Clinical Commissioning Policy Statement: Rituximab For Systemic Lupus Erythematosus (SLE)

December 2012
Reference : NHSCB/A3C/1b
NHS Commissioning Board
Clinical Commissioning Policy
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Systemic Lupus
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First published: December 2012

Prepared by the NHS Commissioning Board Clinical Reference Group for
Specialised Rheumatology

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First published December 2012
Published by the NHS Commissioning Board, in electronic format only.
**POLICY STATEMENT:**

**Rituximab for Systemic Lupus Erythematosus (SLE)**

| Treatment: | Rituximab (Mabthera)  
Roche Products Limited |
|------------|----------------------|
| For the treatment of: | Systemic Lupus Erythematosus (SLE).  
SLE is a disease where the immune system stops recognising parts of the body, and mounts an immune response against them, causing inflammation driven by the patient's own immune system. This can result in mild manifestations such as aches and pains and fatigue, but can also cause potentially life threatening disease by affecting vital organs such as the kidneys, heart, lungs and brain.  
Patients with more severe disease need steroid anti-inflammatory drugs, and drugs that suppress the malfunctioning immune system. For some these approaches are inadequate, and they require biological drugs that attack specific parts of the immune and inflammatory systems that are driving the disease.  
Rituximab is a drug that kills B lymphocytes, which are white blood cells that are important in driving SLE. |
| Background: | Rituximab in SLE patients is an unlicensed use of rituximab, and will not be subject to a NICE review.  
It is estimated that approximately 1 to 2 per 100,000 population will require rituximab for SLE in one year.*  
Cost of 2 infusions (one cycle) is approximately £4300 (in addition £814, tariff for day case admissions, HD23c).  
Fifty percent of patients will require subsequent doses as defined above between 6 and 18 months (median 12 months) post initial infusions, i.e. up to 50% of patients gain >18 months response from 1 cycle of rituximab.  
There are approximately 20,000-25,000 of patients with lupus in the UK predominantly women with a peak incidence at the |
age of 25-30. Its onset however varies from children under 5 to adults over the age of 60. The prevalence is higher in African-Caribbean, South Asian and Chinese populations compared to European whites, and the disease also tends to be more severe in these ethnic subsets (particularly a higher incidence of renal involvement). While criteria have been developed for the classification of SLE, a number of patients do not fulfil complete criteria but quite reasonably can be diagnosed as SLE.

In addition, SLE itself frequently overlaps with other connective tissue disease such as Sjogren's syndrome, antiphospholipid syndrome, systemic sclerosis and myositis. At the time of diagnosis, many will have symptoms related to their disease for at least 5 years. It is not known how much of this delay is due to the insidious nature of initial symptoms (e.g. arthralgia, fatigue) or diagnostic delay due to lack of awareness in both primary and secondary care.

The majority of cases are likely to be referred initially to a local rheumatologist or dermatologist although some will have renal disease as their presenting feature, and renal involvement occurs in up to 40% of cases, and can occur many years after diagnosis, though is usually apparent within 5 years.

Because of the potential for Lupus to affect any organ system, sequentially or at the same time, effective management involves accurately assessing both disease activity and damage. Capturing disease activity and distinguishing it from damage (i.e. permanent change) is important. There are several validated scoring systems for this purpose (BILAG 2004, SLEDAI, SLICC) although these are not in widespread use outside of specialist centres or clinical trials.

The aim of drug therapy is to treat disease activity, according to organ involvement and severity, and prevent disease flares. Hydroxychloroquine, Azathioprine and Methotrexate are commonly prescribed. However, 10 -15% of patients will continue to have high disease activity despite standard therapy. These patients are likely to need more specialist advice, and require IV cyclophosphamide, mycophenolate or access to Biologic Drugs e.g. rituximab.

* Based on rapid analysis of the patients attending the Leeds clinic, it is estimated there are approximately 500 prevalent patients in Leeds from which 10 per year will require rituximab. The estimated incidence of 1 to 2 /100,000 needing rituximab per year is based on local consensus which may be a slight over estimate as Leeds takes referrals from other centres.

| Commissioning | Rituximab is not routinely funded for use in Systemic Lupus Erythematosus (SLE) |
Evidence Summary: The randomised controlled trials EXPLORER$^2$ and LUNAR$^3$ did not meet primary end points and suggested that rituximab was not effective in SLE. However, results from local and international experience are better than those seen in these studies. This is thought to be because the patient population in the trials was not representative of those in the open label series - the trial patients had less severe disease, had not generally failed cyclophosphamide and had received higher doses of steroids.$^4$

Benefits of rituximab in this cohort of patients have been derived from case series data. The largest series from the UK are from Leeds and UCH, London$^5$. These demonstrate response rates of 70-80% in patients who have mostly failed Cyclophosphamide or Mycophenolate; these studies have used objective markers of response with BILAG$^6$ and other validated outcome measures.

Only 40% of 105 patients at UCH have required re-treatment in the past 12 years, though in Birmingham this is higher at 60-70%, possibly reflecting more severe patients being treated. Fifty percent of patients have responses of 18 months or longer – the median time for retreatment of these patients is 24 months. The other 50% require retreatment at 6-18 months, with a median time of 12 months.$^4$

The response duration is bimodal. Patients who respond to rituximab also have less dependence on steroids, which also renders this approach more cost-effective by reducing the expenses of long-term steroid related side effects.$^4$

There is an economic argument in favour of using rituximab in place of cyclophosphamide. Assuming that cyclophosphamide is given IV as a day case the tariff for day case admissions is £407 (HD23c – planned same day tariff for inflammatory spine, joint or connective tissue). 1 cycle of 6 pulses would therefore cost £2442. Many if not most patients will be given a minimum of 2 cycles at a cost of £4884; this is especially the case in cases presenting with aggressive multi organ involvement. This is compared to a course of rituximab £4300 + 2 day case admissions – total cost of £5114. The costs of treating side effects or long term complications are not factored into this calculation for either treatment strategy.

Neither rituximab or cyclophosphamide will cure, it is expected that retreatment will be required in patients treated with both.
Equality Impact: The NHS Commissioning Board (NHS CB) is committed to ensuring equality of access and non-discrimination, irrespective of age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex (gender) or sexual orientation. In carrying out its functions, the NHS CB will have due regard to the different needs of different protected equality groups. This applies to all the activities for which they are responsible, including policy development, review and implementation.

Responsible CRG: Specialised Rheumatology CRG

Date approved by NHS CB Clinical Assurance Group:

Date approved by NHSCB Board: To be confirmed

Policy review date: To be confirmed

Version: 1

Supersedes: N/A

Responsible Officer/Contact:

Distribution/Target Audience:

References


