NICE National Institute for Health and Care Excellence

NICE guidance

Voclosporin with mycophenolate mofetil for treating lupus nephritis

Technology appraisal guidance
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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 Voclosporin with mycophenolate mofetil is recommended, within its marketing authorisation, as an option for treating active class 3 to 5 (including mixed class 3 and 5, and 4 and 5) lupus nephritis in adults. It is only recommended if the company provides voclosporin according to the commercial arrangement.

Why the committee made this recommendation

Treatment options for active lupus nephritis include immunosuppressants such as mycophenolate mofetil. There are several other immunosuppressant options depending on factors such as condition severity, previous treatments and other conditions such as organ damage.

Clinical trial evidence suggests voclosporin with mycophenolate mofetil is more effective at stopping lupus nephritis from getting worse than mycophenolate mofetil alone. Indirect comparisons suggest voclosporin with mycophenolate mofetil is more effective than other immunosuppressant options.

The most likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources. So, voclosporin with mycophenolate mofetil is recommended.

2 Information about voclosporin

Marketing authorisation indication

2.1 Voclosporin (Lupkynis, Otsuka) is indicated 'in combination with mycophenolate mofetil for the treatment of adult patients with active class 3, 4 or 5 (including mixed class 3/5 and 4/5) lupus nephritis'.

Dosage in the marketing authorisation

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

Price

2.3 Voclosporin costs £1,000 per 180-pack of 7.9 mg soft capsules (excluding VAT; company submission). Voclosporin costs £12,167 for 12 months of treatment. The list price of mycophenolate mofetil is £6.23 per 50-pack of 500 mg tablets (excluding VAT; BNF online accessed March 2023).

2.4 The company has a commercial arrangement. This makes voclosporin available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The evaluation committee considered evidence submitted by Otsuka, 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.

Clinical need

Nature of the condition

3.1 Lupus nephritis is a complication of systemic lupus erythematosus, a chronic condition that causes inflammation in connective tissues. It occurs in around 40% to 60% of people with systemic lupus erythematosus and affects the kidneys, specifically glomeruli cells. Clinical experts highlighted the high unmet need for people with lupus nephritis because the condition is not curable. The disease follows a cycle of relapsing and remitting. Some people develop end-stage renal disease if their condition does not respond to treatment and need dialysis or kidney transplants to survive. Lupus nephritis is a debilitating disease which significantly impacts the lives of people with the condition and those who care for them. Patient experts highlighted the most challenging aspects for people with lupus nephritis are the symptoms, reduced ability to work and impact on mental wellbeing. Patient experts explained that in a 2020 survey of 67 people with lupus nephritis, 81% reported fatigue as the most difficult symptom, followed by joint pain and swelling (60%). People with the condition explained how lack of energy makes every day a challenge. In the same survey 57% of people with lupus nephritis felt isolated once a week and 58% needed help with household care, while 33% needed help with personal care. Carers of people with lupus nephritis are significantly impacted because of helping with daily tasks and having less time to work and socialise. There is also constant anxiety about the health of people with lupus nephritis because of the lack of a cure and because of regular tests to monitor the condition. The committee also heard how carers feel helpless, especially when lupus nephritis symptoms are worse. Patient and clinical experts also explained how current treatments have significant adverse effects.

These side effects can cause other conditions that need separate treatment. They also severely impact quality of life and in some cases may affect adherence to dosing regimens. The committee concluded that lupus nephritis is a debilitating condition and there is high unmet need for effective treatments with manageable side effects.

Clinical management

Treatment options

3.2 Clinical and patient experts highlighted that lupus nephritis is a highly heterogeneous condition. This may result in considerable differences in treatment options because of varying needs and personal circumstances. Clinical experts explained that lupus nephritis rarely happens in isolation and that treatment choices depend on lots of other factors, including disease severity, previous treatments and comorbidities such as organ damage. They explained that lupus nephritis follows a cycle of relapsing and remitting, meaning treatments are used to either induce or maintain remission. They added that treatments varied only by the immunosuppressives taken with hydroxychloroquine and tapered doses of corticosteroids. The immunosuppressives used to induce remission include methylprednisolone with mycophenolate mofetil, low- and high-dose cyclophosphamide, rituximab with mycophenolate mofetil, and tacrolimus with or without mycophenolate mofetil. Maintenance treatments include mycophenolate mofetil, azathioprine and tacrolimus monotherapy. The committee concluded that the treatment options for lupus nephritis are highly heterogenous and are expected to frequently change based on disease response.

Treatment positioning of voclosporin

3.3 Clinical experts explained that voclosporin, a calcineurin inhibitor, would be an add-on treatment to mycophenolate mofetil and corticosteroids for treating lupus nephritis. The company highlighted that the marketing authorisation for voclosporin does not specify a treatment line. Clinical experts expressed uncertainty about how voclosporin would be used in clinical practice. Some experts agreed it would be used as a first-line

induction treatment or a later add-on treatment for people whose condition doesn't respond to mycophenolate mofetil alone, like in the AURORA trials (see section 3.4). Other experts suggested that voclosporin may be used hesitantly in the first line because of the lack of long-term evidence and that use after other treatments is more likely. The EAG explained that calcineurin inhibitors were usually used as later-line treatments. So, clinician hesitation would be expected for using voclosporin as a first-line induction treatment. But it said that mycophenolate mofetil alone was the most suitable comparator if voclosporin was to be used as a first-line treatment. It added that tacrolimus plus mycophenolate mofetil would be the most suitable comparator for later-line treatments. Clinical experts and the Innovative Medicines Fund clinical lead explained that voclosporin would be used to induce remission and not as a maintenance treatment. Clinical experts added that considering induction or maintenance treatment positioning is more appropriate than considering first-line and later lines of treatment. Lupus nephritis follows cycles of relapse and remission so a treatment previously used to induce remission could be considered a treatment option in the future. The company highlighted that voclosporin was used in the AURORA trials as a first- or subsequent-line induction treatment. So, mycophenolate mofetil alone or with tacrolimus are the most appropriate comparators. Stakeholder responses to draft guidance consultation also highlighted the use of voclosporin as an induction treatment. The committee considered that the AURORA trials only showed an ability to induce remission, but voclosporin's mechanism of action suggests maintenance use may also be possible. But it recalled clinical experts' opinion that voclosporin would be used to induce remission and not typically for more than 9 to 12 months, although it may be used again if it was effective at inducing remission. So, the committee concluded that voclosporin would be used to induce remission and not as a long-term maintenance treatment. Based on this, it identified mycophenolate mofetil alone or with tacrolimus as the most appropriate comparators (see section 3.2).

Clinical evidence

Pivotal clinical trials and outcome measures

3.4 The clinical evidence for voclosporin was from the phase 3 AURORA 1 and AURORA 2 trials. These were multicentre, double-blind, placebo-controlled randomised trials. AURORA 2 was a 24-month long-term continuation study for people who had completed the 12-month AURORA 1 study. People had voclosporin or placebo, plus mycophenolate mofetil and low-dose corticosteroids. The primary endpoint of AURORA 1 was complete renal response at 12 months, which was 40.8% for voclosporin and 22.5% for placebo. AURORA 1 recruited 357 people from 27 countries, 216 of whom also enrolled in AURORA 2. Clinical experts noted that complete renal response in the AURORA trials was a composite endpoint, comprising several measures. This included changes to the urine protein to creatinine ratio and estimated glomerular filtration rate, as well as the use of rescue medication and prednisone. Partial renal response depended only on changes to the urine protein to creatinine ratio. Clinical experts explained that changes in the urine protein to creatinine ratio do not always necessarily lead to meaningful long-term changes in the disease. They suggested using kidney biopsy results as an alternative measure of response but noted the practical challenges of doing kidney biopsies. Although the AURORA trials had some limitations, the committee concluded that they show voclosporin plus mycophenolate mofetil had clear clinical advantages over placebo plus mycophenolate mofetil in inducing renal response when measured by protein in the urine.

Generalisability of clinical trials

3.5 The EAG noted that the AURORA trials (see section 3.4) included no people from the UK, so generalisability to the NHS may have been limited. Clinical experts considered that the population included in the AURORA trials is reflective of the population seen in the NHS. However, clinical experts did question the generalisability of the AURORA trials because of the corticosteroid doses used. An expert highlighted that the doses were lower than recommended by guidelines and used in NHS

clinical practice. The EAG explained it had clinical advice that agreed the steroid use was lower than in clinical practice, but that the dose would still be effective and in line with clinical guidelines. It also noted that both treatment arms of the AURORA trials had lower-dose steroids. Patient and clinical experts emphasised that a key benefit of voclosporin is the potential ability to have lower-dose steroids. The reduced use of steroids is desirable because of reduced side effects, especially damage to the immune system. However, clinical experts raised concerns that some clinicians would not use lower steroid doses with voclosporin, like in the AURORA trials, and would use standard higher doses based on previous experience. At draft guidance consultation, some stakeholder responses highlighted that steroid use in clinical practice is similar to use in the AURORA trials. Others highlighted that while there is a trend towards using lower doses of steroids within the NHS, this is not yet standard clinical practice. The committee recalled that both treatment arms of the AURORA trials used lower doses of steroids than standard practice and that there was no direct evidence comparing voclosporin's use with higher and lower doses of steroids. The committee concluded that the AURORA trials are generalisable to the UK population but that the steroid doses used may not be reflective of established NHS clinical practice.

Attrition bias

3.6 It was noted that 39.5% of people from AURORA 1 did not enrol into AURORA 2. The committee was concerned with the possibility of attrition bias (that is, that discontinuation may not be random and there may be systematic differences between the population who discontinued AURORA 1 and the population who continued enrolment to AURORA 2). The EAG explained that the rate of and reasons for discontinuation were comparable across the trial arms, reducing the risk of bias. But the break in randomisation caused a high risk of bias in AURORA 2. It also noted that response outcomes significantly increased at 12 months and 18 months, caused by the switch from AURORA 1 to AURORA 2 data. In response to committee requests, the company provided scenario analyses that assumed different responses for people who did not enrol in AURORA 2. This included the following 3 scenarios which assumed:

- last observed response state carried forward

- people who had voclosporin plus mycophenolate mofetil were 'non-responders' and people who had mycophenolate mofetil had complete response
- people who had mycophenolate mofetil were 'non-responders' and people who had voclosporin plus mycophenolate mofetil had complete response.

The EAG commented that only the last observation carried forward assumption was appropriate because the other scenarios are highly unlikely in clinical practice. The committee acknowledged the efforts of the company to explore accounting for attrition bias in the AURORA 2 data. It noted that only the last observation carried forward scenario was likely to be clinically plausible and that this slightly reduces the cost-effectiveness estimates. The committee concluded that there was some remaining uncertainty about the impact of attrition bias. But, the company had done as much as could be reasonably expected and the provided scenarios had allowed enough exploration of the sensitivity of the results.

Network meta-analysis

3.7 Because of the lack of direct evidence comparing voclosporin plus mycophenolate mofetil with other relevant comparators besides mycophenolate mofetil, the company developed a network meta-analysis. The analysis included complete and partial renal response data for the treatment options outlined in section 3.2. Data was identified by a systematic literature review. The company's original base case included a fixed effects network meta-analysis. The company justified this approach because random effects network meta-analysis estimates were not converging. The EAG suggested implementing a random effects network meta-analysis using informative priors. This is because considerable variation across the included trials could lead to heterogeneity. The company provided a random effects analysis during technical engagement and explained that the fixed and random effect analyses produced similar results. Based on the committee's preference, the random effects network meta-analysis was implemented in the company's updated base case. This suggested that voclosporin plus mycophenolate mofetil was more effective than the comparators. The committee concluded that the network meta-analysis used in the company base case was appropriate but noted that heterogeneity across

the populations and included trial outcomes increased uncertainty of the results.

Economic model

Company's model structure

3.8 The company developed a cohort-level state-transition Markov model to estimate the cost effectiveness of voclosporin plus mycophenolate mofetil compared with relevant comparators. People were modelled to transition between 3 lupus nephritis-related chronic kidney disease (CKD) states (stages 1 to 3a, stages 3b to 4, stage 5) and death. People with stages 1 to 3a CKD could move between active disease, partial response and complete response substates. People with stages 3b to 4 CKD were only modelled in an active disease substate. People with stage 5 CKD could move between dialysis and kidney transplantation. During technical engagement, the company updated the model to allow disease progression from stages 1 to 3a to stages 3b to 4 CKD, apply consistent death costs, apply correct relative dosing intensity, and reassure the EAG of accurate model inputs and formulas. These changes were to align with some aspects of the EAG's preferred base case, but some issues remained. For instance, in the updated company base case, people with stages 3b to 4 CKD could not have a response in the model. In response to a committee request, the company provided scenario analyses allowing for 2.5% of people with stages 3b to 4 CKD to have a response (based on expert estimates). But the company did not implement the assumption in its base case. It explained that the impact on the cost-effectiveness estimates was small and that experts agreed assuming no response for this subgroup was reasonable. The EAG agreed that the scenario may only have a small impact. But, it also noted that clinical experts had agreed that the number of people who would have a response was not zero, and that this should be reflected in the company base case. The EAG also identified that transition probabilities were uncertain for voclosporin and mycophenolate mofetil. This is because transitions for AURORA 1 and AURORA 2 participants were derived by the 'count method', which is associated with limitations because of small sample sizes. The company explained that it attempted

to use alternative statistical methods to estimate transition probabilities, but the approaches provided unrealistic outcomes that did not match the trial data. The EAG acknowledged the company's efforts to reduce uncertainty and agreed with the company's explanation, but it noted that inherent uncertainties with the 'count method' remained. Other modelling issues included:

- The estimated proportion of people with stage 5 CKD who had kidney transplant was too high in the company's original base case. The EAG included a transplantation rate of 65% in its base case based on clinical advice. The company included this assumption in its updated base case, accepting the preference of the committee.
- Model transparency was raised as a key issue because the EAG found errors in the model (for example, with adverse event disutility calculations) and multiple instances of insufficient descriptions of calculations and sources of information. At the second committee meeting, the EAG considered that while the model lacked some flexibility to refer to previous treatment settings, overall model transparency had improved and the company had made changes to resolve concerns with model inputs.

  The committee noted that the company had satisfactorily explored the assumption that people with stages 3b to 4 CKD could not have a response in the model. It concluded that the cost-effectiveness estimates were insensitive to this assumption, and it was not a key uncertainty. The committee noted the company's model still had limitations because it lacked flexibility and prevented the EAG from implementing its preferred base case and cross-checking calculations in the model. However, the committee concluded that the uncertainty had been reduced after draft guidance consultation and model transparency had improved.

Modelling of costs

3.9 Modelled monitoring costs were raised as an issue by the EAG because the company excluded additional monitoring costs for voclosporin. This was inconsistent with the modelled costs for tacrolimus, the other calcineurin inhibitor in the model. The company suggested this is because voclosporin has a predictable pharmacokinetic and

pharmacodynamic relationship allowing for fixed dosing and no therapeutic drug monitoring, whereas tacrolimus has a complex and unpredictable pharmacokinetic profile that requires monitoring. The committee noted that the summary of product characteristics for voclosporin recommends careful monitoring of renal function. Clinical experts and the Innovative Medicines Fund clinical lead explained that this would be included within routine monitoring for lupus nephritis. They explained that tacrolimus needs therapeutic drug monitoring to confirm optimal dosing and renal toxicity. However, voclosporin does not need this extra monitoring. The committee concluded that extra monitoring costs for voclosporin were not appropriate because of the different monitoring requirements for tacrolimus and voclosporin. The EAG further raised modelled costs as a key issue because the company assumed no treatment discontinuation for non-trial comparators. The company explained this was because of a lack of evidence. Based on clinical expert input, the EAG considered this was a clinically implausible assumption. In response to a committee request, the company updated its base case to include treatment discontinuation for non-trial comparators by assuming discontinuation equal to voclosporin. The EAG preferred to assume discontinuation equal to mycophenolate mofetil in its base case. The committee noted the efforts of the company to include treatment discontinuation for non-trial comparators. The committee considered that there was uncertainty in determining treatment discontinuation of non-trial comparators. However, it concluded that the assumptions of the company and EAG did not have a significant impact on the cost-effectiveness estimates.

Long-term treatment effects

3.10 AURORA 1 and AURORA 2 data on voclosporin plus mycophenolate mofetil used in the company's model covered 3 years. So, the company used assumptions to extrapolate data for approximately 69 further years. To do this, the company assumed:

- long-term transition probabilities for treatments equalled the average transition probabilities for month 30 and month 36, combined with a treatment waning effect

- for active disease and partial response states, voclosporin plus mycophenolate mofetil transition probabilities equalled those of mycophenolate mofetil alone
- for complete response states, voclosporin plus mycophenolate mofetil transition probabilities equalled the average of voclosporin plus mycophenolate mofetil and mycophenolate mofetil alone
- transition probabilities for other comparators were the same as the active disease state.

The EAG expressed considerable uncertainty in using on-treatment short-term data to predict off-treatment long-term outcomes. It explained the uncertainty was likely to only be reduced with additional long-term data or clinical expert input. Submissions from stakeholders highlighted that a long-term treatment effect is an unproven assumption, but that short-term benefits can be predictive of improved longer-term outcomes. In response to the uncertainty, the company provided:

- additional scenario analyses that assumed no relative effect for voclosporin after 36 months

- evidence of external model output validity by comparing modelled outcomes to those reported in external literature. It claimed that the percentage of people with end-stage renal disease at 5 years and 10 years estimated by the model was comparable to figures reported in Tektonidou et al. (2016) and Gisca et al. (2021).

  The EAG agreed the comparisons with external literature to validate the model were reasonable, but noted high uncertainty in health states other than end-stage renal disease. This is because only literature reporting on end-stage renal disease, and not on other outcomes estimated in the model, was available. The EAG preferred to assume voclosporin plus mycophenolate mofetil and mycophenolate mofetil alone were equal based on the average transition probabilities for month 30 and month 36. But this functionality was removed in the company model during consultation. Because of this, the EAG was unable to implement its preferred base case, instead adopting a different approach. It assumed voclosporin plus mycophenolate and mycophenolate mofetil alone were equal for all health states. The EAG also recalled the efforts at multiple stages of this evaluation to explore different durations of treatment effect for voclosporin, including no relative effect after 36 months. But it reiterated that the key uncertainty was using short-term data to inform long-term transitions and outcomes, which could not be resolved in the current model and with current efficacy data. The committee determined that the long-term extrapolations could better reflect the relapsing and remitting nature of the disease. It would have preferred to see repeated uses of induction treatment reflected, instead of induction followed by maintenance treatment with other therapies for over 69 years. However, it acknowledged that modelling such extrapolations would be difficult to construct. The committee concluded that longer-term efficacy is difficult to establish and extrapolate from short-term data such as that used in the network meta-analyses, particularly when these are associated with heterogeneity (see section 3.6). It also recalled the lack of model flexibility for the EAG to implement its preferred base case (see section 3.8). The committee noted that if the EAG had been able to implement its preferred base case, the associated incremental cost-effectiveness ratios (ICERs) were expected to reduce. There is uncertainty with both the company's and EAG's approaches to the long-term treatment effect extrapolations.

Treatment duration

3.11 The company's model assumed treatment stops at 36 months, in line with the available AURORA data. The company explained that clinical experts supported this modelling assumption. The marketing authorisation for voclosporin does not specify a stopping rule but the summary of product characteristics recommends a risk–benefit analysis at 24 weeks. Clinical advice to the EAG also supported stopping treatment at 36 months in the model. The clinical experts explained that induction treatment with voclosporin is unlikely to be for 36 months. This is because the relapsing and remitting nature of the condition means treatment would be expected for about 9 months to 12 months. But retreatment with voclosporin to induce response would be expected and desirable in the future. In response to a committee request, the company provided scenario analyses for treatment durations of 12 months and 18 months for all treatments (when appropriate). The scenarios also adopted varying response assumptions to reflect the changing treatment duration. The EAG noted that the updated scenarios were helpful in reflecting different treatment durations but results were uncertain because retreatment was not included in the model. The committee noted the efforts of the company in providing scenario analyses that reflected different treatment durations. It considered that not including retreatment in the company's model was a key uncertainty but acknowledged the difficulties in doing so. It concluded that assuming treatment stops at 36 months was arbitrary because treatment discontinuation included in the model captured the treatment durations shown in the clinical trials. It noted that although the modelled treatment duration was 36 months, almost half of people who started voclosporin in AURORA 1 had stopped treatment by this point. This was more people still having treatment at 36 months than expected by clinical experts, who suggested treatment would last roughly 12 months. However, the committee also recalled that retreatment would be expected, meaning it was difficult to determine whether the model accurately reflected treatment durations expected in clinical practice. The committee concluded that modelling an accurate treatment duration was an uncertainty.

Cost-effectiveness estimates

Company and EAG cost-effectiveness estimates

3.12 The deterministic cost-effectiveness results include confidential prices for voclosporin and other treatments. Therefore, the exact results cannot be reported here. The company's deterministic base-case ICER for voclosporin plus mycophenolate mofetil against mycophenolate mofetil alone was within what NICE normally considers cost effective. The EAG's corresponding base-case ICER was also within what NICE normally considers cost effective. ICERs varied for other comparator treatments. The committee recalled that the main difference between the EAG's and company's base cases was the approach to extrapolating long-term treatment effects (see section 3.10). It recalled that voclosporin may be associated with additional benefits of lower steroid doses (see section 3.5 and section 3.13). However, it also considered that:

- without long-term data, both the EAG's and company's base cases were associated with uncertainty
- model functionality prevented the EAG from implementing its preferred base case (although this would likely decrease the ICERs)
- the model did not reflect likely retreatment with induction treatments, prompting uncertainty in the ICERs.

Given the level of uncertainty associated with the company's model and therefore the cost-effectiveness estimates, the committee determined that the maximum acceptable ICER was towards the lower end of the range normally considered a cost-effective use of NHS resources. The committee concluded voclosporin plus mycophenolate mofetil is likely a cost-effective use of NHS resources.

Other factors

Innovation

3.13 Clinical experts suggested that there may be potential uncaptured benefits within the company's model. They highlighted the significant impact of lupus nephritis and treatments on people's immune systems and fertility. In addition, they noted the potential use of voclosporin with lower doses of steroids (see section 3.5) would enable a reduction in the significant harmful effects associated with higher doses of steroids. Experts suggested that such benefits were not captured in the model because the comparator arm also used a lower dose of steroids. The committee recognised the lower dose of steroids used with voclosporin may be an uncaptured benefit but noted that there was some uncertainty around this (see section 3.5). It recalled that that there was no evidence comparing the use of voclosporin with higher and lower doses of steroids. It considered this in its discussion of the cost-effectiveness estimates (see section 3.12). The committee also considered whether voclosporin was innovative. It heard from clinical experts that voclosporin is not considered a step change in treatment for lupus nephritis. This is because other calcineurin inhibitors such as tacrolimus are already used in practice. So, the committee concluded that voclosporin was not innovative for treating lupus nephritis.

Equality issues

3.14 Patient and clinical experts identified that people with Indian Asian, African or Caribbean, and Chinese family backgrounds are more likely to have poorer outcomes with lupus nephritis. However, clinical experts also noted that there was no evidence to suggest voclosporin showed different effectiveness for different subgroups of people. The committee heard that women are disproportionately affected by lupus nephritis. It also heard from patient experts how current treatments such as cyclophosphamide can cause infertility or increase the risk of birth defects in a developing fetus. The committee was grateful for these issues being raised but noted that voclosporin is taken with mycophenolate mofetil and steroids. It recalled that mycophenolate

mofetil cannot be used during pregnancy and so this would also apply to voclosporin. However, it did note that voclosporin was unlikely to be associated with a risk of permanent infertility. So, it would provide an alternative option to treatments such as cyclophosphamide. The committee also noted that the differences in prevalence cannot usually be resolved in a technology appraisal, although the committee can consider whether a specific equality issue has a significant impact on access to treatment. Overall, the committee agreed that its recommendation would not have a different effect on people protected by the equality legislation than on the wider population. The committee concluded that there were no equality issues that would alter its recommendation.

Conclusion

Recommendation

3.15 The committee recalled the uncertainty associated with the company's model and long-term treatment effect estimations. It also acknowledged the efforts of the company to address some of the committee's concerns discussed in draft consultation guidance. It recalled that both the EAG's and company's base case were associated with uncertainty. But, plausible cost-effectiveness estimates were sufficiently low enough to be considered a cost-effective use of NHS resources. This means voclosporin plus mycophenolate mofetil is recommended for treating lupus nephritis.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation 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 guidance 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 draft guidance.

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 lupus nephritis and the doctor responsible for their care thinks that voclosporin plus mycophenolate mofetil is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

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

Dr Megan John
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 and a project manager.

Owen Swales
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