NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Rituximab in combination with corticosteroids for treating anti-neutrophil cytoplasmic antibody-associated vasculitis

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: Lorraine Harper

Name of your organisation Renal Association

Are you (tick all that apply):

- √ a specialist in the treatment of people with the condition for which NICE is considering this technology?
- √ a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

ANCA-associated vasculitis is usually treated with non-specific immunosuppression as first line therapy. Induction therapy is with cyclophosphamide and high dose tapering steroids for 3-6 months. As disease enters remission therapy is changed to an anti-proliferative agent such as azathioprine and low dose steroids are maintained. This maintenance therapy is given for at least 2 years. Further treatment is dependent on the toxicity associated with therapy and the risk of disease relapse. Rituximab is frequently being used in patients who relapse and require re-induction therapy to limit cyclophosphamide toxicity. The toxicity associated with cyclophosphamide is cumulative and cumulative doses <20 g should be used. In addition those at risk of infertility due to cyclophosphamide or are intolerant of cyclophosphamide are currently treated with Ritutuximab as first line therapy. As experience grows with the use of rituximab by professionals its use as a first line agent is increasing. It is perceived that rituximab is safer than cyclophosphamide as there are no reported risks of malignancy unlike cyclophosphamide. It has however not been shown to be associated with fewer adverse evetns in clinical trials.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology? No

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?
This technology would be used in secondary care, by specialist clinicians. A national vasculitis service is being proposed to improve the care of patients with ANCA-associated vasculitis and coordinate use of new technologies such as Rituximab. At present nothing like this exists in England but development of networks to provide guidance on care and use of new technologies would be beneficial.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?
Rituximab is being used by experts as described above. This is outwith its current licensing indications although the FDA have licensed rituximab for use in ANCA-associated vasculitis. Variability in the frequency of its use occurs across the country due to requirements for approval of use due to its high cost nature, this therefore limits its use in many areas.

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Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

British Society of Rheumatology is producing guidelines based on published clinical trials for the management of ANCA-associated vasculitis. This will include indications for the use of rituximab. NHS Evidence protocols are followed for the compilation of these guidelines.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

The technology is administered as an infusion either weekly for 4 weeks or 2 doses separated by 2 weeks. The technology is no more difficult to administer than pulsed cyclophosphamide which is the comparator for safety. It remains unclear at the moment what additional drugs need to be administered, if any, to maintain disease remission. Relapse is associated with the technology. Septrin should be considered for use 6 months following rituximab to prevent pneumocystis and 200mg methylprednisolone should be given at the time of infusion to reduce infusion reactions. Vaccination should be considered prior to its use but should not delay treatment. Patients should be counselled about its side-effects and consent taken but this is no different than best practice when using the alternative treatments.

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation. Not applicable

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

The clinical trials which have investigated the efficacy of this drug in ANCA-associated vasculitis have been based at least to a degree in the UK and reflect conditions observed in clinical practice. Time to remission as assessed using BVAS, relapse and adverse events were all recorded and are extremely important. The surrogate end-points used in the trial predict long-term outcomes.

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What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

The most important adverse event is infection, which includes hepatitis B reactivation and PML. All current therapies have similar risks of infection. Using current therapies the most common cause of death in patients is due to infection and infection is also the most frequent reason for hospital admission. The risk of infection with rituximab is probably the same or less than current therapies.

Equality and Diversity

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 this appraisal:

- Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed; not applicable
- 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; not applicable
- Could lead to recommendations that have any adverse impact on people with a particular disability or disabilities not applicable

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts no evidence

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

No additional sources of evidence

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Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

NHS nursing staff would need to be trained in the administration of rituximab. However there are sufficient numbers of trained nurses who administer rituximab for lymphoma or rheumatological conditions that this would not be an issue.
No additional resources would be required