NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final draft guidance

Epcoritamab for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic treatments

1 Recommendations

1.1 Epcoritamab is recommended as an option for treating relapsed or refractory diffuse large B-cell lymphoma (DLBCL) in adults after 2 or more systemic treatments, only if:

- they have had polatuzumab vedotin, or if polatuzumab vedotin is contraindicated or not tolerated, and
- the company provides epcoritamab according to the commercial arrangement (see section 2).

1.2 This recommendation is not intended to affect treatment with epcoritamab 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

Usual treatment for DLBCL after 2 or more treatments is rituximab-based chemoimmunotherapy, polatuzumab vedotin with bendamustine plus rituximab (polatuzumab-BR), or axicabtagene ciloleucel. People have rituximab-based chemoimmunotherapy or axicabtagene ciloleucel if they have already had polatuzumab vedotin.

Issue date: January 2024

© NICE 2024. All rights reserved. Subject to Notice of rights.

Epcoritamab has not been directly compared with usual treatment in a clinical trial. An indirect comparison suggests that people having epcoritamab live for longer than people having rituximab-based chemoimmunotherapy, but the results are uncertain. It is not clear from indirect comparisons if people having epcoritamab live longer or have longer before their cancer gets worse than people having polatuzumab-BR or axicabtagene ciloleucel.

The most likely cost-effectiveness estimates for epcoritamab compared with rituximab-based chemoimmunotherapy and axicabtagene ciloleucel are within what NICE normally considers an acceptable use of NHS resources. Because of their similar clinical effectiveness, only the difference in cost between epcoritamab and polatuzumab-BR was considered, and epcoritamab is more expensive. So epcoritamab is recommended, but only for people who have had treatment containing polatuzumab vedotin, or if polatuzumab vedotin is contraindicated or not tolerated.

2 Information about epcoritamab

Marketing authorisation indication

2.1 Epcoritamab (Tepkinly, AbbVie) is indicated for 'adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for epcoritamab 4-mg/0.8 ml concentrate for solution for injection and epcoritamab 48-mg solution for injection.

Price

2.3 The list price for epcoritamab is £6,568 per 48-mg vial and £547.33 per 4-mg vial (excluding VAT; company submission).

2.4 The company has a commercial arrangement (simple discount patient access scheme). This makes epcoritamab available to the NHS with a

© NICE 2024. All rights reserved. Subject to Notice of rights.

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 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.

Clinical need and treatment pathway

Evolving treatment pathway

3.1 At the time of this evaluation, there have been several recent changes to the treatment pathway for relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after 2 or more systemic treatments. Polatuzumab vedotin in combination with rituximab, cyclophosphamide, doxorubicin and prednisolone (polatuzumab R-CHP) has recently been recommended for untreated DLBCL (NICE technology appraisal guidance 874). So its use earlier in the treatment pathway has increased, which is likely to lead to a reduction in the use of polatuzumab vedotin with bendamustine plus rituximab (polatuzumab-BR; NICE technology appraisal guidance 649) at later stages of treatment. Additionally, axicabtagene ciloleucel, a chimeric antigen receptor T-cell (CAR-T) therapy, is used after 2 or more treatments (NICE technology appraisal guidance 872) and is available in the Cancer Drugs Fund (CDF) after first-line chemoimmunotherapy (NICE technology appraisal guidance 895). At the time of the second committee meeting, glofitamab, which has a similar mechanism of action to epcoritamab, had been recommended (NICE technology appraisal guidance 927). An evaluation of loncastuximab tesirine in the same indication was also underway. The committee concluded that the treatment pathway has changed rapidly and that this would be considered in the decision-making process.

© NICE 2024. All rights reserved. Subject to Notice of rights.

New treatment option

3.2 DLBCL is an aggressive type of cancer. Symptoms usually develop rapidly and progress quickly. Treatments aim to cure DLBCL, but in many people, it is refractory to treatment, or it relapses after initial treatment. Patient and clinical experts highlighted the need for more treatment options after 2 or more treatments, because of the relapsing nature of DLBCL and the limited number of available options. They explained the significant impact that DLBCL has on quality of life for both people with DLBCL and their carers. The patient and clinical experts advised that the available treatments all have limitations. Although there are a number of CAR-T centres in the UK, another option such as epcoritamab would be useful for some people; these include people whose disease is rapidly progressing, people who live a long way from a CAR-T therapy centre, and those who do not want to be separated from their families for the duration of their treatment and monitoring. The clinical experts noted that bispecific antibodies such as epcoritamab can be administered in the outpatient setting in non-CAR-T centres and this can improve access to treatment. Epcoritamab is the only subcutaneous treatment currently available. The clinical and patient experts noted that this could improve access to treatment compared with other treatments such as CAR-T therapies because it can be delivered in a day setting. This can be particularly useful for people who would like to avoid longer stays in hospital to avoid potentially catching other illnesses. The clinical expert noted that epcoritamab needs less hospital time and is easier to deliver because it does not need a cannula to be put in, unlike current treatments. But they noted that epcoritamab is taken until progression or unacceptable toxicity, rather than for a fixed number of cycles, which some people may find burdensome. Rituximab-based chemoimmunotherapy (R-based CIT) can be debilitating because of its side effects, and the time needed to administer the treatment can interfere with everyday life. The committee concluded that there is an unmet need

© NICE 2024. All rights reserved. Subject to Notice of rights.

in this population and that epcoritamab offers a potential new treatment option after 2 or more treatments.

Comparators

3.3 The committee noted that treatment options for relapsed or refractory DLBCL after 2 previous systemic treatments depend on which treatments the person has previously had and whether they are eligible for CAR-T therapy. After 2 or more previous treatments, the available options at the time of this evaluation were:

- polatuzumab-BR (see NICE's technology appraisal guidance on polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma)
- axicabtagene ciloleucel (see NICE's technology appraisal guidance on axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal large B-cell lymphoma after 2 or more systemic therapies)
- pixantrone (see NICE's technology appraisal guidance on pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma)
- R-based CIT regimens.

The company used R-based CIT as the comparator for people who cannot have or choose not to have intensive treatment ('population A') and axicabtagene ciloleucel for people who can have intensive treatment ('population B'). Intensive treatment was defined as either an autologous stem cell transplant or CAR-T therapy. The company did not consider polatuzumab-BR a relevant comparator in the third line but did a scenario analysis in population A with polatuzumab-BR as a comparator. This was because polatuzumab vedotin is now being used in untreated disease as part of polatuzumab R-CHP (see section 3.1) and would not likely be used again. The company's clinical experts had noted that, by approximately February 2025, they would expect less

© NICE 2024. All rights reserved. Subject to Notice of rights.

than 5% of people to be having polatuzumab-BR as third-line treatment. A clinical expert at the committee meeting agreed with this, and noted that bendamustine is often avoided because it might reduce CAR-T therapy efficacy in a later line. The EAG considered that polatuzumab-BR was a relevant comparator because its clinical experts noted it will still be an option for some people. The clinical experts and the NHS England CDF clinical lead advised that axicabtagene ciloleucel and polatuzumab-BR are still relevant comparators after 2 or more treatments, despite their increasing use at earlier stages of treatment. Additionally, they advised that some people would have R-based CIT because of not being eligible for axicabtagene ciloleucel or polatuzumab-BR. The company did not consider pixantrone a relevant comparator because it is rarely used in clinical practice; this was confirmed by the clinical experts during the first meeting. The committee noted that NICE had very recently recommended glofitamab, but it could not be considered a comparator because it was not yet routine clinical practice. A clinical expert noted that while the treatment pathway previously depended on eligibility for intensive treatment, it now depended on time to relapse after initial treatment because of the introduction of more treatments that are easier to deliver. At consultation, Gilead, the company representing axicabtagene ciloleucel, questioned if it was appropriate to consider separate analyses based on eligibility for intensive treatment (for example, population A or population B) because axicabtagene ciloleucel is recommended for relapsed or refractory disease after 2 or more systemic therapies. It noted that people with an Eastern Cooperative Oncology Group (ECOG) performance status of 2 (ECOG 2) may be considered eligible for axicabtagene ciloleucel in the UK. The EAG considered the division into these analyses appropriate, noting that people with an ECOG performance status of 2 were not excluded from population B. The committee concluded that although the pathway is changing quickly, axicabtagene ciloleucel,

© NICE 2024. All rights reserved. Subject to Notice of rights.

polatuzumab-BR and R-based CIT are the relevant comparators after 2 or more systemic treatments.

Clinical evidence

Data sources

3.4 Clinical evidence for epcoritamab came from the expansion part of an ongoing single-arm, phase 1 to 2 trial (EPCORE TM NHL-1) collecting data on 3 cohorts of people having epcoritamab. One of the cohorts included adults with DLBCL and other types of large B-cell lymphoma (LBCL) that had relapsed after, or had not responded to, at least 2 previous systemic treatments, and was included in the submission. The EAG noted that EPCORE TM NHL-1 only included people with ECOG scores of 0 to 2, and people who were ineligible for an autologous stem cell transplant or for whom the transplant failed, but the decision problem was broader than this. The EAG's clinical expert noted that most people who would have epcoritamab in clinical practice would have ECOG scores of 0 to 2. But, the clinical expert preferred not to exclude people with higher ECOG scores. Clinical experts at technical engagement noted that approximately 5% to 10% of people eligible for epcoritamab will have an ECOG score of 3. They also noted that most people who are eligible for epcoritamab will be ineligible for an autologous stem cell transplant. The clinical experts considered that a high proportion of people in the trial had complete remission of disease with epcoritamab (the company considers the exact figures confidential so they cannot be reported here). The committee concluded that the study was broadly generalisable to clinical practice and the results were promising.

Indirect comparison

3.5 There were no trials directly comparing epcoritamab with any of the comparator treatments. So, the company did an indirect treatment comparison against each comparator, in which data from the pivotal epcoritamab trial, EPCORE TM NHL-1, was compared with data from

© NICE 2024. All rights reserved. Subject to Notice of rights.

1 key trial for each comparator. All comparisons were made between single arms and so were unanchored. Matching-adjusted indirect comparisons (MAICs) were done in which the epcoritamab trial population was matched to the populations included in the comparator trials on important reported characteristics. In the MAICs, data for some people in the epcoritamab population was removed to match the population in the comparator trial (see section 3.9). The remaining observations were matched and re-weighted based on the baseline characteristics of the comparator trial. This considerably reduced the effective sample size of the epcoritamab population for each comparison.

3.6 The company used MAICs that were adjusted for only some reported factors ('partially adjusted') in its economic model base case. The EAG had substantial concerns about the partially adjusted MAICs and considered that full adjustment for all reported baseline characteristics is necessary for unanchored MAICs, as noted in the NICE Decision Support Unit's technical support document 18. The company provided MAICs with adjustment for all reported factors ('fully adjusted') for all comparators but considered that these produced clinically implausible results. The company also considered that the fully adjusted MAICs had a risk of over-adjustment, because UK clinical experts noted that several variables are correlated (such as disease stage and International Prognostic Index score). It noted that bias may be introduced by reducing the sample size further. The EAG acknowledged that the smaller sample sizes in the fully adjusted MAICs made the results less precise and more uncertain (that is, increased the confidence intervals), but it preferred accuracy of results over precision. The EAG considered that using partially adjusted MAICs did not make the trials more comparable, but instead obscured the potential lack of comparability between trials. It noted that it was possible that the differences between studies may be too great to adjust for.

3.7 At consultation, clinical experts and professional groups noted that EPCORE TM NHL-1 was done more recently than the comparator trials,

© NICE 2024. All rights reserved. Subject to Notice of rights.

after more treatments have become available at earlier lines of therapy. So, the population in EPCORE TM NHL-1 had tried and had no response to, or relapsed after, more effective treatments and so may have had a worse prognosis. The EAG acknowledged this but noted that better matching of comparator studies, such as excluding the group with previous CAR-T therapy and matching for prognostic factors, should reduce differences between the trials to some extent.

3.8 The EAG preferred using fully adjusted MAICs for the polatuzumab-BR and axicabtagene ciloleucel comparisons, and an analysis with 9 of 10 reported variables adjusted in the comparison with R-based CIT because the fully adjusted MAIC produced clinically implausible results. At consultation, the company provided fitted curves from the fully adjusted MAICs (to enable the results to be used in the model). In general, the committee was concerned about the lack of direct treatment comparisons, because indirect comparisons are inherently uncertain and potentially biased. This is because it is not possible to fully account for all the confounding variables and differences between populations. The committee concluded that the results from the indirect treatment comparisons were very uncertain. But it preferred using results from the MAIC with 9 of 10 reported variables adjusted for the comparison with R-based CIT, and the fully adjusted MAICs for the comparisons with polatuzumab-BR and axicabtagene ciloleucel in the model.

People who cannot have or do not want intensive treatment (population A)

3.9 For the MAICs for population A, the company included a subgroup from EPCORE TM NHL-1 that only included people who had not had CAR-T therapy. This was because the comparator trials did not include people who had had CAR-T therapy. The EAG noted that in clinical practice some people will have had CAR-T therapy and that it was unclear if results from the MAICs would apply to this population. The EAG was also concerned that it was unclear whether the EPCORE TM NHL-1 population

© NICE 2024. All rights reserved. Subject to Notice of rights.

included in the MAICs was ineligible for intensive treatments, because it was possible some eligible people were also included. After consultation, the company provided additional information from ECPORE TM NHL-1, including baseline characteristics and efficacy outcomes for the subgroup ineligible for intensive treatments. The EAG noted that the subgroup ineligible for intensive treatments had reduced fitness and poorer survival outcomes compared with the overall DLBCL population. It agreed with the company that it was not appropriate to adjust the population for epcoritamab without adjusting the population in the comparator trials, which could not be done without individual patient data from comparator populations. The EAG considered that some unresolvable uncertainty remained about whether the results were applicable to people ineligible for intensive treatments. But it noted this may become less important because treatment choice is now more often being made based on time to relapse after first treatment (see section 3.3). The committee concluded that the population included in the MAIC for population A was appropriate for decision making. But it noted that there is some unresolvable uncertainty about whether the analyses are applicable to people who had previously had CAR-T therapy and whether the populations included in the MAICs were ineligible for intensive treatments.

Comparison with rituximab-based chemoimmunotherapy

3.10 For the comparison with R-based CIT, data from EPCORE TM NHL-1 was matched to data from SCHOLAR-1. This was a retrospective observational study which pooled together data from 2 phase 3 clinical trials and 2 observational cohorts of people with refractory LBCL having R-based CIT. The data used in the company's submission was taken from a paper published by Neelapu et al. (2021) which included 340 people from SCHOLAR-1. The company used a partially adjusted MAIC in its base case (7 adjusted factors) but the EAG preferred the MAIC with 9 of the 10 reported variables adjusted for (see section 3.8). The EAG noted that several factors were still unbalanced in the MAIC with 9 of 10 reported variables adjusted for (3 or more lines of chemotherapy,

© NICE 2024. All rights reserved. Subject to Notice of rights.

autologous stem cell transplantation, and stem cell transplantation any time after refractory disease). The EAG noted limitations of the Neelapu et al. paper so at consultation the company provided additional MAICs using another paper reporting results from SCHOLAR-1, Crump et al. (2017). The EAG noted that adjusting for its preferred number of variables in the MAIC with Crump et al. (9 of 10 reported variables) resulted in a smaller sample size than with Neelapu et al. and that the groups were not well matched after adjustment. So, it agreed with the company that it was appropriate to use Neelapu et al. in its base case. The EAG also noted some unresolvable limitations in the SCHOLAR-1 cohort, which contributed to the overall uncertainty in the MAIC. These included that all participants' cancer was refractory to at least 1 previous treatment, whereas in EPCORE TM NHL-1, the participants' cancer could be relapsed or refractory. The EAG noted that this was particularly important because refractory status is a prognostic factor. It was also unclear how many people had had R-based CIT. The company acknowledged the limitations but noted that 21% of people in SCHOLAR-1 experienced relapse within 12 months of an autologous stem cell transplant, which was comparable to EPCORE TM NHL-1. Both the company's and EAG's preferred comparisons showed that epcoritamab was more effective than R-based CIT for all of the efficacy outcomes evaluated (the company considers the exact results to be confidential, so they cannot be reported here). But the committee noted that there was a considerable level of unresolvable uncertainty because of a lack of comparability between the studies and a small effective sample size (see sections 3.5 and 3.6). The committee concluded that the comparison appeared to show that epcoritamab was more effective than R-based CIT.

Comparison with polatuzumab-BR

3.11 For the comparison with polatuzumab-BR, data from EPCORE TM NHL-1 was matched to data from the GO29365 trial. The company used data from the EUnetHTA submission for baseline characteristics, and from Sehn et al. (2020) and Sehn et al. (2022) to estimate survival curves. The

© NICE 2024. All rights reserved. Subject to Notice of rights.

GO29365 trial compared polatuzumab-BR with BR alone after 1 or more treatments, and included 131 people in the polatuzumab-BR arm. The EAG noted unresolvable limitations in GO29365, which contributed to the overall uncertainty in the MAIC. The EAG considered that the polatuzumab-BR survival outcomes may have been overestimated compared with a UK population (based on a real-world study by Northend et al. 2022). It noted that this may bias the cost-effectiveness results against epcoritamab. It also noted that GO29365 did not report on primary refractoriness, which is a potentially important prognostic factor. The company did additional MAICs including a subgroup from the Northend et al. study that included people who already had 2 or more treatments.

3.12 At consultation, the company noted that its clinical experts considered that the true efficacy of polatuzumab-BR in NHS clinical practice is likely to fall between the estimates from GO29365 and Northend et al. So, it considered that results from both estimates should be considered. The EAG did not consider it appropriate to use the study by Northend et al. in the base case because comparing trial evidence with real-world data would introduce more bias. The company used a partially adjusted MAIC in its base case (6 factors adjusted), but the EAG noted that some factors were still unbalanced (refractory to last anti-lymphoma treatment, 2 lines of treatment, and 3 or more lines of chemotherapy and autologous stem cell transplantation). So it preferred to use the fully adjusted MAIC in its base case (10 factors adjusted; see section 3.5). Both the company and EAG's preferred comparisons showed that there were no significant differences in overall survival (OS) or progression-free survival (PFS) between epcoritamab and polatuzumab-BR (the company considers the exact results to be confidential, so they cannot be reported here). The clinical experts highlighted concerns with comparing EPCORE TM NHL-1, which was done more recently when more treatments were available at previous lines, with the GO29365 trial, noting that patients in EPCORE TM NHL-1 may have had a worse prognosis (see section 3.7). They noted

© NICE 2024. All rights reserved. Subject to Notice of rights.

that while the studies do not appear to show statistically significant differences in outcomes between epcoritamab and polatuzumab-BR, it is plausible that epcoritamab is more effective than polatuzumab-BR. The committee noted the considerable level of uncertainty because of the lack of comparability between the studies and the small effective sample size (see section 3.5 and 3.6). It also noted very wide confidence intervals for the results and that the hazard ratio for overall survival using its preferred MAIC was close to 1. The committee concluded that there do not appear to be substantial differences in efficacy between epcoritamab and polatuzumab-BR but noted the substantial uncertainty around the results.

Comparison with axicabtagene ciloleucel

3.13 For the comparison with axicabtagene ciloleucel, data from EPCORE TM NHL-1 was matched to data from the single-arm ZUMA-1 trial, which included 101 people with LBCL who had axicabtagene ciloleucel after 2 or more treatments. The company included the DLBCL population from EPCORE TM NHL-1 in the analyses to align with the marketing authorisation. But the EAG preferred to use the LBCL population from EPCORE TM NHL-1 (plus adjustment for type of LBCL) to align more closely with the ZUMA-1 population. The EAG noted that the definition of PFS varied between EPCORE TM NHL-1 and ZUMA-1 (Lugano versus International Working Group criteria, respectively) and that this may have biased the results against epcoritamab. The EAG noted additional unresolvable limitations in ZUMA-1 which contributed to the overall uncertainty in the MAIC. The EAG and company noted that the available data from ZUMA-1 was for the treated population rather than the intention-to-treat population, so did not include people who were assigned to axicabtagene ciloleucel in the trial but did not have it. The clinical experts advised that the people who did not have axicabtagene ciloleucel would have had cancer that rapidly progressed between being approved for treatment and having the infusion. They also advised that axicabtagene ciloleucel often needs a period of bridging therapy before it is administered. So, people who could not wait long enough for treatment

© NICE 2024. All rights reserved. Subject to Notice of rights.

were unlikely to have been referred for axicabtagene ciloleucel treatment at all. So, the clinical experts considered that the population in ZUMA-1 may have had a better prognosis than the population in EPCORE TM NHL-1. The EAG agreed that this could bias the indirect comparison in favour of axicabtagene ciloleucel, but that it was not possible to quantify the extent of this bias. The EAG noted that 1 potentially important prognostic factor (refractory to last anti-lymphoma treatment) was not reported in ZUMA-1 so could not be adjusted for. The company used a partially adjusted MAIC in its base case (7 factors adjusted; see section 3.6). But the EAG noted that some factors were still unbalanced (DLBCL versus other LBCL, International Prognostic Index score of 3 or more, 3 or more previous treatment lines, and refractory to second-line or subsequent therapy) so it preferred to use the fully adjusted MAIC in the model (11 factors adjusted) that was focused on LBCL. Both the company and EAG's preferred comparisons showed that there were no significant differences in efficacy outcomes (PFS, OS, complete remission and overall response) between epcoritamab and axicabtagene ciloleucel (the company considers the exact results to be confidential, so they cannot be reported here). The committee noted that there was a considerable level of uncertainty because of the lack of comparability between the studies and the small effective sample size (see section 3.5 and 3.6). It also noted very wide confidence intervals for the results. The committee concluded that there are likely to be no substantial differences in efficacy between epcoritamab and axicabtagene ciloleucel, but noted the substantial uncertainty around the results.

Economic model

Company's model

3.14 The company used a partitioned survival model to estimate the cost effectiveness of epcoritamab. The model included 3 health states: progression free, progressed disease and death. The probability of being in a given health state was calculated using the OS and PFS curves that

© NICE 2024. All rights reserved. Subject to Notice of rights.

were based on the MAICs. The committee concluded that the model structure was acceptable for decision making.

Long-term remission assumptions

3.15 At consultation, the company applied a long-term remission assumption for people who were progression free from 3 years after starting treatment with epcoritamab or its comparators. This was aligned with the committee's preferred assumptions for the NICE technology appraisal of glofitamab (TA927). The EAG noted that people have glofitamab for a fixed duration of 12 cycles or until disease progression or toxicity, whereas people have epcoritamab until disease progression or toxicity. It questioned if it was clinically plausible for people having epcoritamab to be in long-term remission, which means they are discharged from follow up, while still on treatment. The EAG did scenarios removing the long-term remission assumption for epcoritamab which had a large impact on the incremental cost-effectiveness ratio (ICER). The clinical experts considered that relapses after 3 years of being progression free are rare in this condition, noting that around 90% of disease that recurs will do so within 2 years. They considered that although there is limited evidence of the impact of stopping epcoritamab while in long-term remission, around 50% of people are likely to stop treatment after their disease has been progression free for 3 years and relapse is unlikely after stopping treatment. The experts noted that this proportion may increase in time as data on stopping epcoritamab becomes available. In the company's and EAG's base cases, the time point at which people stop having epcoritamab is based on the time to treatment discontinuation (TTD) curve from EPCORE TM NHL-1 (see section 3.17). The committee considered scenarios in which 100% of people stopped having epcoritamab when they entered long-term remission, noting that the results favoured epcoritamab. The committee concluded that it was appropriate to apply the long-term remission assumption 3 years after starting epcoritamab or its comparators, as done in TA927. It concluded that there is limited evidence on the proportion of people who stop

© NICE 2024. All rights reserved. Subject to Notice of rights.

epcoritamab when they have long-term remission, so the proportion of people in the model who stop epcoritamab when entering long-term remission should be based on the TTD curve from EPCORE TM NHL-1.

Flexible survival curves

3.16 At the first committee meeting, the committee concluded that standard parametric distributions did not fit the survival data well, so more flexible survival models should be explored. The EAG had noted that the company's parametric extrapolations did not capture the change in underlying hazards and underestimated survival for the comparators, for which there was longer follow-up data. At consultation, the company noted that there was not sufficiently robust evidence to implement spline or mixture-cure models, but provided scenario analyses using piecewise models for all comparisons. These scenarios used Kaplan–Meier data for the first 24 months (12 months for the analysis with Northend et al. based on shorter follow up) and then fitted parametric extrapolations beyond this point. The EAG noted that the piecewise models had not been implemented correctly and that the 24-month cut-point was not justified. It noted that the piecewise models should only represent the initial section of the Kaplan–Meier data and the extrapolation should join a predetermined point of the Kaplan–Meier curve. Despite the limitations, the EAG considered the piecewise models were the best available option and mitigated many of the EAG's issues around capturing the points at which the Kaplan–Meier curves crossed or overlapped in the MAIC. So it used piecewise models in its base case. The EAG noted that the concerns with applying the piecewise models were less likely to impact the cost-effectiveness results if the long-term remission assumption was applied for epcoritamab and comparators. The committee noted the concerns about the implementation of the piecewise models and considered that this increased uncertainty. But it also noted its conclusion that applying the long-term remission assumption was appropriate (see section 3.15), which mitigated the EAG's concerns with the application of the models. So it considered that these models were suitable for decision

© NICE 2024. All rights reserved. Subject to Notice of rights.

making. The committee considered that the company's extrapolations lacked internal validity because the extrapolated models did not fit the available trial data well. It considered that the EAG's piecewise models best reflected the available trial data. So, it preferred to use piecewise models with the 24-month cut-point for the model's extrapolations. See sections 3.17 to 3.24 for more details on the company's and EAG's extrapolations.

Epcoritamab treatment duration in the model

3.17 There is no stopping rule for epcoritamab except for disease progression or toxicity. The comparators are each taken for a fixed duration. The company confirmed that some people remained on epcoritamab and were progression free in the latest data cut of EPCORE TM NHL-1 (median follow up 25.7 months). The company estimated the long-term duration of treatment with epcoritamab in the model by fitting exponential curves to the TTD Kaplan–Meier data from EPCORE TM NHL-1. Clinical experts consulted by the company said that the modelled TTD curve would be similar to but lower than the PFS curve. This is because people are likely to remain on treatment until progression, as epcoritamab is well tolerated. At technical engagement, the company's clinical experts stated that people are unlikely to remain on treatment after 5 years. The EAG considered that this was inconsistent with the clinical expert opinion in the company's original submission. It also noted that the exponential modelled TTD curves for epcoritamab were not consistent with the underlying Kaplan–Meier data from EPCORE TM NHL-1. The EAG preferred to use the piecewise models with the 24-month cut-point to estimate TTD for epcoritamab (see section 3.16). It preferred to use log-normal curves to estimate TTD beyond 24 months for epcoritamab compared with all comparators because it considered this best fitted the data. The committee concluded that it preferred the EAG's approach.

Extrapolations for the comparison with rituximab-based chemoimmunotherapy

© NICE 2024. All rights reserved. Subject to Notice of rights.

3.18 For the comparison with R-based CIT, the committee preferred using the MAIC results from the company's scenario with 9 of 10 reported variables adjusted (see section 3.8). The EAG considered that the company's preferred OS curves overpredicted survival for epcoritamab, and underpredicted it for R-based CIT compared with the SCHOLAR-1 data reported in both Neelapu et al. and Crump et al. at 5 years. Because PFS was not reported in SCHOLAR-1, the company estimated PFS for R-based CIT by applying the hazard ratio from the MAIC for OS versus epcoritamab to the PFS curve for epcoritamab. The EAG preferred to use the hazard ratio between the epcoritamab OS and PFS Kaplan–Meier curves applied to the OS curve for SCHOLAR-1 for R-based CIT, to estimate a PFS curve for R-based CIT. The committee noted that the approach to estimate PFS did not have a big impact on the cost-effectiveness results. So, given the uncertainty, it concluded that it preferred to use the EAG's approach to estimate PFS.

3.19 The company assumed that the TTD curve for R-based CIT would be the same as the PFS curve, based on expert opinion and lack of suitable data on discontinuation of R-based CIT. The EAG considered that it was implausible to assume people on R-based CIT do not stop treatment for reasons other than progression, because of the high toxicity of the treatment. The EAG preferred to assume that 10% of people stop treatment with R-based CIT for reasons other than progression. However, the EAG considered that, even with this adjustment, the company's TTD curve overestimated treatment costs for R-based CIT. The committee concluded that, given the toxicity of R-based CIT, it was reasonable to assume that people would stop treatment for reasons other than progression. So, it preferred to apply the 10% adjustment to the PFS curve for R-based CIT to estimate the TTD curve.

3.20 The EAG noted that there was a substantial difference between the mean PFS and mean TTD for epcoritamab in the company's base case. The exact difference between mean PFS and mean TTD when using the

© NICE 2024. All rights reserved. Subject to Notice of rights.

company's and EAG's preferred curves is considered to be academic in confidence by the company and so it cannot be reported here. The EAG considered that the company's TTD curve for epcoritamab (exponential) underestimated costs. The EAG preferred the piecewise models to extrapolate OS, PFS and TTD (see section 3.16). Beyond the 24-month cut-point, most of the EAG's preferred extrapolations differed from the company's, because it considered they better fitted the data and were more clinically plausible. The committee considered the shape of the EAG's preferred OS curve (exponential) for epcoritamab with the long-term remission assumption applied. It noted that this may be more pessimistic than would be expected in clinical practice, but considered this curve was more plausible than the company's preferred OS curve (log-normal). The committee acknowledged the uncertainty with the extrapolations but concluded that it preferred to use the partially adjusted MAIC (9 of 10 reported variables adjusted; see section 3.8) with piecewise models for OS, PFS and TTD, and the EAG's preferred extrapolation curves that better fitted the data.

Extrapolations for the comparison with polatuzumab-BR

3.21 For the comparison with polatuzumab-BR, the committee preferred using the results from the fully adjusted MAIC with 10 variables adjusted (see section 3.11). As with R-based CIT (see section 3.19), the company assumed that the TTD curve for polatuzumab-BR would be the same as the PFS curve. The EAG considered that this was implausible and overestimated the cost of polatuzumab-BR. The EAG preferred to assume that 10% of people stop treatment with polatuzumab-BR for reasons other than progression. The committee concluded that, given the toxicity of polatuzumab-BR, it was reasonable to assume that people would stop treatment for reasons other than progression. So, it preferred to apply the 10% adjustment to the PFS curve for polatuzumab-BR to estimate the TTD curve.

© NICE 2024. All rights reserved. Subject to Notice of rights.

3.22 The EAG noted that the company's preferred OS curve for epcoritamab (generalised gamma) overestimated the benefit of epcoritamab compared with the fully adjusted MAIC, which showed the epcoritamab and polatuzumab-BR curves converging at around 15 months. The EAG noted that the company's preferred OS curve for polatuzumab-BR (log-logistic) underestimated survival with polatuzumab-BR compared with that reported from the GO29365 trial. It noted that no parametric extrapolation curves represented the possible plateau in OS seen in GO29365 between 18 and 27 months. It also noted that the extrapolated PFS curves (generalised gamma for epcoritamab and gamma for polatuzumab-BR) had a poor fit to the MAIC-adjusted Kaplan–Meier data used by the company for epcoritamab, and to the data from GO29365 for polatuzumab-BR which had a potential plateau at 24 months. The EAG used a slightly better fitting TTD curve in its exploratory analyses. As with the comparison with R-based CIT, the EAG noted a substantial difference between mean PFS and mean TTD for epcoritamab in the company's base case. The exact difference between mean PFS and mean TTD when using the company's and EAG's preferred curves is considered academic in confidence by the company and so it cannot be reported here. The EAG considered the company's TTD curves to underestimate costs for epcoritamab and overestimate costs for polatuzumab-BR. The committee preferred the EAG's curves for the extrapolation of TTD for both epcoritamab and polatuzumab-BR because they fitted the data better than the company's extrapolations.

3.23 The committee noted that in the company's base case, epcoritamab generated more quality-adjusted life years (QALYs) than polatuzumab-BR whereas in the EAG's base case, polatuzumab-BR generated more QALYs than epcoritamab. The clinical experts considered that it was plausible that epcoritamab was more effective than polatuzumab-BR. The committee recalled the high level of uncertainty in the evidence base comparing epcoritamab and polatuzumab-BR and that both the partially and fully adjusted MAICs did not show statistically significant differences

© NICE 2024. All rights reserved. Subject to Notice of rights.

(see section 3.12). The committee recalled that in the appraisal on loncastuximab tesirine, polatuzumab-BR was assumed to have equal OS and PFS to loncastuximab tesirine in the committee's preferred base case and the MAICs showed similar efficacy between loncastuximab tesirine and polatuzumab-BR. The committee also noted that in the company's base case, most of epcoritamab's clinical benefit compared with polatuzumab-BR occurred during the extrapolation period. This was inconsistent with clinical expert input that clinical benefit would normally be seen in the first 2 years. Because of the high level of uncertainty in the evidence base comparing epcoritamab and polatuzumab-BR, the committee concluded that it preferred to assume equal efficacy between epcoritamab and polatuzumab-BR.

Extrapolations for the comparison with axicabtagene ciloleucel

3.24 For the comparison with axicabtagene ciloleucel, the committee preferred using the results from the fully adjusted MAIC including the LBCL population with 11 variables adjusted (see section 3.11 and 3.13). The EAG considered that the company's preferred OS and PFS curves (Gompertz for all) did not align with the Kaplan–Meier curves for either treatment. For PFS, the EAG considered that the company's curve for epcoritamab was clinically implausible. The EAG also noted that the company's base case had a large difference between mean PFS and mean TTD that was unlikely to be plausible, and so underestimated the costs for epcoritamab. The exact difference between mean PFS and mean TTD when using the company's and EAG's preferred curves is considered academic in confidence by the company and cannot be reported here. The EAG applied a hazard ratio of 1.2 to the epcoritamab PFS curve to estimate the TTD curve in its base case. However, the committee considered that the mean TTD for epcoritamab was implausibly large in the EAG's base case. It noted that the EAG's modelled TTD was much higher than the clinical experts' estimation that people would be unlikely to stay on epcoritamab longer than 2 or 3 years. The committee noted that removing the hazard ratio of 1.2 from the EAG's

© NICE 2024. All rights reserved. Subject to Notice of rights.

base case resulted in a more clinically plausible mean TTD for epcoritamab and decreased the total costs for epcoritamab. The committee concluded that it preferred to use fully adjusted MAICs including the LBCL population (see section 3.13) with piecewise models for OS, PFS and TTD, after which it preferred to use the EAG's preferred extrapolation curves. It preferred to remove the EAG's application of a 1.2 hazard ratio to estimate TTD for epcoritamab.

Subsequent treatments

3.25 At the first committee meeting, the committee concluded that there was uncertainty in the most appropriate subsequent treatments to include in the model for each population and that this had a substantial impact on the cost-effectiveness estimates. It requested further scenarios in which the subsequent treatments included in the model better reflected NHS clinical practice. Or, if this was not possible, it preferred that subsequent treatments in the model were aligned with EPCORE TM NHL-1. In the company's original submission, the subsequent treatments used in the model were based on UK clinical expert feedback. However, the EAG considered that, based on its clinical expert input, the values provided by the company did not represent NHS clinical practice. It considered that subsequent treatment will differ based on the third-line treatment used and that the company's estimation of the proportion of people having CAR-T therapy after epcoritamab was too low. It also considered that people who had R-based CIT or polatuzumab-BR at third line would not have further R-based CIT but would instead have palliative chemoimmunotherapy. While the company noted that the proportion of people having subsequent treatment with CAR-T therapy in its original submission might have been too small, it noted the EAG's analyses included a higher proportion of people having CAR-T therapy after epcoritamab than in EPCORE TM NHL-1. The exact proportions of people having subsequent CAR-T therapy in EPCORE TM NHL-1 are considered academic in confidence by the company so they cannot be reported here. The EAG noted that in the most recent data cut from EPCORE TM NHL-1,

© NICE 2024. All rights reserved. Subject to Notice of rights.

the proportion of people having subsequent CAR-T therapy was similar to the EAG's clinical experts' opinion of 11% for population A. The EAG's preferred estimate of 30% of people having CAR-T therapy after epcoritamab for population B was higher than in EPCORE TM NHL-1. The clinical experts at the first meeting had noted that the EAG's assumption of 30% of people having CAR-T therapy after epcoritamab in population B was higher than they would expect in clinical practice.

3.26 At consultation, the company sought additional clinical expert input on subsequent treatments used for each third-line treatment. The EAG was concerned that the company's use of subsequent treatments, including CAR-T therapy use after epcoritamab and use of rituximab-based treatment after R-based CIT and polatuzumab-BR, still did not represent clinical practice, based on its clinical expert input. The committee noted the overall uncertainty in the appropriate subsequent treatments that would be used in clinical practice, noting inconsistent advice from different clinical experts. The committee noted that while the choice of subsequent treatment did impact the cost-effectiveness results, it did not affect the decision about whether epcoritamab was cost effective or not. The committee concluded that there was uncertainty about the subsequent treatments used in clinical practice. It concluded it would prefer to use the proportions based on the feedback from the EAG's clinical experts for the purposes of the analyses, because these were most aligned with EPCORE TM NHL-1.

Epcoritamab follow-up treatment costs

3.27 At the first meeting, the committee concluded that it was appropriate to reduce the intensity of follow up (such as the number of appointments and tests) once people having epcoritamab had a complete remission. But the costs used in the model in this situation should be clinically validated. In the company's model, people having epcoritamab were assumed to incur lower follow-up costs after the point of median PFS for partial responders in EPCORE TM NHL-1. The company considers the exact time point to be

© NICE 2024. All rights reserved. Subject to Notice of rights.

academic in confidence so it cannot be reported here. It was also the point at which the dosing frequency of epcoritamab decreased from once weekly to every other week. The company noted that most people who experienced a complete response had done so by this time point. The company's clinical experts and the clinical experts at the first committee meeting agreed that the intensity of follow up for people having epcoritamab was likely to decrease over time after they have a complete response.

3.28 At consultation, the company provided a revised PFS for 'low intensity' resource use while on epcoritamab based on an interview with 5 clinical experts. It applied this at the same time point as in its original submission. The resource use determined from clinical experts was lower than the original resource use estimates used for the comparators, which the company considered were not clinically plausible because people having the comparators would no longer be having treatment. So, the company used the same PFS for 'low intensity' resource use for epcoritamab and the comparators. The EAG considered the change to the original resource use assumption was not sufficiently justified, particularly the increased use of specialist nurse and haematologist time. So, it preferred to use the company's original values in its base case. The EAG also considered it inappropriate to use median PFS as the time point for the switch from 'high intensity' to 'low intensity' follow up. It considered that the rationale for why the median PFS from the trial should dictate resource use for people having epcoritamab was unclear. So, the EAG switched from 'high' to 'low intensity' after 1 year in its base case and ran a scenario in which the switch happened 2 years after starting treatment. The committee concluded that there was uncertainty about how much the intensity of follow up would reduce after people having epcoritamab have a complete remission, and at what time point the intensity would reduce. It noted that while this assumption impacted the cost-effectiveness results, it did not affect the decision about whether epcoritamab was cost effective or not. Given the uncertainty, and the lack of sufficient justification for the

© NICE 2024. All rights reserved. Subject to Notice of rights.

changes to resource use, the committee preferred to use the level of resource use in the company's original submission. Also, given the uncertainty in the time point at which resource use would be lower, the committee preferred to use a more conservative assumption that applied lower intensity costs from 1 year after starting epcoritamab.

3.29 The clinical experts noted that people in long-term remission would likely have further follow up, because people having treatment at this stage will have had several relapses so would likely prefer some follow up. However, the experts disagreed on the frequency of follow up in long-term remission, with estimates ranging from every 3 to 4 months to an annual telephone call. The committee noted that the model assumed no further follow up after long-term remission, but the CDF clinical lead noted that the additional costs of follow up were not likely to substantially impact the cost-effectiveness results. So, the committee concluded that it was appropriate to assume that people having epcoritamab would have no further follow up after entering long-term remission.

Severity

3.30 The committee may apply a greater weight to QALYs (a severity modifier) if technologies are indicated for conditions with a high degree of severity. The committee considered the severity of DLBCL after 2 previous treatments (the future health lost by people living with the condition and having standard care in the NHS). The company provided absolute and proportional QALY shortfall estimates in line with NICE's health technology evaluations manual. Based on the QALYs generated from the company's and EAG's models, the company and EAG agreed it was not appropriate to apply a severity modifier for the comparison with axicabtagene ciloleucel. The company and EAG agreed that for the comparison with R-based CIT, the QALYs should have a higher weighting (1.2 times). When the committee's preferred assumptions were applied for the comparisons with polatuzumab-BR, the threshold for a severity modifier was not met. The committee concluded that it was appropriate to

© NICE 2024. All rights reserved. Subject to Notice of rights.

apply the severity weight of 1.2 to the QALYs for the comparison with R-based CIT but that it was not appropriate to apply a severity modifier to the comparison with polatuzumab-BR or axicabtagene ciloleucel.

Cost-effectiveness estimates

Acceptable ICER

3.31 NICE's manual on health technology evaluations notes that above a most plausible ICER of £20,000 per 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, but will also take into account other aspects including uncaptured health benefits. The committee noted the high level of uncertainty, specifically:

- whether the intervention and comparator trials were sufficiently comparable to draw meaningful results from the MAICs (see sections 3.10 to 3.13)
- whether the results for population A (people who cannot have or do not want intensive treatment) were applicable to people who had CAR-T therapy (see section 3.9)
- whether the populations included in the MAICs for population A were ineligible for intensive treatments (see section 3.9)
- the appropriateness of the indirect comparison with R-based CIT (unresolvable limitations of the SCHOLAR-1 study, and whether it was appropriate to assume the PFS gain for R-based CIT would be similar to the OS gain; see sections 3.10 and 3.18)
- the appropriateness of the indirect comparison with polatuzumab-BR (including unresolvable limitations of the GO29365 trial; see section 3.11 and 3.12)
- the appropriateness of the indirect comparison with axicabtagene ciloleucel (including differing definitions of PFS across studies, that the

© NICE 2024. All rights reserved. Subject to Notice of rights.

ZUMA-1 study did not include an intention-to-treat population, and other unresolvable limitations of ZUMA-1; see section 3.13)

- poor fitting of the company's parametric extrapolations for OS, PFS and TTD for epcoritamab and all comparators to the available data and in how the piecewise models were implemented (including the time point to extrapolate beyond the Kaplan–Meier data; see sections 3.16, and 3.18 to 3.24)
- the appropriate proportions of people having each subsequent treatment, to best reflect UK clinical practice (see section 3.25 to 3.26)
- follow-up costs for people having epcoritamab (see section 3.27 to 3.29)

So, the committee concluded that an acceptable ICER would be towards the lower end of the range normally considered a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

Cost-effectiveness estimates

3.32 Because of confidential commercial arrangements for epcoritamab, the comparators, and other treatments in the model, the exact cost-effectiveness estimates are confidential and cannot be reported here. The company's ICERs for epcoritamab compared with R-based CIT were at the lower end of the range of what is normally considered a cost-effective use of NHS resources. In the company's base case, epcoritamab cost less but produced more QALYs than axicabtagene ciloleucel. However, there were limitations with the company's base case that incorporated MAICs in which some factors were still unbalanced between comparator groups (see sections 3.10 to 3.13). The EAG's base-case deterministic ICER for epcoritamab compared with R-based CIT was at the lower end of the range normally considered a cost-effective use of NHS resources. The EAG's base case ICERs for the comparison with axicabtagene ciloleucel were higher than what is normally considered a cost-effective use of NHS resources.

© NICE 2024. All rights reserved. Subject to Notice of rights.

The committee's preferred assumptions included:

- Using the partially adjusted MAIC (9 of 10 reported variables) for the comparison with R-based CIT (see section 3.10) and the fully adjusted MAIC in the LBCL population for the comparison with axicabtagene ciloleucel (see section 3.8)
- Applying the long-term remission assumption 3 years after starting epcoritamab or its comparators and using the TTD curve to determine the proportion of people stopping epcoritamab when entering long-term remission (see section 3.15)
- Using piecewise models with the 24-month cut-point and the EAG's preferred extrapolations for PFS, OS and TTD for R-based CIT and axicabtagene ciloleucel (see sections 3.16 to 3.24), but removing the hazard ratio that the EAG had applied to estimate TTD for epcoritamab in the comparison with axicabtagene ciloleucel (see section 3.24).
- Assuming epcoritamab and polatuzumab-BR have equal efficacy (see section 3.23)
- Using the EAG's preferred assumptions for subsequent treatments and follow-up costs on epcoritamab (see sections 3.25 to 3.29).

The deterministic ICER using the committee's preferred assumptions for epcoritamab compared with R-based CIT was at the lower end of the range normally considered a cost-effective use of NHS resources. With the committee's preferred assumptions, epcoritamab cost less but produced more QALYs than axicabtagene ciloleucel. Because the committee preferred to assume equivalent efficacy between epcoritamab and polatuzumab-BR, it only considered the difference in costs, and epcoritamab was substantially more expensive than polatuzumab-BR. The committee concluded that epcoritamab was a cost-effective treatment option compared with R-based CIT and axicabtagene ciloleucel, but not compared with polatuzumab-BR.

Uncaptured benefits

© NICE 2024. All rights reserved. Subject to Notice of rights.

3.33 The committee did not identify any additional benefits of epcoritamab not captured in the economic modelling. So it concluded that all of the benefits of epcoritamab had already been taken into account.

Equality

3.34 The company, clinical experts and patient experts outlined that there are barriers related to the delivery of CAR-T therapies, with many people having to travel long distances, or being unable to travel to therapy centres. The committee agreed that access was an issue with CAR-T therapies, but that access to therapy centres could not be directly addressed through its recommendations. The patient experts noted that epcoritamab may need to be delivered in larger transplant or CAR-T therapy centres before training and support is provided to smaller centres, particularly to manage the potential adverse events. They noted that this may introduce short-term inequities for people who live further from treatment centres and cannot pay for travel or are unable to travel longer distances. The clinical experts acknowledged this but noted that many regional hospitals are having training in managing side effects. They noted that bispecific monoclonal antibodies are deliverable by non-CAR-T centres in an outpatient setting and that these treatments have been delivered successfully in exceptional circumstances through individual funding requests. They noted that, overall, offering another treatment such as epcoritamab would improve access to treatment for people with relapsed or refractory DLBCL, particularly for those who have to wait to have CAR-T therapy. The committee acknowledged that disability (which may contribute to the inability to travel long distances) is a protected characteristic under the Equality Act 2010. It noted that socioeconomic status and geographical distance are not protected characteristics, but that NICE has due regard to promote the reduction of health inequalities. The committee considered that the addition of epcoritamab as another treatment option that does not need people to travel to a specialist centre could help ensure more people have access to effective treatments.

© NICE 2024. All rights reserved. Subject to Notice of rights.

Conclusion

3.35 Because of their similar clinical effectiveness, only the difference in cost between epcoritamab and polatuzumab-BR was considered, and epcoritamab was substantially more expensive. The deterministic ICER incorporating the committee's preferred assumptions for epcoritamab compared with R-based CIT was at the lower end of the range normally considered a cost-effective use of NHS resources. Epcoritamab cost less but produced more QALYs than axicabtagene ciloleucel. The committee considered that R-based CIT or axicabtagene ciloleucel would be used after polatuzumab vedotin, or when polatuzumab vedotin was contraindicated or not tolerated (see section 3.3). So, epcoritamab is recommended for use in the NHS for treating relapsed or refractory DLBCL in adults who have had 2 or more systemic treatments, but only if they have had polatuzumab vedotin, or if polatuzumab vedotin is contraindicated or not tolerated.

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 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early

© NICE 2024. All rights reserved. Subject to Notice of rights.

Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 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.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic treatments and the doctor responsible for their care thinks that epcoritamab 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 C.

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

© NICE 2024. All rights reserved. Subject to Notice of rights.

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

Steve O'Brien

Chair, technology appraisal committee C

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.

Heather Stegenga

Technical lead

Lizzie Walker

Technical adviser

Louise Jafferally

Project manager

ISBN: [to be added at publication]

© NICE 2024. All rights reserved. Subject to Notice of rights.