Appendix D – Clinical specialist statement template

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Tocilizumab for the treatment of systemic juvenile idiopathic arthritis

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: Dr Jeremy Camilleri

Name of your organisation: Welsh Government, Department of Health

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? X
- 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)

Appendix D – Clinical specialist statement template

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

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?

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?

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)?

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?

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.

Treatment of Systemic Onset Juvenile Idiopathic Arthritis (SOJIA) is usually carried out in secondary care in specialised paediatric rheumatology units and treatments are typically used in a stepwise fashion depending on clinical response. High dose NSAIDS can be used as a first treatment but are not usually effective enough as a stand alone treatment. Corticosteroids usually given orally are usually effective in high doses of 1 to 2 mg/kg daily initially. The steroid dose is then tapered but it is usually the case that the dose of steroid needed to maintain control of symptoms and signs of joint inflammation is unacceptably high because of the side effects caused by the steroids. Methotrexate is usually added to the treatment regime either at the start of treatment with steroids or when symptoms appear on steroid dose reduction. The dose is usually given according to the British Society for Paediatric and Adolescent Rheumatology(BSPAR) guidelines. If despite the maximal dose of Methotrexate with minimal or no steroid, disease control is not achieved then Biologic DMARDS are usually added. Anti TNF treatments such as Etanercept or Humira can be effective in the polyarticular phase of the disease (after the systemic phase has subsided) NICE guidance TA35 Nov 2002.
Anti TNF treatments are often only partially effective in SOJIA and for this reason some practitioners would now prefer to treat with other Biologics such as Tocilizumab if Methotrexate is not effective.
There is now a substantial body of clinical evidence that Tocilizumab is effective in the treatment of polyarticular forms of JIA.
Patients with persistent joint pain and swelling despite treatment with steroids and methotrexate are at high risk of poor outcome with long term disability. These are the patients who should be considered for treatment with Tocilizumab.

Appendix D – Clinical specialist statement template

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

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?

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.

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?

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?

Tocilizumab is licensed for the treatment of adults with Rheumatoid Arthritis. My personal experience is that it is effective after failure of conventional DMARDS and also after failure of anti TNF treatments. The recognised adverse effects such as hyperlipidaemias and raised bilirubin levels were seen in the clinical trials and are frequent but not usually a reason for stopping treatment. Neutropenias and infection

Appendix D – Clinical specialist statement template

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

also occur with moderate frequency and can be a cause for discontinuation of treatment and severe adverse events usually due to infection.
I have not been involved in clinical trials of Tocilizumab in SOJIA. I am currently treating three patients with JIA with Tocilizumab, two with SOJIA and one with polyarticular JIA. All three have responded to treatment after failure of steroids, DMARDS and Anti-TNF treatments. Two have neutropenia requiring alterations in the treatment schedule reducing he dose and frequency of administration. One has hyperbilirubinaemia that is mild and stable and not a cause for concern
In my opinion Tocilizumab should only be given in a specialised unit with experience administering biologics and specialist nurse support.

Appendix D – Clinical specialist statement template

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

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.

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.

Appendix D – Clinical specialist statement template

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

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)?

Units treating paediatric rheumatology patients will already have the staff, and facilities to administer intravenous biologic treatments in specialised children's treatment units.
The clinical staff using the technology will need to have knowledge of the drug and its adverse effects but additional resources will not be needed for the treatment to be administered.