust policies for the safe prescribing and monitoring of off-label licensed medications including compliance with the Medicines and Healthcare products Regulatory Agency (MHRA) safety alerts. Prescribers need to also be aware of their responsibilities as specified in MHRA Drug Safety Update volume 10 issue, 12 July 2017:2.

Each provider organisation treating children with a medicine approved under this policy will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the Trust's Drugs and Therapeutics Committee (or similar) and NHS England can ask for documented evidence that these processes are in place.

Provider organisations must register all patients on rituximab for SLE, using software such as a prior approval system and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

## 11 Proposed Mechanism for Funding

Rituximab for the treatment of refractory SLE will be commissioned and funded by NHS England Specialised Commissioning under existing arrangements for the provision of Specialised Rheumatology Services. All associated activity should be recorded to NCBPS26Z Rheumatology service line.

## 12 Proposed Audit Requirements

All patients receiving rituximab for SLE must be registered with the BILAG-BR ([www.bilagbr.org](http://www.bilagbr.org)) or the UK JSLE Cohort Study until their transition to the adult service.

## 13 Documents That Have Informed This Policy Proposition

This document updates and replaces the Interim Clinical Commissioning Policy Statement: Rituximab for the treatment of Systemic Lupus Erythematosus in adults (August 2013) Reference: NHS ENGLAND A13/PS/a

European Medicines Agency. 2017 Biosimilar medicines: overview. Available at: <https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview>

Joint Formulary Committee. 2018 *British National Formulary*. Available at: <http://www.medicinescomplete.com>

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NHS England. 2019 Evidence review: Policy 1853.

NHS England. 2017 Commissioning Medicines for Children in Specialised Services policy (170001/P)

## 14 Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or not for routine commissioning.

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