NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Upadacitinib for treating giant cell arteritis

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using upadacitinib in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Note that this document is not NICE's final guidance on upadacitinib. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using upadacitinib in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 4 February 2026
- Second evaluation committee meeting: TBC
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Upadacitinib should not be used to treat giant cell arteritis in adults.

1.2 This recommendation is not intended to affect treatment with upadacitinib 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 healthcare professional consider it appropriate to stop.

What this means in practice

Upadacitinib is not required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because there is not enough evidence to show upadacitinib offers benefit or is value for money in this population.

Why the committee made these recommendations

Usual treatment for giant cell arteritis is corticosteroids, which are gradually reduced over time. Tocilizumab or methotrexate (off-label use) may be added when the condition relapses.

Evidence from a clinical trial shows that, compared with placebo, upadacitinib results in:

- an increase in the number of people with sustained or complete remission of giant cell arteritis
- people being able to reduce corticosteroid use.

How effective it is compared with placebo after 1 year is unknown. Also, it has not been directly compared with tocilizumab or methotrexate. The results of an indirect

comparison with tocilizumab suggest that they may be similarly effective, but this is very uncertain.

There are uncertainties in the economic model, including the modelling of:

- a 2-year treatment stopping rule
- sequencing of treatments after relapse
- time to a first flare in people with new-onset giant cell arteritis
- giant cell arteritis flare-related complications
- corticosteroid-related complications.

Because of the uncertainties in the clinical evidence and economic model, it is not possible to determine the most likely cost-effectiveness estimates for upadacitinib. So, it should not be used.

2 Information about Upadacitinib

Marketing authorisation indication

2.1 Upadacitinib (RINVOQ, AbbVie) is indicated for 'the treatment of giant cell arteritis in adult patients'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for upadacitinib.

2.3 The list price for upadacitinib is £805.56 for a pack of 28 x 15 mg tablets (excluding VAT; BNF online, accessed December 2025).

2.4 The company has a commercial arrangement. This makes upadacitinib available to the NHS with a discount and it would have also applied to this indication if upadacitinib had been recommended. The size of the discount is commercial in confidence.

Carbon Reduction Plan

2.5 Information on the Carbon Reduction Plan for UK carbon emissions for AbbVie will be included here when guidance is published.

3 Committee discussion

The evaluation committee considered evidence submitted by AbbVie, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

3.1 Giant cell arteritis (GCA) causes inflammation in the walls of the arteries in the head and neck. Less commonly, it can cause inflammation in the aorta, which is known as large vessel GCA. The inflammation causes the affect arteries to narrow, which restricts blood flow. This leads to symptoms such as headache, jaw pain, fatigue, and muscle and joint pains. More serious complications include sight loss, stroke, aortic aneurysm and dissection, and myocardial infarction. The patient experts explained that living with GCA can be difficult. They explained that it is an unpredictable condition with relapses, flares and remissions. They also noted that, during acute phases of the condition, symptoms can be so debilitating that they often need to rely on carers to help them with day-to day-tasks. The patient experts emphasised that the main treatment for the condition is corticosteroids, which can lead to serious side effects at higher doses or with prolonged use. They noted that corticosteroid-sparing agents such as upadacitinib are very important for people with GCA, especially when the condition is relapsing or refractory, so needing prolonged corticosteroid use. The clinical expert explained that GCA is a serious condition, and the initial presentation can be a medical emergency. They noted that delays to initial diagnosis in some regions are not uncommon. They explained that there is wide variability in the speed at which diagnostic procedures such as biopsies and vascular imaging are available. Delays to treatment can lead to serious complications such as

complete sight loss, stroke or end-organ failure. This can have a devastating long-term impact for people with the condition. The committee concluded that GCA has a high disease burden that substantially affects people's lives.

Treatment pathway

3.2 Initial treatment in the NHS for people presenting with visual symptoms and with new-onset GCA is high-dose corticosteroids, usually prednisolone. Once the condition is in remission, the dose is tapered gradually over 12 to 24 months to minimise the risk of a flare. For relapsing GCA, the corticosteroid dose can be increased to the last effective dose for a minor relapse. Higher doses of corticosteroids are offered for major relapses. The clinical and patient experts noted that corticosteroids are effective at managing GCA. But they added that high doses of corticosteroids over time may cause several serious debilitating problems, including skin problems, weight gain, diabetes and osteoporosis. Another treatment option for relapsed GCA is tocilizumab. NICE's technology appraisal on tocilizumab for treating GCA (from here, TA518) recommends tocilizumab as an option for treating GCA in adults with relapsing or refractory GCA for up to 1 year of uninterrupted treatment. For people who have a relapse after treatment with tocilizumab, there are no alternative licensed corticosteroid-sparing options. There is also unmet need for effective treatments in people who cannot have tocilizumab or corticosteroids. The clinical experts further noted that there may be some off-label use of immunosuppressants such as methotrexate in clinical practice but that this is not consistent across the NHS. The patient experts added that methotrexate can be associated with adverse effects. The committee concluded that people with GCA would welcome a new treatment option that reduces flares and prolonged corticosteroids use.

Relevant comparators

3.3 The company positioned upadacitinib with a 26-week tapering course of corticosteroids for everyone with GCA, that is people with new-onset and relapsing GCA. The NICE scope included tocilizumab and methotrexate as relevant comparators in relapsed GCA, but the company did not include them as comparators in its submission. The company said that it excluded tocilizumab as a comparator because:

- it can only be used for up to 1 year
- the restricted duration of use has had led to lower than anticipated tocilizumab use in NHS clinical practice.

It did not think methotrexate was a relevant comparator because its clinical experts said that methotrexate use varies widely depending on healthcare professional judgement. The clinical experts at the committee meeting noted that tocilizumab is routinely used in NHS clinical practice for relapsed GCA. They also noted that, although there is limited evidence for methotrexate's effectiveness, it is still used in the NHS in some areas because there is no better alternative. The committee noted that, because tocilizumab and methotrexate are relevant comparators in relapsed GCA, it would need to consider relapsed GCA and the new-onset GCA subgroup separately. But, to capture the full pathway for the new-onset GCA subgroup, the modelling should also include what happens after relapse. The committee concluded that the relevant comparators are corticosteroids in the new-onset subgroup and corticosteroids, tocilizumab and methotrexate in the relapsed subgroup.

Clinical effectiveness

SELECT-GCA

3.4 The main clinical-effectiveness data for upadacitinib came from SELECT-GCA. This was a phase 3, randomised, double-blind, multicentre, placebo-controlled trial. It compared upadacitinib (15 mg) plus a 26-week

tapering course of corticosteroids (n=209) with placebo plus a 52-week tapering course of corticosteroids (n=112) in adults 50 years and over with active new-onset or relapsing GCA. Period 1 of the trial comprised a 52-week double-blind placebo-controlled phase. Period 2 was a 52-week blinded extension. It evaluated the safety and efficacy of continuing upadacitinib compared with stopping it in terms of maintaining remission in people who had remission in period 1. The primary endpoint of the trial was the proportion with sustained remission at 52 weeks. Other efficacy endpoints included:

- the proportion with sustained complete remission (defined as the absence of GCA signs and symptoms) from week 12 to week 52
- time to first GCA flare
- the proportion with at least 1 GCA flare up to week 52
- cumulative corticosteroid exposure.

SELECT-GCA period 1 results

3.5 Results for the intention-to-treat (ITT) population from the period 1 data showed that a greater proportion of people in the trial had sustained remission at week 52 in the upadacitinib arm (46.4%; 95% confidence interval [CI] 39.6 to 53.2) than in the placebo arm (29.0%; 95% CI 20.6 to 37.5). Also, a greater proportion of people had:

- sustained complete remission from week 12 to week 52 in the upadacitinib 15 mg arm (37.1%; 95% CI 30.5 to 43.7) compared with the placebo arm (16.1%; 95% CI 9.3 to 22.9)
- a corticosteroid-sparing effect with a reduction in cumulative corticosteroid exposure up to week 52 (1,615 mg; 95% CI 1,615 to 1,635) compared with the placebo arm (2,882 mg; 95% CI 2,762 to 3,253]).

The company also provided results from the trial for the new-onset and relapsed subgroups. New-onset GCA was defined as diagnosis of GCA within 8 weeks of baseline. Relapsing GCA was defined as active GCA

in a person who's corticosteroid taper had failed at least once. There was a statistically significant greater proportion of people with either new-onset or relapsing GCA that reached the primary endpoint of sustained remission at week 52 in the upadacitinib arm compared with the placebo arm. In the new-onset GCA group, 48.1% in the upadacitinib arm had sustained remission at week 52 compared with 32.2% in the placebo arm. In the relapsing GCA group, 42.3% had sustained remission at week 52 compared with 22.2% in the placebo arm. The committee concluded that upadacitinib improved GCA control compared with corticosteroids.

SELECT-GCA period 2 data

3.6 The company used data from period 1 of SELECT-GCA to inform its clinical- and cost-effectiveness results. The EAG noted that the time to first flare data included in the submission was limited to only 1 year. It thought that time to first flare data from period 2 would be useful to inform the longer-term extrapolation. The company noted that, in period 2 of the trial, participants whose GCA was in remission for at least 24 weeks were rerandomised to either continue upadacitinib or switch to placebo. It noted that this represented a different population from period 1, so period 2 data was not methodologically suitable for determining time to first flare across both periods. So, it thought that the data should not be used to inform model extrapolations. The committee noted that it understood the implications of the trial design. So, it asked the company to provide additional data from period 2 to enable robust modelling of parameters like time-to-flare extrapolations, treatment duration, stopping treatment and relapse rates.

Indirect treatment comparison

3.7 The company did not include any indirect treatment comparisons (ITCs) with tocilizumab because it did not think that tocilizumab was a relevant comparator for people in the relapsed-GCA subgroup (see section 3.3). The EAG did an ITC comparing upadacitinib (SELECT-GCA) and

tocilizumab (the GiACTA trial). The EAG used reported risk ratios and hazard ratios for outcomes for remission at 52 weeks, having at least 1 flare by week 52 and time to first flare. The results were presented for the ITT group, new-onset and relapsed subgroups. The results are confidential and cannot be reported here. But they suggested that there was no statistically significant difference between the clinical effectiveness of upadacitinib and tocilizumab. The EAG also compared the Kaplan–Meir (KM) plots from the ITT populations of both trials for time to first flare at 52 weeks. It noted that the KM plots of time to first flare at 51 weeks showed a larger benefit for tocilizumab compared with placebo than for upadacitinib compared with placebo. The EAG noted that that this was a large enough difference to suggest that clinical inferiority of upadacitinib compared with tocilizumab cannot be ruled out. It suggested that a more robust analysis would be helpful to determine the relative clinical effectiveness of upadacitinib. The committee asked the company whether it thought that an ITC with tocilizumab is technically feasible. The company noted that it had done and submitted an ITC with tocilizumab for other health technology agencies. This was because of different reimbursement arrangements in those countries compared with the NHS. The committee noted that the EAG did not have access to the data from SELECT-GCA that the company had, which would have enabled a more robust indirect comparison. Also, no comparison with methotrexate was done, which is a relevant comparator (see section 3.3). The committee asked the company to provide a more robust ITC analysis to compare upadacitinib with tocilizumab, which is technically feasible, and with methotrexate, if it is technically feasible.

Economic model

Company's modelling approach

3.8 The company presented a semi-Markov model structure in line with the model used in TA518. It compared upadacitinib with a 26-week corticosteroid taper and a 2-year treatment duration with placebo and a 52-week corticosteroid taper. The model consisted of 4 health states

representing GCA flare-related complications: pre-flare remission, flare, post-flare remission and death. The starting point in the model was in pre-flare remission. The transition from the pre-flare remission state to the flare state is informed by the secondary endpoint of time to first flare from SELECT-GCA. The company also provided cost-effectiveness results split into the subgroups of new-onset and relapsing GCA. The company chose a 1-week cycle length, a lifetime horizon and a model starting age of 71.1 years based on SELECT-GCA. The EAG noted that, in TA518, the model starting age was 73 years, which is the approximate mean age of GCA in the UK. So, the EAG updated its base case to include a starting age of 73 years. The committee concluded that the EAG's starting age was appropriate. It also noted that the overall model structure was appropriate for decision making.

Treatment sequencing

3.9 For the new-onset subgroup, the company compared upadacitinib with 26-week corticosteroid tapering with placebo with 52-week tapering. It did not allow switching on relapse to either upadacitinib (with a tapering course of corticosteroids or as monotherapy), tocilizumab or methotrexate. The company thought that modelling of treatment sequencing without robust individual patient data and comparative effectiveness risked producing misleading cost-effectiveness results. It added that the relapsing subgroup already captured the post-flare experience for relapses on corticosteroids alone. The EAG highlighted that there is data from the SELECT-GCA trial for time to first flare and time to subsequent flare for the new-onset subgroup. It also noted that the opinion of the EAG's clinical experts suggested that potentially around 40% of people with new-onset GCA will successfully taper their corticosteroids and not have another flare. This is in line with TA518, in which 30% to 50% of people did not have any flaring by 5 years based on longitudinal data. The EAG suggested that it could be useful to incorporate some treatment sequencing for this group.

The committee queried why some people stopped treatment in both arms of SELECT-GCA. It thought that people who stopped treatment in the trial in either the upadacitinib or placebo arms could have gone on to have tocilizumab. The clinical experts noted that, without robust evidence, it is difficult to give an indication of the appropriate proportions for who would go on to have different treatments on relapse. But they noted that, in clinical practice, people whose GCA relapses are offered tocilizumab and, if upadacitinib was available, could go on to have upadacitinib after tocilizumab treatment. The committee concluded that it wanted to see further exploration of treatment sequencing in the modelling. It clarified that this should include treatment with tocilizumab after relapse and treatment with upadacitinib after tocilizumab. The committee would also like to understand what subsequent treatments were available in SELECT-GCA.

Modelled treatment duration

3.10 In the company's base case, a 2-year treatment duration for upadacitinib was assumed, although longer durations of treatment were also explored. The marketing authorisation does not stipulate any stopping rule. The company stated it did not consider the 2-year treatment duration in the model a 'stopping rule', but instead reflected the likely duration of treatment in clinical practice. It added that treatment duration for GCA should be guided by disease activity, healthcare professional judgement and patient choice. The company thought that a formal stopping rule would prevent flexible treatments for people with GCA and should be avoided. The clinical experts agreed that more flexibility would be valuable to healthcare professionals to allow them to apply an individualised approach to the needs of people with GCA. The committee asked the clinical experts if, in practice, they would expect to be able to use upadacitinib indefinitely. The clinical experts noted that, ideally, some form of tapering schedule, like those used successfully in other countries for tocilizumab, could be implemented. The patient experts added that GCA relapses are unpredictable, and that they would welcome being able to

access treatment that has worked well for them in the past when needed.

The committee noted that, if the cost-effectiveness estimates were based on the costs of treatment stopping at 2 years in the model, the recommendations would need to reflect this. The committee was aware that stakeholder submissions had highlighted the stopping criteria in TA518 as a significant barrier to treatment. The stopping criteria were supported by people with GCA and healthcare professionals at the time the evaluation was done. But experience from using this drug in routine practice has highlighted that the 1-year treatment duration and the inability to restart treatment is a significant barrier to its uptake. The committee noted that data from SELECT-GCA, from periods 1 and 2, provided valuable information on treatment duration and stopping treatment, which the company had not used. The committee asked the company to:

- provide KM estimates for time to stopping treatment in SELECT-GCA
- use the data, with the appropriate adjustments when needed
- extrapolate treatment duration and stopping treatment
- provide data on restarting treatment in a proportion of people with GCA to be modelled.

Time to first flare in the new-onset subgroup

3.11 The company's base case for the new-onset subgroup selected Gompertz extrapolation curves to extrapolate time to first flare data for both upadacitinib and placebo. The company then applied placebo probabilities of flare in the upadacitinib arm for stopping treatment at 2 years. The company noted that its choice of extrapolation was based on healthcare professional feedback. It said that it thought that this was the most important consideration, given the uncertainties around extrapolating from short-term data. The EAG highlighted that, in TA518, expert opinion suggested that the Gompertz curve was too optimistic when modelling the placebo arm at 10 years. It thought that the log-normal at 10 years was appropriate. The EAG used the log-normal curve in its base case and

explored the generalised gamma curve in a scenario. The choice of curve had a large impact on the cost-effectiveness results in the new-onset group. The EAG also commented that, for both upadacitinib and placebo, the company's choice of curve showed little to no probability of flare from year 3. So, rather than there being a waning of effect, the treatment effect was maintained indefinitely. The EAG noted that its clinical expert's opinion was that upadacitinib is unlikely to be disease modifying. So, the upadacitinib curve should converge towards the placebo curve after stopping treatment at 2 years.

The clinical experts explained that there was too much uncertainty to determine whether upadacitinib is disease modifying. They also noted that the optimal treatment duration is not yet established. They explained that some people having corticosteroid treatment alone might remain in corticosteroid-free remission after tapering. So, an observed plateau might be reasonable in this situation. They estimated that around 40% of people would not have a flare. But they added that, for many people, corticosteroid tapering can trigger a flare or a period of instability in the control of GCA. The committee thought that, based on clinical judgement, there may be some clinical basis for a plateau in GCA that does not relapse. But it said that it had not been provided with robust long-term data to underpin this assumption. The committee questioned whether there was evidence to suggest that upadacitinib:

- increased the proportion of people reaching the plateau, or
- delayed the time it took for that proportion of people to reach the plateau.

The committee understood that corticosteroid use in people with GCA has been the mainstay of treatment for many years. So, there should be evidence available to underpin this assumption in the placebo arm. The committee asked the company for more evidence from its trial and the literature, with appropriate adjustments when needed, to underpin

its assumptions around its time to first flare extrapolations in the new-onset group.

Modelling of GCA flare-related complications

3.12 In the company's base case, risks of GCA flare-related complications were converted to weekly probabilities in line with the model cycle length. The company noted that, because these serious complications are rare and were not seen during SELECT-GCA, the risks were derived from the literature. The EAG suggested that some of the literature sources used by the company gave estimates for people with GCA in general. So the data may not have been specifically related to flares. It noted that its clinical expert opinion was that the rates of complications at presentation may be higher than at subsequent flares because of diagnosing pre-existing conditions. The EAG suggested that the rates of complications associated with flares in the relapsed subgroup during period 1 of SELECT-GCA could be used to improve accuracy when modelling GCA flare-related complications, as well as rates from other relevant literature sources. The EAG included a scenario analysis of a reduced risk of stroke-related complications of 50% and 20% of the company's base case. This had a moderate effect on the cost-effectiveness results.

The clinical experts noted that a diagnosis of GCA relapse is usually quicker than the first diagnosis because people are experienced in managing their GCA. This may reduce the risk of some of the more severe complications. But some complications, such as sight loss, can still occur in new-onset GCA if there are delays in diagnosis. The clinical experts noted that the EAG's scenarios around reducing the risk of complications of stroke seemed reasonable. The committee asked the company for more evidence from the literature for its modelling assumptions on GCA-related complications. It also asked the company to provide scenarios around a reduction in the risk of stroke-related complications of between 20% and 50% of the company's base case.

Source of corticosteroid-related complications

3.13 The company used a US-based health data base to determine rates of adverse events for corticosteroid use. The company noted that overall and corticosteroid-related adverse event rates in SELECT-GCA were low. This was likely because of the long-term nature of these adverse events, the controlled environment and the relatively short follow-up period (52 weeks). The company noted that the US-based health data base analysed data from 4,115 people with GCA having oral corticosteroid over an exposure period of 1 to 60 months. Follow up was up to 5 years and a minimum of 1 year. It also noted that the population characteristics were thought to be broadly reflective of UK clinical practice. This was based on clinical expert input it received as part of its submission. The EAG was concerned that there were large differences between the company's source of corticosteroid-related adverse event rates and those reported in SELECT-GCA.

The committee noted that the reduction in corticosteroid-related complications was the key model driver in the company's cost-effectiveness modelling. The committee noted that the rates of adverse events had come from the US health system, which is not comparable with the NHS in England. It thought that the company could have potentially found evidence for adverse event rates from comparable countries in the UK or EU. The committee concluded there was uncertainty around the company's choice of corticosteroid-related adverse event rate datasets. It asked the company to provide a more relevant data source to inform its adverse event rates from corticosteroid use. It also asked it to provide scenarios using SELECT-GCA data to inform corticosteroid-related adverse events. Method used to estimate cumulative corticosteroid burden

3.14 To estimate the cumulative corticosteroid burden, the company stratified people with GCA in the modelling into 4 risk groups based on their average daily corticosteroid dose. It then applied the rates of adverse

events to each risk group using the US-based health database data (see section 3.13). The EAG noted that it had several concerns with the company's approach:

- It took the rate of adverse events from the year of GCA diagnosis and applied it to subsequent years. The EAG did not think this approach was appropriate because it is likely that some people with GCA are diagnosed with pre-existing conditions rather than new corticosteroid-related complications.
- It assumed that a similar cumulative dose of corticosteroid in the year around diagnosis results in the same annual risk as the same dose built up over 20 years. The EAG did not think that the company had provided sufficient evidence that this relationship holds.
- The EAG noted that associating an increased risk of complications with the total cumulative corticosteroid dose since baseline may be reasonable for conditions in which the damage is permanent, such as osteoporosis. But it is less reasonable for adverse events that would likely subside once corticosteroids are stopped. The EAG's clinical expert identified several conditions such as gastrointestinal perforation, sepsis and sleep disorders that this may apply to. The EAG did a scenario analysis that revised the risks of these conditions to be dependent on the total corticosteroid dose of the previous year rather than the total corticosteroid dose since diagnosis. This had a large impact on the cost-effectiveness results.

The clinical experts noted that most of the issues they see in clinical practice relating to corticosteroid-related adverse events is from cumulative use. The committee agreed with the EAG that several assumptions relating to the reduction of adverse events from corticosteroids using upadacitinib lacked faced validity and were not based on evidence. The committee concluded that it wanted to see an updated company model. It said that this should use SELECT-GCA data, other validated sources (see section 3.13) and healthcare

professional judgement to model the impact of upadacitinib on corticosteroid-related adverse events.

Modelling differences

3.15 The EAG noted that it had found several errors relating to how the company had modelled corticosteroid- and GCA-related complications. So, it made changes to its preferred base case:

- The company's modelling of corticosteroid-related adverse events was based on the cumulative prior dose of corticosteroids, which was assumed to be 0 at baseline. The EAG's approach was to model the people with new-onset GCA with a baseline cumulative dose of 0 mg, and estimate baseline cumulative dose in people with relapsed GCA from average duration of diagnosis from SELECT-GCA. This had a small impact on the cost-effectiveness results.
- In the company's model, people not on corticosteroids during any cycle were assumed to have no risk of corticosteroid-related adverse events. The EAG thought that there is a background risk of developing certain conditions (for example, type 2 diabetes) and that this risk does not fall to zero risk for any patient population. The EAG corrected this in its base case, which had a large impact on the cost-effectiveness results.
- The EAG thought that the company's choice of retaining the 26-week corticosteroid tapering after a flare in the upadacitinib arm after stopping treatment at 2 years was incorrect. It preferred to switch to the 52-week taper modelled for the placebo arm. This resulted in a smaller reduction in the cumulative corticosteroid dose from upadacitinib. This was generally maintained over the lifetime of people with GCA rather than continuously increasing. This had a large impact on the cost-effectiveness results.
- The EAG noted that the company had not conditioned the mean corticosteroid dose for a model cycle by the proportion surviving, so it corrected for this. This had a small impact on the cost-effectiveness results.

- The EAG noted that the company had not weighted the cost of prednisolone by market share and corrected for this. This had a small impact on the cost-effectiveness results.
- The EAG thought that the company had overestimated the incidences of corticosteroid-related conditions because it did not take the prevalence of these conditions into account. This also included not taking into account the prevalence of the conditions at baseline.
- The EAG also thought the company's approach of taking annual incidence rates of complications of flares into weekly probabilities without adjusting the eligible population led to an overestimation of the rate of complications.

The company thought that the EAG's base-case modelling changes did not constitute errors in the company modelling but were EAG preferences. The committee agreed with the EAG that several assumptions relating to corticosteroid-related adverse events and GCA flare-related complications in the company's modelling lacked faced validity. The committee concluded that the EAG's model changes were appropriate. This is subject to structural changes that the company may make to address the committee's requests around sequencing of treatments. If these issues are superseded by new modelling, then the committee has asked the company to clearly explain this.

Utility values

Quality-of-life decrements

3.16 The company distinguished between transient and lifelong conditions relating to GCA flares and corticosteroid-related adverse events. For transient adverse events, the disutility was applied only in the model cycle in which the event occurred, specifically to people with GCA in the flare health state. The EAG noted that, because of the model cycle lengths, this implied that the duration of all these conditions is 1 year. It noted that clinical expert opinion suggested that, for, electrolyte disorders, sepsis and infections needing hospitalisation, the estimated duration is 1 month.

So, it updated this in its preferred base case. The EAG also noted that the duration was likely 6 months for fractures, palpitations, ulcers or gastrointestinal bleeds, gastritis, sleep disorders, bruising, skin thinning, impaired wound healing, Cushing's syndrome and hypertension. In the committee meeting, the company agreed that the EAG's changes to the duration of disutilities were valid. But it was still concerned that some transient utility effects were still assumed to last 1 year without any clinical justification. The clinical experts noted that several corticosteroid-related conditions are more common in older people in general, so the utility decrements applied may have been overestimated. The committee noted that some of the decrements lacked face validity, including those applied for prediabetes and dyslipidaemia. The company applied a transient disutility value for prediabetes but a lifelong value for hyperlipidaemia. The committee explained that conditions such as prediabetes and hyperlipidaemia do not have an impact on daily living unless they progresses to type 2 diabetes or a cardiovascular event. It also that the source of the disutility was not clear. So, it thought that the decrement was not appropriate. The committee concluded that the EAG's approach to the modelling of quality-of-life decrements was appropriate. But it noted that some of the transient effects were still assumed to last for 1 year. It said that there should be revisions, including for hospitalisation for adrenal insufficiency and hospitalisation for treatment of exacerbated diabetes. It also said that it would like to see an updated company model using revised and properly justified disutility values.

Costs

Frequency of rheumatology visits during corticosteroid tapering

3.17 The company said that the costs for managing GCA were derived based on weighted costs for each service and weighted weekly resource use for each health state. The company used estimates from TA518, which were based on a market survey in that technology appraisal. The EAG noted that the survey suggested that people generally needed to visit rheumatology outpatients monthly when tapering corticosteroids. The

company noted that monthly visits related to all healthcare visits considered in the economic modelling, including to rheumatology. EAG expert opinion suggested that 75% of people with GCA manage with fewer visits than this. It also suggested that the other 25% are more or less equally split between people needing slightly more visits and people needing monthly visits. This means that, during corticosteroid tapering, rheumatology visits take place about every other month. The opinion of the EAG's clinical experts indicated that visits could even be as little as once every 3 or 4 months. So, the EAG did a scenario analysis with the ongoing monitoring costs reduced by half. This had a moderate impact on the incremental cost-effectiveness ratio.

The clinical experts noted that, in UK clinical practice, the frequency of visits was likely to be lower than once a month in most cases, but that it depends on stage of GCA. They explained that visits may be more clustered in new-onset GCA, and may be monthly during tapering or a flare. But they said that, in remission, visits could be about every 2 to 3 months. They also added that, in practice, some monitoring is done by other means than a face-to-face clinic, such as telephone consultations. The patient experts also agreed that, in their experience, visits had been less frequent than once a month when they were not having a GCA flare. The committee concluded that there was uncertainty around the frequency of visits during initial, and after successfully completing, corticosteroid tapering. It concluded that, based on clinical expert opinion, visits every 2 months are appropriate. It also concluded that the company should capture that the nature of these visits is variable, depending on disease stage.

GCA-related complication costs

3.18 The company used NHS Reference Costs and published literature to estimate GCA-related complication costs. The EAG reviewed the estimates for costs relating to several conditions, including stroke, glaucoma, hypertension, type 2 diabetes, ulcers and gastrointestinal

bleeding, severe infections, dyspnoea, sleep disorders and major adverse cardiovascular events. The EAG updated the costs for these based on its own assumptions on resource use. The committee noted that several of the company's assumptions around GCA-related complication costs were not underpinned by evidence. The committee concluded that there was uncertainty in the company's GCA-related complication costs. It asked for more evidence to support the assumptions.

Cost-effectiveness estimates

Committee's preferred assumptions

3.19 The committee noted that its preferred assumptions were:

- including comparisons with tocilizumab and methotrexate (if feasible) in the relapsed subgroup (see section 3.3), and modelling the pathway after relapse in the new-onset subgroup
- using a model starting age of 73 years (see section 3.8)
- applying the EAG's modelling changes for assumptions relating to GCA flare- and corticosteroid-related complications (see section 3.15)
- modelling of the frequency of rheumatology visits every 2 months (see section 3.18).

Uncertainty in the cost-effectiveness estimates

3.20 The committee noted that, before it could establish a plausible cost-effectiveness estimate for upadacitinib, more evidence and analysis was needed for several assumptions in the company's model. It asked for the following analyses from the company:

- a more robust ITC using SELECT-GCA data (see section 3.7)
- further exploration of treatment sequencing after relapse (see section 3.9
- using data from SELECT-GCA to extrapolate treatment duration and stopping, and modelling on restarting treatment in a proportion of people with GCA (see section 3.10)

- more evidence supporting the company's choice of curve for extrapolating time to first flare in the new-onset placebo arm and using literature sources to underpin the treatment-waning and placebo-arm assumptions (see section 3.11)
- more evidence from the literature to support modelling assumptions about GCA-related complications and scenarios around reducing the risk of stroke-related complications (see section 3.12)
- an updated company model using SELECT-GCA data or other validated sources for the rates of adverse- and corticosteroid-related complications to further explore the impact of these assumptions (see section 3.13)
- updated modelling using revised quality-of-life disutility values about GCA flares and corticosteroid-related complications (see section 3.15)
- more evidence for the GCA complication-related costs used in the modelling to reduce the uncertainty (see section 3.17).

Other factors

Equality

3.21 The committee noted that GCA disproportionately affects older people because it is common in people 50 years and over. Also, the incidence of GCA increases in each subsequent decade. It is also more common in women than men. The committee heard that current treatment with tocilizumab is prescribed in specialist centres. People living in rural areas, frailer people or people with a disability may face challenges accessing these specialist centres. People on lower incomes may also be disproportionately affected by having to travel further distances to access treatment if upadacitinib was to be prescribed in specialist centres. The committee noted that issues of differences in GCA prevalence cannot be addressed in a technology appraisal evaluation. But the committee carefully considered the needs of the people who would have upadacitinib in clinical practice in its decision making.

Uncaptured benefits

3.22 The committee considered whether there were any uncaptured benefits of upadacitinib. It did not identify additional benefits of upadacitinib not captured in the economic modelling. So, it concluded that all additional benefits of upadacitinib had already been taken into account.

Conclusion

3.23 Because of the uncertainty in the clinical- and cost-effectiveness evidence, the committee was unable to establish a plausible cost-effectiveness estimate. It concluded that additional evidence is needed, so upadacitinib should not be used to treat GCA.

4 Evaluation committee members

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

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

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

Chair

Raju Reddy
Vice Chair, technology appraisal committee D

NICE project team

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

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