NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Mogamulizumab for previously treated mycosis fungoides and Sézary syndrome

1 Recommendations

1.1 Mogamulizumab is not recommended, within its marketing authorisation, for treating mycosis fungoides or Sézary syndrome in adults who have had at least 1 previous systemic treatment.

1.2 This recommendation is not intended to affect treatment with mogamulizumab 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

Standard care for mycosis fungoides or Sézary syndrome in people who have had at least 1 previous systemic treatment includes methotrexate, bexarotene, peginterferon and chemotherapy.

The clinical trial evidence is very uncertain because mogamulizumab is compared with vorinostat, a treatment that is not used or licensed in the UK. Also, many people switch treatments and there are a lot of differences among the trial population. Indirectly comparing the mogamulizumab trial evidence with evidence from patients having treatment in the NHS in England is also uncertain.

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Mogamulizumab does not meet NICE's criteria to be considered a life-extending treatment at the end of life. The most likely cost-effectiveness estimates are much higher than what NICE normally considers an acceptable use of NHS resources. So mogamulizumab cannot be recommended for routine use in the NHS.

Collecting further data is unlikely to address the clinical uncertainty because of the limitations in the trial design. So mogamulizumab cannot be recommended for use within the Cancer Drugs Fund.

2 Information about mogamulizumab

Marketing authorisation indication

2.1 Mogamulizumab (Poteligeo, Kyowa Kirin) is indicated for 'the treatment of adult patients with mycosis fungoides or Sézary syndrome who have received at least one prior systemic therapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of mogamulizumab is £1,329 per vial containing 4 mg of mogamulizumab per ml (excluding VAT; BNF online, accessed December 2020). The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee considered evidence submitted by Kyowa Kirin, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence.

Treatment pathway

People with mycosis fungoides or Sézary syndrome would welcome a new treatment option

3.1 Cutaneous T-cell lymphoma is a rare type of non-Hodgkin lymphoma that affects the skin. It includes mycosis fungoides, the most common type, and Sézary syndrome, which is closely related. The clinical experts explained that Sézary syndrome is an aggressive disease and prognosis tends to be poor. Both patient experts described how living with a scaly itching rash all the time significantly affects their health-related quality of life. Sleep is affected. Cracks and open wounds are common, particularly on the hands and feet, which limits the ability to walk and carry out daily activities. The clinical experts explained that the disease particularly affects people's appearance and people sometimes rely on carers to help with daily activities. They confirmed that the treatments recommended in the British Association of Dermatologists and UK Cutaneous Lymphoma Group guidelines after at least 1 systemic treatment were used in clinical practice. These included methotrexate, bexarotene, peginterferon and chemotherapy. The patient experts said that treatments such as chemotherapy had little benefit but mogamulizumab had a dramatic improvement. Mogamulizumab improved their itching and skin condition, so they could carry out daily activities more easily, and considerably improved their quality of life. The committee concluded that people with mycosis fungoides or Sézary syndrome who have had at least 1 systemic treatment before would welcome an additional treatment option.

The company proposes mogamulizumab for a subgroup of the population covered by the marketing authorisation

3.2 Mogamulizumab is indicated for treating mycosis fungoides or Sézary syndrome after at least 1 previous systemic treatment (see section 2.1). But the company proposed mogamulizumab as an option for a subgroup of the population covered by the marketing authorisation; that is, after at

least 1 systemic treatment for people with severe disease that has progressed with brentuximab vedotin or if it is not appropriate. Severe disease was defined as stage 2B and above for mycosis fungoides and all stages of Sézary syndrome. Brentuximab vedotin is recommended as an option for severe CD30-positive disease after at least 1 treatment (see NICE's technology appraisal guidance on brentuximab vedotin for treating CD30-positive cutaneous T-cell lymphoma). The committee understood that mogamulizumab would most likely be used as an option after 1 systemic treatment for CD30-negative disease and after 2 systemic treatments for CD30-positive disease. But it noted that brentuximab could also be used later in the treatment pathway. The clinical experts explained that around 15% to 20% of people have CD30-positive disease. They also confirmed that the company's proposed subgroup with severe disease was clinically relevant. The committee concluded that the company positioned mogamulizumab for a subgroup of the population covered by the marketing authorisation and it would account for this in its recommendations.

Standard care is the most appropriate comparator

3.3 The company originally submitted cost-effectiveness analyses which used clinical effectiveness data comparing mogamulizumab with vorinostat, a treatment that is not licensed or used in the UK (see section 3.4). In its revised base case after technical engagement, the company included the costs of having bexarotene alone for everyone in the standard care arm because it considered it to be the most commonly used NHS treatment for mycosis fungoides and Sézary syndrome. A clinical expert explained that triple therapy with bexarotene, extracorporeal photopheresis and peginterferon is used in clinical practice. But bexarotene alone would not generally be used, particularly for Sézary syndrome, because it was not effective. Another clinical expert suggested that chemotherapy may also be an option for people who were eligible for mogamulizumab. The committee considered that the company's approach may oversimplify a complex treatment pathway. The company also submitted clinical

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effectiveness data for standard care from the health episode statistics (HES) database, including other relevant treatments in the standard care arm. These included methotrexate, bexarotene, peginterferon and chemotherapy. Overall, the committee concluded that standard care was the most appropriate comparator.

Clinical evidence

There is no trial evidence comparing mogamulizumab with standard care so the relative treatment effect is uncertain

3.4 The clinical evidence for mogamulizumab came from MAVORIC, a phase 3, open-label randomised controlled trial. MAVORIC compared mogamulizumab with vorinostat in 372 adults with stage 1B to 4B relapsed or refractory mycosis fungoides or Sézary syndrome. There was no evidence directly comparing mogamulizumab with treatments currently used as NHS standard care (see section 3.3). In NICE's technology appraisal guidance on brentuximab vedotin for treating CD30-positive cutaneous T-cell lymphoma, the ALCANZA trial was used. It compared brentuximab with the physician's choice of treatment (methotrexate or bexarotene). The committee understood that:

- An anchored indirect treatment comparison using ALCANZA was not possible because there was no common treatment to connect the 2 trials.
- The population in ALCANZA was different to MAVORIC because people with Sézary syndrome were excluded, everyone had CD30-positive disease, and some had primary cutaneous anaplastic large-cell lymphoma (a subtype of cutaneous T-cell lymphoma).
- There was a high level of crossover in ALCANZA and the company did not have access to individual patient level data to calculate crossover-adjusted survival estimates for the comparator arm.

The company assumed that vorinostat was a suitable proxy for standard care in the NHS based on:

- similar progression-free survival to the physician's choice arm in ALCANZA
- clinical expert opinion and
- similar response rates to those seen in bexarotene clinical trials.

The ERG explained that if vorinostat and the physician's choice were similar, people in the physician's choice arm in ALCANZA would have longer progression-free survival and overall survival because they had less severe disease. However, overall survival for the physician's choice arm was shorter than with vorinostat. The clinical experts could not comment on vorinostat's clinical effectiveness because it is not available in the UK. However, they emphasised that mogamulizumab had been shown to be effective in delaying disease progression and improving quality of life both in the trial and in their clinical experience. The committee noted that:

- mogamulizumab improved progression-free survival in MAVORIC compared with vorinostat (hazard ratio 0.43, 95% confidence interval 0.31 to 0.58)
- the overall survival estimates were uncertain because MAVORIC was not powered to detect overall survival differences
- 72% of people in the severe disease subgroup crossed over from vorinostat to mogamulizumab, so crossover adjustment was needed (see section 3.8).

Overall, the committee was concerned about using these clinical effectiveness data because vorinostat was not licensed for use in the UK and did not represent NHS standard care. The committee considered that the evidence for mogamulizumab was limited and concluded that its relative treatment effect compared with NHS standard care was uncertain.

A reliable estimate of the relative treatment effect cannot be obtained using HES data

3.5 After consultation, the company submitted an unanchored indirect treatment comparison comparing mogamulizumab outcomes from MAVORIC with real world data from England's HES database. The HES data had been presented by the company at the first committee meeting and used to support it's preferred approach to extrapolating survival for the comparator arm from MAVORIC (see section 3.9). The committee noted that, unlike the MAVORIC data (see section 3.4), the HES analysis did not need any crossover adjustment. The committee noted that NICE Decision Support Unit technical support document 18 states that all effect modifiers and prognostic factors should be accounted for in an unanchored indirect treatment comparison. This is because 'failure of this assumption leads to an unknown amount of bias' in the comparison. It noted that the MAVORIC data were only matched to the HES data for the proportion of people with mycosis fungoides and Sézary syndrome. Age (a known prognostic factor) and sex (which can potentially affect survival) were not matched. This was because the company considered that these were similar between the MAVORIC and HES data and wanted to avoid reducing the sample size unnecessarily. The ERG explained that age and sex should have been matched and pointed out that differences in mean age increased by 2.5 years after matching. The committee was aware that several additional prognostic factors recognised in the literature and in a study by the Cutaneous Lymphoma International Consortium include:

- stage of disease
- levels of lactate dehydrogenase and
- large-cell transformation.

However, information on these and other prognostic factors were not available in the HES database and so could not be matched. The company considered that, in the HES database, people having systemic therapy had an Eastern Cooperative Oncology Group (ECOG) stage of 1

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or less and adequate haematological, liver, and kidney function. But no evidence to support this was provided. The ERG considered that insufficient information had been provided on the methodology of the unanchored indirect comparison to assess the reliability of the results. Overall, the committee recognised that the HES analysis addressed some of the issues with the original submission and commended the company on its efforts. But the limitations of the data, the lack of information on prognostic factors and the difficulty in assessing its reliability meant that the HES analysis results were uncertain. The committee was unable to draw a conclusion about the relative treatment efficacy of mogamulizumab compared with standard care based on this analysis.

The MAVORIC subgroup with severe disease is clinically relevant but the results create uncertainty

3.6 The company used clinical effectiveness data from a post hoc subgroup of 287 people with severe disease in MAVORIC to reflect its proposed positioning (see section 3.2). The committee recalled that severe disease was considered a clinically relevant subgroup. But it noted that in this subgroup it could not easily determine the proportion of people who had disease progression after brentuximab (CD30-positive disease) and those not eligible for brentuximab (CD30-negative disease). It was also concerned that the clinical effectiveness data included people at different stages in the treatment pathway and did not differentiate between mycosis fungoides and Sézary syndrome. It considered that this may not be appropriate given the differences in expected survival between the conditions. The committee would have liked to have seen separate analyses by disease type and line of treatment. It recalled that all analyses used vorinostat as a comparator, which did not represent NHS standard care (see section 3.4). Based on the evidence, the committee concluded that the MAVORIC subgroup with severe disease was clinically relevant. But using a mixed population, which grouped several lines of treatment together, created uncertainty. Also, MAVORIC did not compare mogamulizumab with a relevant comparator.

Economic model

The company's model structure is acceptable, but there is uncertainty in the data sources

3.7 In the company's partitioned survival model 3 different treatment pathways were modelled:

- people who did not have an allogeneic stem cell transplant
- people who had an allogeneic stem cell transplant after current treatment (that is, mogamulizumab or standard care)
- people who had an allogeneic stem cell transplant after subsequent treatment.

The company initially used clinical expert advice to estimate the proportion of people having an allogeneic stem cell transplant after current treatment because this was not allowed in MAVORIC. After consultation, the company used HES data (see section 3.5) for this proportion. The committee was aware that the estimated treatment effect in MAVORIC may have differed if allogeneic stem cell transplant had been allowed. It recognised that some people may have an allogeneic stem cell transplant in clinical practice. But in the model it preferred removing allogeneic stem cell transplant after current treatment, to avoid double-counting survival benefit in MAVORIC and to reduce potential bias. It understood that this had a small effect on the cost-effectiveness estimates. The company originally modelled standard care using MAVORIC clinical effectiveness data because it considered that vorinostat could be used as a proxy for standard care (see section 3.4). In its revised base case after technical engagement, the company preferred to use the costs of bexarotene alone for 48 weeks to represent the likely costs for people who have NHS standard care. After consultation, the company reverted to the ERG's preferred assumption of using the time on treatment for vorinostat and for relevant standard care treatments. In addition, clinical effectiveness data for the standard care arm were updated to reflect data from the HES

analysis (see section 3.5). The committee concluded that the company's economic model structure was acceptable, but reiterated the uncertainty associated with the available data sources.

Overall survival

The crossover adjustment results for MAVORIC represent the upper and lower range of plausible overall survival in the standard care arm

3.8 In MAVORIC, 72% of people in the severe disease subgroup crossed over from vorinostat to mogamulizumab after disease progression. Therefore, overall survival in the vorinostat arm was heavily confounded. Both the company and ERG agreed that:

- an adjustment was needed to estimate what would have happened in the comparator arm if there was no crossover
- the rank preserving structural failure time model suggested that survival with vorinostat was longer than with mogamulizumab and this was not clinically plausible.

The company preferred the inverse probability of censoring weights (IPCW) method to adjust for crossover because:

- it produced estimates in line with the company's clinical expert advice
- it also accounted for a potential post-progression benefit of mogamulizumab
- the company considered the results to be consistent with HES data and observational studies.

The ERG preferred the 2-stage estimation method to adjust for crossover. It noted that both methods provided estimates that were in line with external data, but significant differences in overall survival estimates between the different external data sources limited any comparisons. The ERG explained that there was bias and substantial uncertainty associated with both approaches and that the estimates of treatment effect varied

widely (exact data are considered confidential by the company and cannot be reported here). The committee was not convinced that the IPCW-adjusted curve was clinically plausible for the average person in the modelled population with severe disease. It understood that the 2-stage estimation adjusted curve showed better survival in the comparator arm, which led to higher cost-effectiveness estimates. The company did not consider the 2-stage estimation method to be plausible, because the analysis showed higher survival estimates than the HES data. Also, it suggested that the long-term predictions using the 2-stage estimation adjusted curve did not account for the potential disease-modifying effect of mogamulizumab. This was because the modelled survival benefit was longer in the comparator arm than in the mogamulizumab arm for people with disease progression after current treatment was stopped, which it considered to be implausible. The ERG questioned whether the main survival benefit of mogamulizumab would be gained when people were on subsequent treatment. It emphasised the lack of evidence to support the disease-modifying effect of mogamulizumab. One patient expert described how their symptoms slowly returned after mogamulizumab was temporarily stopped for around 12 weeks. After consultation, the company suggested that the HES data analysis supported use of the IPCW method. However the ERG commented that the HES analysis, with matching of MAVORIC results based on only 1 variable, was not robust enough to reach this conclusion. The committee was not convinced that mogamulizumab provided a prolonged benefit after disease progression and could be considered disease-modifying. It recognised that the choice of crossover adjustment had a large effect on the cost-effectiveness results. The committee concluded that the results from the 2-stage estimation and IPCW methods represented the upper and lower range of plausible overall survival in the standard care arm.

The ERG's preferred exponential curve for both treatment arms in the MAVORIC analysis is acceptable for decision making

3.9 Alongside the company's preferred IPCW crossover adjustment, it chose a lognormal curve to extrapolate overall survival in the mogamulizumab arm and applied an exponential curve to the standard care arm. The ERG explained that with the company's preferred IPCW crossover adjustment, the exponential curve provided the best statistical fit for the mogamulizumab arm. The committee agreed that the company would need to make a strong case to justify using different parametric curves in each treatment arm. The company explained that:

- based on visual inspection, a lognormal curve provided a better fit to the first half of the curve when more data were available
- it also used observational data to validate the survival predictions from its preferred model
- the HES data were closest to the data from the subgroup with severe disease in its proposed positioning.

But it noted that the HES data only included people who had 1 treatment, and only a small number of them had Sézary syndrome. The ERG preferred to use the 2-stage estimation crossover adjustment and applied an exponential extrapolation for both treatment arms because this gave the best statistical fit. The committee understood that MAVORIC was not powered to estimate differences in overall survival, the data were immature and there was a high level of crossover. Therefore all extrapolations were uncertain. The committee was not convinced that mogamulizumab provided an overall survival benefit compared with standard care. It concluded that the ERG's preferred exponential curve for both treatment arms was acceptable for decision making.

All extrapolations for the HES analysis are uncertain, but the company's approach is acceptable for decision making

3.10 After consultation the committee considered the company's additional HES analysis (see section 3.5), which had been reviewed by the ERG. The company and ERG both chose the exponential curve for the mogamulizumab arm because it was the best statistical fit. However, for the standard care arm, the company also preferred the exponential curve, whereas the ERG preferred the lognormal curve. The committee noted that the generalised gamma curve was the best statistical fit for the standard care arm. However both the company and ERG agreed that this curve was not clinically plausible. The company explained that the lognormal curve (the second-best fit) was also not clinically plausible for the standard care arm because:

- it crosses the mogamulizumab curve
- It predicts that a slightly higher proportion of people on standard care will survive after 30 years than people having mogamulizumab
- it predicts that 21% of people are alive at 5 years.

The committee recalled that using different extrapolations in each arm needs strong justification. It concluded that both extrapolations are associated with uncertainty, however the company's approach was acceptable for decision making.

A 2-year stopping rule is not appropriate

3.11 The company included a 2-year stopping rule for mogamulizumab in its revised base case. There was no evidence to support a stopping rule because it was not included in either the summary of product characteristics or the MAVORIC trial. The committee understood that the estimated treatment effect could have differed if a stopping rule had been used. The company suggested that the treatment effect was unlikely to differ substantially because in MAVORIC only a small proportion of people had mogamulizumab after 2 years (the data are confidential and cannot

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be reported here). The committee recalled that it was not convinced that mogamulizumab was disease-modifying (see section 3.8) or that there would be a prolonged treatment benefit after stopping treatment. Before technical engagement 1 clinical expert suggested that a 2-year stopping rule would not be appropriate if people were still benefitting from treatment. At the committee meeting the clinical experts explained that treatment would not normally be stopped if it was tolerated and there was an ongoing clinical benefit. The patient experts said they would feel distressed if mogamulizumab was stopped at 2 years, leaving them without any effective treatment options. The committee concluded that a 2-year stopping rule was not appropriate.

Utility values

The company's approach to modelling carer health-related quality of life is not appropriate

3.12 The committee recalled that people with this condition sometimes rely on help from informal carers (see section 3.1). The committee noted that some people would have help from district nurses (for example, with wound dressing). Also, costs for community-based care including home visits, skin and wound care and dressings were included in the model. The company's base case modelled the effect of caring on the health-related quality of life of carers by applying an additional utility gain of 0.19 when a person is in the disease control health state. This was the difference between the direct estimates of carer's health-related quality of life when caring for someone in the disease control (0.56) and subsequent treatment states (0.37) from the company's vignette study. Therefore, only the additional time a person spent in the disease control state after having mogamulizumab compared with standard care contributed to improving carer's health-related quality of life. After consultation, the company submitted 2 scenarios for carer utilities, in which:

- the difference between carer utilities for the disease control and subsequent treatment health states was the same as the difference seen for the people in the trial (0.09)
- absolute values for disease control and subsequent treatment states were used to show that the base case reflected a conservative approach.

The committee considered that the company's approach was not robust because the utility gain in the base case for carers was implausibly large compared with the expected utility gain for people with the condition. It recognised that there was a lack of detailed methodology on how to model carer utility. But it noted that the company used vignettes in the general population, which was not in line with NICE's guide to the methods of technology appraisal. The committee also did not consider it acceptable that the difference between carer utilities for the disease control and subsequent treatment health states would be the same as the difference seen for the people in the trial. This was because this was an unvalidated assumption, with no supporting evidence. Overall, the committee was not convinced that the company's approach to modelling carer utility values was appropriate. So it preferred to remove them from the base-case analysis but recognised the burden placed on some carers.

End of life

Mogamulizumab is not considered to be a life-extending treatment at the end of life

3.13 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's guide to the methods of technology appraisal. At the first meeting, using MAVORIC data with the company's preferences, the model predicted a median survival of 21 months and a mean survival of 37 months in the standard care arm. The committee's preferred assumptions (see section 3.15) predicted a mean survival of between 33 months and 59 months in the standard care

arm depending on if an IPCW or 2-stage estimation crossover adjustment was used. The company also submitted HES data, which showed a median overall survival of around 1.3 years for people who have had 1 treatment (see section 3.9). After consultation, the company submitted an updated HES analysis (see section 3.5) and considered that the end of life criteria had been met. The committee recognised that median life expectancy based on the new HES analysis (17.83 months) was less than 24 months. However, it noted that the mean extrapolated discounted and undiscounted life years in the standard care arm of the cost-effectiveness model based on the HES data were 2.87 and 3.31 years, respectively. Also, the committee was aware of a study by the Cutaneous Lymphoma International Consortium. In this, median overall survival for people with advanced mycosis fungoides and Sézary syndrome was 63 months. The committee accepted that there may be differences compared with the HES population. However, it also noted that the people in the study were from specialist centres so the large difference in survival compared with the HES analysis was concerning. More information on important prognostic factors was available in this data than in the HES data aiding interpretation. The committee also recalled that in the professional organisations' response to technical engagement, median survival for people with disease stage 2B and above eligible for second-line treatment in the NHS was estimated to be between 3 to 5 years. The committee noted that NICE's guide to the methods of technology appraisal states that the appraisal committee must be satisfied that:

- the assumptions used in the reference case economic modelling are plausible, objective and robust and
- the estimates of the extension to life are sufficiently robust.

The committee recognised that there was potential value in real-world evidence from the NHS in England to help inform its decision making. However, the committee was concerned about the differences between the median overall survival results from the HES analysis and the mean

results produced when it is used in the model. The cost-effectiveness results and decisions are based on mean quality-adjusted life years and costs. The committee also recalled that it was difficult to assess the reliability of the HES data (see section 3.5). Other sources of data such as that from the Cutaneous Lymphoma International Consortium, the model outputs using the trial data and professional organisation submissions all suggested survival is longer than 24 months. Overall, the committee was not convinced there was robust evidence that the short life expectancy criterion had been met. It concluded that mogamulizumab could not be considered a life-extending treatment at the end of life.

Cost-effectiveness estimate

Because of the uncertainty an acceptable ICER is no higher than the middle of the range normally considered cost effective

3.14 NICE's guide to the methods of technology appraisal notes that above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted the high level of uncertainty associated with the MAVORIC analysis, specifically:

- The relative treatment effect of mogamulizumab compared with NHS standard care was uncertain because MAVORIC did not include the most appropriate comparator (see section 3.4).
- The company's preferred subgroup was limited because it included a mixed population in a single post hoc analysis (see section 3.6).
- There was a high level of crossover, adjustments were potentially biased and the methods produced a wide range of estimates of treatment effect (see section 3.8).

- The overall survival data were immature. Also, overall survival was not a primary endpoint in MAVORIC so the trial was not powered to estimate differences (see section 3.9).

Although the HES analysis addressed some of the issues associated with MAVORIC (for example, comparator and crossover adjustment), the committee noted it was also associated with uncertainty. It recalled that the ERG could not assess the reliability of the HES analysis and because of data limitations, only 1 prognostic factor had been matched (see section 3.5).

Therefore, it agreed that an acceptable ICER would be no higher than the middle of the range normally considered a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

All cost-effectiveness estimates are uncertain but are higher than the middle of the range normally considered cost effective

3.15 The company's updated base-case ICER for mogamulizumab compared with standard care was £31,030 per QALY gained, including the commercial arrangement for mogamulizumab. The company's base case included clinical effectiveness data from the unanchored matching-adjusted indirect comparison using real world data from the HES analysis and reweighted MAVORIC data. It also included carer health-related quality of life. Excluding these increased the ICER to £33,043 per QALY gained. The ERG preferred the original MAVORIC analysis compared with vorinostat for its base case. The committee considered both methods to be associated with uncertainty and so considered ICERs from both approaches for its decision making. It understood that after taking into account all of its preferred assumptions, the most plausible ICER was £33,043 per QALY gained based on HES data and between £42,812 and £80,555 per QALY gained based on MAVORIC data. For the MAVORIC analysis, the lower ICER reflected the IPCW adjustment method, which the committee considered to be potentially clinically implausible. The

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higher ICER reflected the 2-stage estimation method, which it considered may be overly pessimistic. The committee understood that there was a small effect on the ICERs when including the commercial arrangement for bexarotene (data are confidential so cannot be reported here). It noted the substantial uncertainty in all the cost-effectiveness estimates. The committee concluded that, based on its preferred assumptions, all ICERs were much higher than the middle of the range normally considered cost effective. So mogamulizumab could not be recommended for routine use in the NHS.

Cancer Drugs Fund

Mogamulizumab does not meet the criteria to be considered for inclusion in the Cancer Drugs Fund

3.16 Having concluded that mogamulizumab could not be recommended for routine use, the committee then considered if it could be recommended for treating mycosis fungoides and Sézary syndrome within the Cancer Drugs Fund. The committee discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting NICE's Cancer Drugs Fund methods guide (addendum). The committee noted that:

- The company had not expressed an interest in mogamulizumab being available through the Cancer Drugs Fund.
- The most plausible ICER, including all the committee's preferred assumptions, was at least £33,043 per QALY gained and could be as high as £80,555 per QALY gained. The committee considered that even the lower ICER was much higher than the middle of the range normally considered cost effective, so there was no plausible potential to satisfy the criteria for routine use.
- The key uncertainty relates to the crossover adjustment and extrapolation of overall survival in the standard care arm. Data to

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resolve this uncertainty could not be collected as part of the Cancer Drugs Fund.

The committee concluded that mogamulizumab did not meet the criteria to be considered for inclusion in the Cancer Drugs Fund.

Innovation

Mogamulizumab has an innovative mechanism of action but all benefits can be adequately captured in the model

3.17 The company considered mogamulizumab to be innovative because there are limited effective treatment options for people with severe disease who have had at least 1 systemic treatment. The company emphasised the importance of improved health-related quality of life for this disease, which causes lesions that affect people's appearance. The committee recalled this, the reported benefits in improving symptoms and the burden on carers. It also noted that mogamulizumab has an innovative mechanism of action. The committee recognised that using its preferred assumptions, carer utility values had not been included in the model. But it noted that all cost-effectiveness estimates, even those including a carer utility gain in the model, were much higher than the middle of the range normally considered cost effective. The committee concluded that the relevant benefits associated with mogamulizumab could be adequately captured in the model.

4 Review of guidance

4.1 The guidance on this technology will be considered for review 3 years after publication. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

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Stephen O'Brien
Chair, appraisal committee
February 2021

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 D.

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.

Abitha Senthinathan and Fatima Chunara
Technical leads

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