NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Tocilizumab for treating systemic sclerosis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of tocilizumab within its marketing authorisation for treating systemic sclerosis.

Background

Systemic sclerosis (SSc) is a complex condition where the body overproduces connective tissue that interferes in the normal functioning of many organs. The condition can be described as limited cutaneous (lcSSc) or diffuse cutaneous systemic sclerosis (dcSSc) depending upon the extent of skin thickening.[1] The immune system attacks organ tissue and overproduces fibrous connective tissue. This can cause problems such as pulmonary hypertension, heartburn, bowel problems, shortness of breath and increases mortality risk.[2] SSc can also affect the lungs, blood vessels, heart, kidneys, gastrointestinal tract and the musculoskeletal system. Raynaud's phenomenon is often the first sign of SSc, where poor blood circulation leads to a numbing and coldness of the fingers and toes.[3]

The prevalence of systemic sclerosis is estimated at around 31 to 100 per million.[4,5] It is estimated that there are between 1600-5150 adults with SSc in the UK. Women are four times more likely than men to develop SSc, however the disease is more severe in men.[3] Approximately 2 in 3 people with SSc have limited cutaneous SSc, and 1 in 3 have diffuse cutaneous SSc. SSc associated complications are more commonly observed in people with dcSSc.

The aim of treatment is to relieve symptoms, prevent the disease getting worse, detect and treat any complications, and minimise disability through occupational therapy and physiotherapy. Because SSc can affect many different parts of the body, a variety of treatments may be needed to manage the condition.[2] The British society for Rheumatology (BSR) guideline for the treatment of systemic sclerosis includes recommendations on the treatment of SSc[1]. The BSR guideline recommends that people with early diffuse cutaneous SSc should be offered an immunosuppressive agent such as methotrexate, mycophenolate mofetil or intravenous cyclophosphamide. Oral steroid therapy and rituximab may also be options to treat symptoms of skin involvement. Autologous haematopoietic stem cell transplantation could later be offered for some people particularly where there is risk of severe organ involvement. All cases of SSc require symptomatic treatment, and both limited and diffuse cases should be treated for vascular manifestations. The BSR guideline also includes recommendations on the management of complications associated with SSc such as Raynaud’s phenomenon, digital

ulcers, lung fibrosis, pulmonary arterial hypertension, gut disease, renal complications, cardiac disease.

The technology

Tocilizumab (RoActemra) is a humanised monoclonal antibody that inhibits interleukin-6, a cytokine that is thought to play a role in systemic sclerosis.

Tocilizumab does not currently have a marketing authorisation in the UK for systemic sclerosis. It has been studied in two randomised clinical trials of adults with systemic sclerosis compared with placebo. Tocilizumab is administered by subcutaneous injection.

Intervention(s)	Tocilizumab
Population(s)	Adults with systemic sclerosis
Comparators	Established clinical management without tocilizumab, which may include: • methotrexate • mycophenolate mofetil • cyclophosphamide • rituximab • autologous haematopoietic stem cell transplant
Outcomes	The outcome measures to be considered include: • skin thickness (including the modified Rodnan Skin Score [mRSS]) • lung function • pulmonary hypertension • change in digital ulcer count • exercise capacity (including 6 minute walk distance) • renal function • mortality • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	NICE evidence summaries: Skin involvement in systemic sclerosis: rituximab' (2017) NICE evidence summary 7 'Digital ulcers: sildenafil' (2015) NICE evidence summary of unlicensed or off-label medicines 42 'Scleroderma: oral mycophenolate' (2014) NICE evidence summary of new medicines 32
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. (Chapters 4 and 5). NHS England (2017) Next steps on the five year forward view NHS England. 2013/14 NHS Standard Contract for Specialised Dermatology Services (All Ages) Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,2,4,5 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for tocilizumab been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for systematic sclerosis?

What existing treatments for systemic sclerosis and systemic sclerosis associated complications could be displaced by the introduction of tocilizumab?

Is the aim of treatment to relieve symptoms of secondary problems caused by systemic sclerosis or to control skin thickening?

Are the outcomes listed appropriate? Are there any other outcomes that should be included?

Is the modified Rodnan Skin Score (mRSS) a suitable surrogate outcome measure for disease severity and morality in patients with systemic sclerosis?

Are there any subgroups of people in whom tocilizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately (for example, limited cutaneous SSc, diffuse cutaneous SSC, or poor prognosis SSc)?

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:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which tocilizumab 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.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider tocilizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a ‘step-change’ in the management of the condition)?

Do you consider that the use of tocilizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. BSR and BHPR guideline for the treatment of systemic sclerosis, Rheumatology (2016). Accessed: March 2018

2. Scleroderma, NHS Choices. Accessed: March 2018

3. Systemic sclerosis, Orphanet. Accessed: March 2018

4. Systemic sclerosis (2011) Denton and Black in: Oxford textbook of medicine 5th edition. Accessed: March 2018

5. Tocilizumab, Specialist Pharmacy Service. Accessed: March 2018