NICE National Institute for Health and Care Excellence

NICE guidance

Tocilizumab for treating giant cell arteritis

Technology appraisal guidance
Published: 18 April 2018

www.nice.org.uk/guidance/ta518

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Tocilizumab, when used with a tapering course of glucocorticoids (and when used alone after glucocorticoids), is recommended as an option for treating giant cell arteritis in adults, only if:

- they have relapsing or refractory disease
- they have not already had tocilizumab
- tocilizumab is stopped after 1 year of uninterrupted treatment at most and
- the companies provide tocilizumab (branded or biosimilars) according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with tocilizumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Giant cell arteritis is usually treated with a high dose of glucocorticoids, which is gradually reduced over time. High doses of glucocorticoids may cause a number of problems, including skin problems, weight gain, diabetes and osteoporosis.

Clinical trial results show that after having tocilizumab plus a tapering course of glucocorticoids for 1 year, more people stay in remission and need lower doses of glucocorticoids compared with people having glucocorticoids alone.

In the full population, the most plausible cost-effectiveness estimates were above the range normally considered to be a cost-effective use of NHS resource, even when tocilizumab is used for only 1 year. For the subgroup of people with relapsing or refractory disease, using the committee's preferred assumptions (including that tocilizumab is given for 1 year at most), the most likely cost-effectiveness estimate compared with glucocorticoids alone is £24,977 per quality-adjusted life year gained. This is within the range normally considered to be a cost-effective use of NHS resources, so tocilizumab is

recommended.

2 Information about tocilizumab

Marketing authorisation indication

2.1 Tocilizumab (RoActemra, Roche) has a marketing authorisation for 'the treatment of adults with giant cell arteritis'.

Dosage in the marketing authorisation

2.2 Subcutaneous injection (162 mg) once every week in combination with a tapering course of glucocorticoids. Tocilizumab can be used alone following discontinuation of glucocorticoids, but monotherapy should not be used for the treatment of acute relapses. Treatment beyond 52 weeks should be guided by disease activity, physician discretion and patient choice.

Price

2.3 £913.12 for 4 syringes containing 162 mg tocilizumab (excluding VAT). The company of branded tocilizumab (RoActemra, Roche Products) has a commercial arrangement. This makes tocilizumab available to the NHS with a discount. The size of the discount is commercial in confidence. NHS England has completed a national procurement for tocilizumab, which includes the biosimilar versions of tocilizumab. Prices paid for the originator or biosimilar tocilizumab should be in line with the national procurement outcome and should be no higher than that provided through the original commercial arrangement.

3 Committee discussion

The appraisal committee considered evidence submitted by Roche and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

A new treatment option

People would welcome a new treatment that reduces the cumulative amount of glucocorticoids needed

3.1 Giant cell arteritis causes inflammation in the walls of the arteries in the head and neck, and less commonly the aorta (known as large vessel giant cell arteritis). The patient experts explained that this causes symptoms such as headache, jaw pain, fatigue and muscle and joint pains. More serious complications include vision loss, stroke, aortic aneurysm and dissection, and myocardial infarction. It is with visual symptoms that people often first present to health services. Initial treatment in the NHS is with high-dose glucocorticoids, usually prednisolone. The dose is tapered gradually over 18 to 24 months to minimise the risk of the disease flaring up. The clinical experts explained that although glucocorticoids are effective at managing the disease, large cumulative doses can cause serious side effects such as diabetes and osteoporosis. The patient experts also noted unpleasant side effects with glucocorticoids such as skin changes and weight gain. They highlighted that because the disease is most common among people 50 years and older, these side effects are often in addition to existing health problems. The patient experts emphasised that glucocorticoid-sparing agents are very important for people with giant cell arteritis, especially for those with relapsing or refractory disease, who are subject to excessive cumulative dosage of glucocorticoids. The committee concluded that people with giant cell arteritis would welcome a new treatment option that reduces flares of the disease and the cumulative amount of glucocorticoids needed.

Subgroups

People with relapsing or refractory giant cell arteritis have the highest unmet need

3.2 Tocilizumab has a UK marketing authorisation for use in adults with giant cell arteritis. At the first committee meeting, the company presented clinical- and cost-effectiveness analyses which divided the overall population into 2 subgroups: people with newly diagnosed disease and people with relapsing disease. The clinical experts explained that newly diagnosed giant cell arteritis is treated differently to relapsing disease. People with a new diagnosis are usually offered high doses of glucocorticoids (40 mg to 60 mg of prednisolone daily). This is because the priority is to prevent vision loss, and at this stage people have not been exposed to a high cumulative dose of glucocorticoids, so there are fewer concerns about glucocorticoid-related adverse events. People with relapsing disease are usually offered lower doses of glucocorticoids in an attempt to manage flares and minimise additional glucocorticoids exposure; as such, the clinical and patient experts considered that tocilizumab would be most valuable to people with relapsing disease. The committee agreed that there were important differences between the 2 subgroups. It considered how many people with newly diagnosed disease would then go on to have relapses. The clinical experts explained that it is difficult to identify people whose disease may relapse, although there are some whose disease does not respond to initial high doses of glucocorticoids and that never achieve remission. The committee also acknowledged differences within the subgroup of people with relapsing disease: for example, some people's disease may relapse frequently, whereas for others relapses may be rare. Furthermore, the clinical experts explained there were differences in the severity of flares in this subgroup. In response to consultation, the company stated that tocilizumab would be most valuable to people with relapsing or refractory giant cell arteritis and therefore amended its cost-effectiveness model to focus on this subgroup only (section 3.14). It was also noted that, although clinician and patient groups also highlighted a high unmet need in patients with newly diagnosed giant cell arteritis with comorbidities, there was no data available for the company to do an analysis in this subgroup. The committee concluded that the relapsing or refractory subgroup was distinct and biologically plausible and had the highest unmet need. Therefore it

considered both the full population and the relapsing or refractory subgroup in its decision making.

Clinical evidence

The weekly tocilizumab and 52-week glucocorticoid taper arms of GiACTA reflect the license and British Society for Rheumatology guidelines

3.3 The main clinical evidence for tocilizumab came from GiACTA, a multicentre, double-blind, randomised controlled trial. The trial followed patients for 52 weeks, at which point they were enrolled in an open-label extension study which is still ongoing. Patients in the tocilizumab arm had tocilizumab plus glucocorticoids for 26 weeks, followed by tocilizumab alone for the remaining 26 weeks. The primary outcome of the trial investigated whether more people achieve sustained disease remission at 52 weeks with tocilizumab and glucocorticoids compared with glucocorticoids alone. Secondary outcomes included time to first flare after disease remission and cumulative glucocorticoid dose. The trial included 4 arms:

- tocilizumab every week with 26-week prednisone taper (n=100)
- tocilizumab every 2 weeks with 26-week prednisone taper (n=50)
- placebo with 26-week prednisone taper (n=50)
- placebo with 52-week prednisone taper (n=51).

The company presented clinical-effectiveness data for all 4 arms, but in its economic model used only the weekly tocilizumab and the placebo with 52-week prednisone taper arms. This is because weekly tocilizumab reflects the marketing authorisation, and the 52-week glucocorticoid taper reflects the minimum tapering regimen recommended in British Society for Rheumatology guidelines on giant cell arteritis. The committee noted that splitting the trial into 4 arms meant that the numbers in each arm were small, especially when the population was further divided into newly diagnosed and

relapsing subgroups. It also noted that prednisolone, not prednisone, is usually used in the NHS, but considered that the 2 drugs are very similar. The committee concluded that the 2 arms included in the company's economic model (that is, weekly tocilizumab and placebo with 52-week prednisone taper) are most relevant to clinical practice in England.

Patients in GiACTA reflect those with giant cell arteritis in England

3.4 The committee noted a number of differences in the baseline characteristics between the treatment groups in GiACTA, but the ERG explained that these generally balanced out with no obvious skew. However, the committee was concerned that the mean age in the trial was lower than the mean age of people with the disease in the UK (69 years and 73 years respectively). In addition, 40% of patients in GiACTA had large vessel disease, compared with only around 5% of people with giant cell arteritis seen in clinical practice in England. Large vessel disease tends to be associated with a longer disease duration and more relapses than giant cell arteritis affecting the head and neck. However, the clinical experts explained that most people with giant cell arteritis affecting the head and neck also have large vessel disease. It is less likely to be diagnosed in the NHS because there is a lower utilisation of advanced imaging than in the trial. As such, the proportion in the trial is likely to reflect the true proportion with large vessel disease in England. The committee concluded that the patients in the trial reflect those with giant cell arteritis in England.

The 52-week glucocorticoid taper does not reflect clinical practice in England and might bias the results in favour of tocilizumab

3.5 The committee was concerned that 52 weeks (12 months) is the shortest glucocorticoid taper recommended in the British Society for Rheumatology guidelines. The clinical experts explained that in clinical practice, glucocorticoids would usually be tapered over 18 to 24 months. The committee considered that this might mean that the number of flares in the comparator arm (that is, placebo

with 52-week glucocorticoid taper) may be higher, and the time to first flare shorter, than in clinical practice in England. In response to consultation, the company proposed a revision to the comparator arm of the cost-effectiveness model to incorporate the slowest tapering regimen (24 months) recommended by the British Society for Rheumatology guidelines. The committee was also aware that 49% of patients in the comparator arm did not have disease remission after the 6-week screening phase of the trial, but that nonetheless they had to start the 52-week tapering regimen. The committee was concerned that this might bias the primary end point of the trial (sustained remission at 52 weeks) in favour of tocilizumab, because it is less likely that people whose disease has not responded to high-dose glucocorticoids would achieve remission with lower doses. In response to consultation, the company submitted evidence from a new exploratory analysis that suggested there is no difference in primary end point analysed by remission status at baseline in the trial. However, without any statistical analyses from the company to support this conclusion, the committee remained concerned about potential bias in the primary end point in favour of tocilizumab. It concluded that the 52-week glucocorticoid taper arm of the trial does not reflect clinical practice in England and might bias the results in favour of tocilizumab.

Tocilizumab plus a tapering course of glucocorticoids is more effective than glucocorticoids alone

3.6 The company presented results for the overall intention-to-treat population of GiACTA, as well as for both the newly diagnosed and relapsing subgroups. The results showed that tocilizumab plus a tapering course of glucocorticoids was more effective than glucocorticoids alone at increasing the proportion of patients sustaining remission at 52 weeks, and increasing the time to first flare for the overall population and both subgroups (see table 1). The committee recalled that in clinical practice, newly diagnosed disease and relapsing disease are managed differently, but the results were similarly effective across both subgroups. The committee concluded that tocilizumab is more effective than glucocorticoids alone at increasing sustained remission and time to first flare.

Table 1 GiACTA trial results

Population	Sustained remission at 52 weeks (%)	Time to first flare hazard ratio	Median cumulative glucocorticoids dose (mg)
Overall population: tocilizumab (n=100)	56.0	0.39 (0.18 to 0.82)	1,862
Overall population: placebo (n=51)	17.6	0.39 (0.18 to 0.82)	3,818
Newly diagnosed subgroup: tocilizumab (n=47)	59.6	0.44 (0.29 to 1.59)	1,942
Newly diagnosed subgroup: placebo (n=23)	21.7	0.44 (0.29 to 1.59)	3,817
Relapsing subgroup: tocilizumab (n=53)	52.8	0.33 (0.14 to 0.81)	1,385
Relapsing subgroup: placebo (n=28)	14.3	0.33 (0.14 to 0.81)	3,785

Adverse events

Because tocilizumab is taken with glucocorticoids, the extent to which glucocorticoid-related adverse events are reduced is unclear

3.7 The committee considered the benefits of tocilizumab in terms of a reduction in cumulative glucocorticoid dose and risk of glucocorticoid-related adverse events. The committee noted that although the tapering regimen with tocilizumab is shorter than when glucocorticoids are used alone, disease flares are treated by increasing the glucocorticoid dose, and a tapering regimen restarted. As such, people taking tocilizumab could still be exposed to large cumulative doses of glucocorticoids. The committee acknowledged that the median cumulative glucocorticoid dose was lower in the tocilizumab arm of GiACTA (see table 1), but noted that this was over the relatively short 52-week follow-up. It was concerned that despite the lower median cumulative glucocorticoid dose in the tocilizumab

arm, the rate of glucocorticoid-related adverse events was similar between trial arms (50% compared with 49%). The committee acknowledged that this might be because many glucocorticoid-related adverse events only manifest in the longer term. In response to consultation, the company provided new evidence from post-hoc trial analyses that showed a higher rate of glucocorticoid-related adverse events being seen in the comparator arm. However, the committee was concerned that the data were analysed retrospectively and not based on standard or prespecified criteria. In addition, the company did not provide any statistical analyses to support the comparison of glucocorticoid-related adverse events between arms. The committee concluded that because glucocorticoids still need to be taken with tocilizumab, the extent to which glucocorticoid-related adverse events are reduced is unclear.

The company's economic model

The structure of the model is adequate for decision making

3.8 The company's economic model had a 30-year time horizon and included separate health states for remission based on whether patients are having glucocorticoids or not. Patients in the model could also have a flare, giant cell arteritis-related adverse events and glucocorticoid-related adverse events. Both taking glucocorticoids and disease flares were associated with a utility decrement. The committee concluded that the structure of the model was adequate for decision making.

Duration of tocilizumab treatment

A 1-year stopping rule can be implemented in NHS practice

3.9 In its original model, the company assumed that treatment with tocilizumab stops after 2 years. The committee was concerned that in clinical practice treatment may continue well beyond 2 years. This is because the risk of relapse continues, and there is no evidence that tocilizumab modifies the underlying disease when

treatment stops (it may just supress it for the duration of treatment). In addition, tocilizumab treatment may be stopped and restarted in the event of a relapse. After consultation, however, the company argued that most patients would not need the full 2 years of tocilizumab treatment. It proposed that, based on clinical expert opinion, up to 1 year of treatment would be sufficient to sustain remission in the longer term and to reduce the cumulative glucocorticoid burden. The company therefore implemented a 1-year stopping rule in its revised economic model for people with relapsing or refractory disease. This stopping rule assumed that patients only had 1 course of treatment, even if they had another flare. It supported its position by providing supporting evidence from a literature review of published case reports of tocilizumab in giant cell arteritis, in which most patients had tocilizumab for less than 1 year (range 1 to 53 months). However, the committee was concerned that the evidence was based only on case reports, and that most included no follow-up details. Nevertheless, it noted that GiACTA showed that 1 years' treatment with tocilizumab is effective in sustaining remission and reducing cumulative glucocorticoid burden. It also noted that the 1-year treatment duration provided results that were most internally valid. Both the clinical and patient experts agreed that many patients are likely to need less than 1 year of tocilizumab to achieve sustainable remission, and that a 1-year stopping rule would be acceptable. As a relevant commissioner, NHS England specialised services also stated that a 1-year stopping rule could be implemented in NHS practice. The committee therefore concluded that it would include the 1-year stopping rule in its decision making.

Extrapolation of time to first flare

The company's extrapolation after 52 weeks lacks validity

3.10 In order to extrapolate time to first flare beyond the 52 weeks of the trial, the company fitted separate parametric models to the 2 arms (weekly tocilizumab with 26-week prednisone taper and placebo with 52-week prednisone taper) in its economic model. It used a Weibull distribution for the weekly tocilizumab arm (implying a decreasing risk of flare over time) and an exponential distribution for the comparator arm (implying a constant risk of flare over time). The committee was concerned that extrapolating in this way meant that the benefit of

tocilizumab over glucocorticoids alone was assumed to continue for the 30-year time horizon of the model, despite tocilizumab treatment stopping at 2 years. Moreover, the extrapolation for the comparator arm was based on the glucocorticoid taper period, when the risk of flare is highest. The committee was concerned that this would exaggerate the risk of flare for patients in the comparator arm that had successfully completed the 52-week glucocorticoid taper. The clinical experts explained that after 10 years, they would expect around 25% of people who had successfully completed a glucocorticoid taper to not have disease relapse; in contrast, at the same time point, the company's model predicted that almost all patients in the comparator arm would have disease relapse. Longitudinal cohort data also suggest that at 5 years, 30% to 50% of people having glucocorticoids alone will not have disease relapse; at the same time point, the company's model predicted this to be less than 2%. The committee concluded that the company's extrapolation of time to first flare lacked validity.

The ERG's approach to extrapolation is more appropriate

3.11 The ERG suggested an alternative approach to extrapolating time to first flare for the comparator arm, in which it switches to the same Weibull distribution as the weekly tocilizumab arm after 2 years. The committee considered that this addressed the issue of the relative benefit of tocilizumab continuing after treatment stops, because all patients that have successfully completed the taper in either arm have the same decreasing risk of disease relapse. Using this approach, the ERG predicted that at year 5 around 12% of patients in the comparator arm would not have relapsing disease (falling to 8% by year 10). The committee concluded although the ERG's approach may still overestimate the risk of flare in the comparator arm, it provided more clinically realistic estimates of the proportion of patients with disease relapse after having glucocorticoids alone.

Estimating rates of subsequent flares

The ERG's approach results in more realistic estimates of subsequent flares

3.12 The company used GiACTA data to estimate rates of subsequent flares that were used in the economic model. The ERG noted that the company's estimate for the tocilizumab newly diagnosed subgroup was higher than for the relapsing subgroup, which is clinically implausible. In addition, the company's model predicted a high number of flares for people having glucocorticoids alone, which lacks validity. For example, over the same period of 10 years, a longitudinal cohort study of people with giant cell arteritis taking glucocorticoids alone (Labarca et al. 2016) reported less than half the flares predicted by the company's model. The ERG derived probabilities based on this study that were logically consistent across the subgroups. The committee considered that when the ERG's probabilities for subsequent flare are combined with its approach to time to first flare extrapolation, the predicted mean number of flares over the model time horizon for the comparator arm is more plausible than the company's approach. In the company's revised model for people with relapsing or refractory disease, it proposed an additional 10% adjustment to the ERG's estimated rates of subsequent flares to provide a better estimate in the control arm of the relapsing subgroup. The ERG stated that this had already been accounted for in its own estimates, so no adjustments were needed. The committee concluded that the ERG's approach to estimating the probability of subsequent flares was more appropriate.

Utility values in the model

The company's model adequately captures the negative effect of flares and glucocorticoids on quality of life

3.13 The company used a common utility value for the remission health state in both treatment arms, and applied a utility decrement of -0.13 for 4 weeks to capture how a flare negatively affects quality of life. The company accounted for the

negative effects of glucocorticoids by including increased probabilities of diabetes and fracture in the model, which are associated with costs and disutilities. In addition, all patients having glucocorticoids in the model were assigned a utility decrement of -0.07 for the duration of their treatment, reflecting the negative effects of common side effects such as weight gain and skin changes. The committee acknowledged that the disutility estimate does not include an exhaustive list of adverse events that can result from glucocorticoid treatment, but considered the source to be the most relevant reference. The ERG noted that within the disutility estimate is a separate 'base' disutility estimate (-0.03) to capture common side effects for all patients having glucocorticoids. This was applied during each cycle patients were in the subsequent remission state. It assumed, after a relapse, people would continue to incur both the 'base' disutility and the specific side effects for the remainder of their lifetime. The ERG considered that unless patients continued to have lifelong treatment with glucocorticoids, it might not be appropriate to continue applying the 'base' disutility. Nevertheless, the committee concluded that the company's model adequately captures the negative effect of flares and glucocorticoids on quality of life.

The company's updated economic analysis

The company's ICER for tocilizumab in relapsing or refractory disease is £18,801 per QALY gained with a 1-year stopping rule

3.14 The company's original base-case deterministic incremental cost-effectiveness ratio (ICER) for the overall population was £28,272 per quality-adjusted life year (QALY) gained. This was based on a 2-year stopping rule and included a confidential patient access scheme discount for tocilizumab. In response to consultation, the company updated its economic model to focus only on the subgroup of people with relapsing or refractory giant cell arteritis. The updated economic model included the committee's preferred assumptions, specifically:

- a mean age of 73 years (section 3.4)
- switching the time to first flare extrapolation for glucocorticoids alone to the same Weibull function as tocilizumab after 2 years (section 3.10)

- basing the probabilities of subsequent flares on longitudinal cohort data (section 3.12).

  The updated model also included a number of company-preferred assumptions and corrections, specifically:

- incorporating a 1-year stopping rule for tocilizumab (section 3.9)
- incorporating the slowest glucocorticoid taper regimen (24 months) in the comparator arm to match NHS practice
- incorporating the costs for emergency department visits
- updating the costs of glucocorticoid-related adverse events to reflect 2017 health care utilisation, specifically:
  - including additional costs for a yearly DEXA scan and prophylaxis medication
  - inflating diabetes costs from 2005 to 2017 estimates
  - revising fracture costs (based on Kanis et al. 2007)
  - revising infection costs (based on Sarnes 2011)
- adjusting the ERG's flare rate to better reflect relapsing or refractory giant cell arteritis in the comparator arm of GiACTA
- correcting 2 programming errors: using the average weight of the relapsing and refractory population in GiACTA to calculate concomitant medication dosage (instead of the UK population), and correcting the yearly concomitant medication costs applied to the comparator arm.

  When incorporating these changes, the deterministic ICER for tocilizumab plus prednisolone compared with prednisolone alone, incorporating the confidential patient access scheme, was £18,801 per QALY gained in people with relapsed or refractory giant cell arteritis (a probabilistic ICER was not provided).

The ERG's updated alternative economic analysis

The ERG's ICER for tocilizumab in relapsing and refractory disease is £24,977 per QALY gained when a 1-year stopping rule is applied

3.15 The ERG's original base-case probabilistic ICER for the overall population was £65,801 per QALY gained. This was based on a 2-year stopping rule and included the committee's preferred assumptions. A confidential patient access scheme discount for tocilizumab was also applied. The ERG's revised economic model included a 1-year stopping rule, and focused only on people with relapsing or refractory disease. It made a number of other changes in its revised model, specifically:

- using both the average weight and body surface area estimates of the relapsing or refractory population in GiACTA to calculate the dosages of concomitant medication
- incorporating an alternative estimate for emergency department visits based on NHS reference costs
- including costs for a single DEXA scan, instead of yearly scans, and using average generic cost estimate for oral therapies (taken from NICE's technology appraisal guidance on bisphosphonates for treating osteoporosis)
- using fracture cost estimates that are consistent with those used in NICE's technology appraisal guidance on bisphosphonates for treating osteoporosis.

  The ERG did not consider the company's proposed change to the glucocorticoid tapering regimen to be appropriate, because only the cost of the comparator glucocorticoid taper regimen was adjusted and no adjustment was made to address the uncertainties about how this may affect the number of flares and time to first flare. The ERG also noted that the reference data used to update the infection costs in the company's updated economic model was taken from a US study (Sarnes 2011), so the generalisability of the findings to the NHS is unclear. In addition, the ERG considered the company's proposed additional adjustment to the ERG's estimated rates of subsequent flares (section 3.12) to be inappropriate. The

ERG therefore did not make these changes in its revised analysis. When the ERG made its adjustments, the revised model produced ICERs for tocilizumab plus prednisolone compared with prednisolone alone of £24,977 (deterministic) and £24,032 (probabilistic) per QALY gained in people with relapsed or refractory giant cell arteritis (including the patient access scheme discount).

The most plausible ICER after consultation

Tocilizumab is cost-effective only for relapsing or refractory giant cell arteritis and when a 1-year stopping rule is applied

3.16 The committee preferred the ERG's estimates for both the overall population and people with relapsing or refractory giant cell arteritis, because they better reflected its preferred assumptions. It therefore concluded that the most plausible ICERs for tocilizumab plus prednisolone compared with prednisolone alone, incorporating the confidential patient access scheme, were £65,501 (2-year treatment duration) and £36,960 (1-year treatment duration) per QALY gained for the overall population and £55,924 (2-tear treatment duration) and £24,977 (1-year treatment duration) per QALY gained for people with relapsing or refractory giant cell arteritis. The ICERs for the overall population were higher than the range normally considered to be a cost-effective use of NHS resources (usually £20,000 to £30,000 per QALY), as were the ICERs when a 2-year treatment duration was applied, so the committee concluded that it would recommend tocilizumab as a cost-effective use of NHS resources only for treating relapsing or refractory giant cell arteritis and if a 1-year stopping rule is applied.

Other factors

There are no additional benefits that are not captured in the QALY calculations

3.17 The clinical experts highlighted that tocilizumab is the first new treatment for giant cell arteritis in several years. The committee was aware that before its marketing authorisation was granted, tocilizumab received a Promising Innovative Medicines designation for this indication. The patient experts explained that high doses of glucocorticoids are needed to treat flares and afterwards the tapering regimen must be restarted. This can have a large negative effect on quality of life, which may not be captured in the modelling. However, the committee noted that in the model, patients have a substantially lower utility during a flare, which is assumed to last for 4 weeks (section 3.8). In addition, after a disease flare, all patients have glucocorticoids and this is associated with a utility decrement (section 3.13). The committee concluded that there were no additional benefits that had not been captured in the QALY calculation.

The recommendations do not have a different impact on people protected by equality legislation than on the wider population

3.18 The committee discussed equality issues, and agreed that its recommendations apply equally regardless of age. In addition, issues related to differences in prevalence or incidence of a disease cannot be addressed in a technology appraisal. The committee concluded that its recommendations do not have a different impact on people protected by the equality legislation than on the wider population.

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal determination.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has relapsed or refractory giant cell arteritis and they have not previously received treatment with tocilizumab for giant cell arteritis and the doctor responsible for their care thinks that tocilizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee C.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Aimely Lee and Ross Dent
Technical leads

Alexandra Filby
Technical adviser

Stephanie Callaghan
Project manager

6 Update information

June 2024

The wording of the recommendation describing the commercial arrangement (see section 1.1), and in section 2.3, has been updated to include procurement information about tocilizumab biosimilars.

ISBN: 978-1-4731-6167-2