NICE National Institute for Health and Care Excellence

NICE guidance

Ivosidenib with azacitidine for untreated acute myeloid leukaemia with an IDH1 R132 mutation

Technology appraisal guidance
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Your responsibility

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

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

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

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

Contents

1 Recommendations

1.1 Ivosidenib plus azacitidine is recommended, within its marketing authorisation, as an option for untreated acute myeloid leukaemia (AML) with an IDH1 R132 mutation in adults who cannot have standard intensive induction chemotherapy. It is only recommended if the company provides it according to the commercial arrangement.

Why the committee made these recommendations

Usual treatment for newly diagnosed AML with an IDH1 R132 mutation in adults who cannot have standard intensive induction chemotherapy is venetoclax plus azacitidine.

Ivosidenib plus azacitidine has not been directly compared in a clinical trial with venetoclax plus azacitidine. An indirect comparison suggests that ivosidenib plus azacitidine increases how long people live and how long they have before their condition gets worse compared with venetoclax plus azacitidine.

The most likely cost-effectiveness estimates for ivosidenib plus azacitidine are within the range that NICE considers an acceptable use of NHS resources. So, it is recommended.

2 Information about ivosidenib with azacitidine

Marketing authorisation indication

2.1 Ivosidenib (Tibsovo, Servier Laboratories) 'in combination with azacitidine is indicated for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) with an isocitrate dehydrogenase-1 (IDH1) R132 mutation who are not eligible to receive standard induction chemotherapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of a 60-tablet pack of 250 mg ivosidenib is £12,500, or £150,000 for a year of treatment (excluding VAT; BNF online accessed January 2024). At the time of evaluation, the average price of azacitidine was £45.16 per 100 mg powder for suspension for injection vial (excluding VAT; eMIT accessed September 2023).

2.4 The company has a commercial arrangement. This makes ivosidenib available to the NHS with a discount. The size of the discount is commercial in confidence.

3 Committee discussion

The evaluation committee considered evidence submitted by Servier Laboratories, 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.

Acute myeloid leukaemia with an IDH1 R132 mutation

New treatment option

3.1 The patient expert explained that existing treatments for acute myeloid leukaemia (AML) are mainly chemotherapy and stem cell transplant but new options are needed for when these are not suitable. The patient expert described how gruelling intensive induction chemotherapy is, both physically and psychologically, even if you are physically fit. The clinical expert also emphasised the need for an alternative to intensive induction chemotherapy. They said that before venetoclax plus azacitidine was recommended, survival rates for AML had been poor if people could not have intensive induction chemotherapy. They added that since venetoclax plus azacitidine became available, survival rates had substantially improved. Ivosidenib plus azacitidine would be a treatment option for the 6% to 10% of people with AML who have an IDH1 R132 mutation (from now, IDH1 mutation). Ivosidenib is an oral treatment, so preferable to intravenous treatments, for people with AML. The clinical expert said that, for people with an IDH1 mutation, they would prefer to offer ivosidenib plus azacitidine over venetoclax plus azacitidine, because haematological toxicity is an issue with venetoclax plus azacitidine. The committee concluded that people with AML with an IDH1 mutation who cannot have intensive induction chemotherapy would welcome a new treatment option.

Clinical management

Treatment pathway

3.2 The first treatment option for AML is intensive induction chemotherapy to bring about remission, then consolidation chemotherapy, followed by maintenance therapy, and then a stem cell transplant. But more than 50% of people with AML cannot have intensive induction chemotherapy and stem cell transplants, for example, because of their age or comorbidities. Standard care for AML if someone cannot have intensive induction chemotherapy is venetoclax plus azacitidine (see NICE's technology appraisal guidance on venetoclax with azacitidine for untreated AML when intensive chemotherapy is unsuitable). Other options are:

- low-dose cytarabine
- azacitidine (for AML with 20% to 30% bone marrow blasts)
- venetoclax plus low-dose cytarabine (for AML with more than 30% bone marrow blasts).

Comparators

3.3 The company said that venetoclax plus azacitidine was the only relevant comparator in people with untreated AML who cannot have intensive induction chemotherapy. But the EAG said that it had clinical advice that venetoclax plus azacitidine was only suitable for people who are well enough, and that the other comparators are offered if people cannot tolerate venetoclax plus azacitidine. The clinical expert said that the main treatment for people who could not have intensive induction chemotherapy was venetoclax plus azacitidine. They acknowledged that there were situations in which other treatments could be considered but said that these were unusual because outcomes for them were so poor. The NHS England Cancer Drugs Fund clinical lead (from here, Cancer Drugs Fund lead) said that most people on venetoclax were having it in combination with azacitidine. The committee was satisfied that most people with untreated AML who cannot have intensive induction chemotherapy have venetoclax plus

azacitidine in clinical practice. It concluded that the most appropriate comparator for ivosidenib plus azacitidine was venetoclax plus azacitidine.

Clinical effectiveness

Literature searches

3.4 The EAG had concerns that the company had narrowed the population element of the literature searches too much. It said that because the search was narrowed to only include articles specifically mentioning the phrases 'first line', 'treatment-naive' or 'untreated' in the database record, relevant literature may have been missed. The EAG identified an extra 1,336 potentially relevant documents. It considered that there was a risk that important comparator trials had been missed. The company responded that its search strategy was in line with the target population and was constructed to exclude irrelevant indications. It also said that the approach had been used in previous systematic reviews submitted for NICE technology appraisals. The clinical expert confirmed that the most important trials had been identified. The committee acknowledged the uncertainty highlighted by the EAG but was reassured that the most important evidence was likely to have been identified.

AGILE trial

3.5 The direct comparative clinical-effectiveness evidence for ivosidenib plus azacitidine came from the AGILE trial. This was a phase 3 multicentre, randomised, placebo-controlled trial comparing ivosidenib plus azacitidine (n=72) with azacitidine plus placebo (n=74). The committee noted that azacitidine monotherapy was not considered a relevant comparator treatment by the company. The trial was in people with previously untreated AML with an IDH1 mutation who could not have intensive induction chemotherapy. Median follow up was 28.6 months and the primary outcome was event-free survival. Secondary outcomes were overall survival, complete remission (CR) or CR without haematological recovery (CRi), and objective response rate. In the AGILE trial, event-free survival was significantly better for ivosidenib plus azacitidine than for

azacitidine plus placebo, with a hazard ratio of 0.33 (95% confidence interval [CI] 0.16 to 0.69; p=0.0011). Overall survival was also significantly better, with a hazard ratio of 0.42 (95% CI 0.27 to 0.65; p<0.0001). The committee concluded that ivosidenib plus azacitidine improved event-free and overall survival compared with azacitidine plus placebo.

Indirect treatment comparison

Network meta-analysis

3.6 Because there was no direct comparative evidence for ivosidenib plus azacitidine compared with venetoclax plus azacitidine, the company did an indirect treatment comparison using network meta-analysis (NMA). This used data from the VIALE-A trial for venetoclax plus azacitidine. VIALE-A was a randomised controlled trial comparing venetoclax plus azacitidine with azacitidine plus placebo in 433 people with untreated AML who could not have intensive induction chemotherapy. The point estimates in the NMA results for event-free survival, overall survival and CR favoured ivosidenib plus azacitidine over venetoclax plus azacitidine. The company considered the exact results confidential and so they cannot be reported here. The committee noted that the credible intervals crossed 1, suggesting that there may be no difference in effect between the 2 treatments. The EAG said that, although the company's NMA had been done to a reasonable standard, it had several concerns. Aside from the uncertainty in the treatment effect, there was heterogeneity across some of the studies. And because the company used fixed effects rather than random effects models, the EAG said that the credible intervals did not properly express this uncertainty. The company acknowledged the uncertainties in the NMA results. At consultation, it pointed out that these were because of the small sample size. The small sample size was a result of the trial being stopped early because there were fewer deaths with ivosidenib plus azacitidine. After consultation, the company provided extra analyses of the NMA outputs, which showed a high probability of added benefit with ivosidenib plus azacitidine compared with venetoclax plus azacitidine. It also provided 3 more indirect comparisons: an anchored matching-adjusted indirect comparison (MAIC) for overall survival, an anchored MAIC for event-free survival and an unanchored MAIC for overall

survival in a subgroup of people with the IDH1 mutation (the IDH1 subgroup). All 3 favoured ivosidenib plus azacitidine, although the confidence intervals crossed 1 for the 2 analyses in the full population. The EAG said that the NMA provided the most robust results, which the company agreed with, and that the MAICs were less theoretically sound. It acknowledged that the only way to provide more certainty was to have more data.

The EAG raised another concern, that the IDH1 mutation could be an important treatment effect modifier. A post-hoc analysis of results from the VIALE-A trial (Pollyea et al. 2022) suggested a stronger treatment effect for venetoclax plus azacitidine in people with IDH1 mutation than in people without it, although the subgroup was small. In its original submission, the company did not include NMA results for the IDH1 subgroup. This was because of the difference in proportions of people with the IDH1 mutation in the AGILE trial (100%) and the comparator trials (around 20%). The company said that venetoclax was not designed to target IDH1 and its efficacy is not expected to be different in people with the mutation and those without. The EAG used the VIALE-A results to do an exploratory NMA effect estimate for overall survival in the IDH1 subgroup. This favoured venetoclax plus azacitidine over ivosidenib plus azacitidine, but the credible intervals crossed 1. The EAG noted that at consultation the company submitted results from an unanchored MAIC for overall survival in the IDH1 subgroup. It considered that these results were of limited value. At consultation the clinical expert said that they had done a further analysis of a large cohort of people who had treatment with venetoclax plus azacitidine and found no difference in survival for people with and without the IDH1 mutation. The committee acknowledged the uncertainty in the NMA, especially around the difference in treatment effect and the potential for IDH1 mutation status to affect the overall results. But it considered that the NMA results were more informative than the MAICs. The committee concluded that there was evidence to suggest that ivosidenib plus azacitidine improved overall and event-free survival compared with venetoclax plus azacitidine.

Economic model

Company's modelling approach

3.7 The company submitted a partitioned survival model with Markov components. The Markov components were the estimates of the proportion of people with CR or CRi, used to estimate modelled utility values, and the proportion moving to the long-term survival state. The model had a 25-year time horizon. It used the endpoints in the AGILE trial to inform the modelled health states: event-free (which contained a long-term survival state), progressed disease or relapse, and death. The EAG noted that model structures for NICE technology appraisals in this area varied: NICE's technology appraisal guidance on venetoclax with azacitidine for untreated AML used a Markov model while NICE's technology appraisal guidance on gilteritinib for relapsed or refractory AML used a partitioned survival model. The company explained that it had chosen to vary its approach from that used in the venetoclax guidance because:

- important elements of the model structure had been redacted from the appraisal papers so were not available for reference
- it did not have person-level data to inform the transitions for venetoclax plus azacitidine.

The committee was aware that the company's model structure differed from other models for AML but concluded that it was appropriate for decision making.

Cure assumption

3.8 In the company's original model, anyone who was still event-free at 3 years in either treatment arm stopped treatment and moved into the long-term survival state (that is, there was a cure assumption). Their risk of death was assumed to be the same as the general population from this point. No medicine acquisition, administration or concomitant medicine costs were applied to people in the long-term survival state. The EAG noted that a higher proportion of people on ivosidenib plus azacitidine entered the long-term survival state than those on

venetoclax plus azacitidine. The EAG noted that the long-term survival state produced most of the quality-adjusted life year (QALY) gain for ivosidenib plus azacitidine. The company argued that the remission rates in the AGILE trial showed a link between CR and overall survival (41% of people on ivosidenib plus azacitidine were estimated to still be alive at 3 years). It said that the plateau in overall survival in this group implied a potential 'cure'.

The company noted that in previous NICE evaluations in AML, cure assumptions have been considered. In NICE's technology appraisal guidance on venetoclax with low dose cytarabine for untreated AML and on venetoclax with azacitidine for untreated AML the committee considered that the evidence for including a cure state in the model was uncertain but it was plausible that some people may be cured. NICE's technology appraisal guidance on gilteritinib for relapsed or refractory AML and on gemtuzumab ozogamicin for untreated AML also incorporated a cure assumption (at 2 to 3 years, and 5 years, respectively).

The clinical expert said that there was not enough long-term data from trials to be able to conclude what proportion of people would be functionally cured. But they said they considered that a cure was possible in a small proportion of people taking combination treatment (that is, venetoclax plus azacitidine or ivosidenib plus azacitidine), probably less than 10%. They added that it was reasonable to assume that if someone was still in remission at 3 years, then they were functionally cured. The EAG said that, if it was possible for people on ivosidenib plus azacitidine to be cured, they would expect the hazard of death to be equal to the general population. But its calculations did not show this, and the point estimate hazard of death remained higher at the end of the AGILE trial than the general population. The committee considered that, because the point estimate hazard of death at the end of the trial remained above that of the general population, it would prefer to see scenarios that increased the standardised mortality ratio (SMR). After consultation, the company increased the hazard of death in the model to above that of the general population by increasing the SMR to 1.2, in line with NICE's technology appraisal guidance on venetoclax with azacitidine. It also provided scenarios with cure points at 2, 3 and 5 years and SMRs of 1.0, 1.1, 1.2 and 2.0. It also amended the model so that only people with CR or CRi moved to the cure state, which the EAG agreed with, if the committee accepted the cure assumption was plausible. The EAG added that increasing the SMR to 1.2 provided a compromise that allowed for increased mortality despite

the 'cure' definition and it included the cure assumption in its post-consultation base case. The committee noted that, in previous NICE technology appraisals, scenarios with cure points of 2, 3 and 5 years had been considered. It considered that an assumption of a cure for people in remission was reasonable. The committee concluded that modelling based on a cure assumption of 3 years and an SMR of 1.2 was appropriate for decision making.

Stopping rule

3.9 The company's original model assumed that everyone stopped treatment at 3 years. The EAG had clinical advice that if AML responded to treatment, some people would continue the treatment beyond 3 years. It estimated from the company's model that a reasonable proportion of people would still be on treatment at 5 years. The summary of product characteristics for ivosidenib says that treatment should be continued until AML progression or until treatment is no longer tolerated. So the EAG removed the 3-year stopping rule from its base case. The clinical expert said that the stopping rule reflected what happened in clinical practice. The committee noted that the stopping rule was only relevant if the cure assumption was removed from the model. This is because if a cure assumption remains at 3 years, treatment stops at that point anyway. The committee recalled that after consultation, the company updated the model so that only people with CR or CRi moved to the cure state (see section 3.8). This meant that a small proportion of people remained in the event-free health state on treatment with no stopping rule applied. The impact on the incremental cost-effectiveness ratio (ICER) of removing the stopping rule for this group of people was small. The committee concluded that the stopping rule had little impact when the cure assumption was incorporated in the model, so the model was acceptable for decision making.

Overall survival: long-term estimates

3.10 Treatment effect data for ivosidenib plus azacitidine was only available from the AGILE trial for a median follow up of 28.6 months. So the company modelled long-term overall survival for ivosidenib plus azacitidine using a log-normal distribution. But the EAG said it had clinical advice that this produced an overall

survival estimate that was implausibly high. Also, when the company's cure assumption was applied, it increased the overall survival estimates even more. The EAG preferred to use a Weibull distribution, which it said produced more plausible estimates. The committee questioned why the company had chosen the log-normal distribution. It noted that 2 out of 3 of the company's own clinical advisers had said they felt the Weibull or exponential distribution (2 of the lowest overall survival estimates) were more plausible. The company responded that it had prioritised statistical goodness of fit when choosing the appropriate extrapolation. The committee noted that at 5 years the percentage of people alive using the company's preferred log-normal curve was 33.2% and using the EAG's preferred Weibull curve it was 28.1%. At consultation, the company agreed with the EAG that the Weibull curve produced plausible long-term overall survival estimates. At the first committee meeting, the clinical expert said that it was difficult to comment on the plausibility of the 5-year survival figures when they had not been adjusted for age and the cure assumption. At the second committee meeting, they said that at 5 years, less than 10% of people were likely to still be alive, taking into account that in clinical practice most patients were aged 70 or over. The committee noted that the survival estimates did not include the cure assumption at 3 years or an SMR of 1.2. The company said that, in the model, the cure assumption meant that from 3 years, survival matched the general population but with an SMR of 1.2. The committee considered that the exponential distribution was likely to produce survival estimates that were too pessimistic. It concluded that the Weibull distribution produced the most plausible long-term overall survival estimates.

Event-free survival: long-term estimates

3.11 In its original submission, the company modelled long-term event-free survival for ivosidenib plus azacitidine using a log-normal distribution. The EAG's clinical advice was that this produced implausibly high long-term event-free survival estimates. Again, the EAG considered that the Weibull distribution produced more plausible estimates. At consultation, the company maintained that the log-normal curve was the most appropriate to estimate event-free survival. It said that estimating long-term event-free survival was a challenge because it was a composite end point, combining deaths before relapse or progression with relapse and progression events. It noted that people who were event-free for a

long time were likely to be in remission. So, the probability of an event-free survival event decreases as the proportion of people who are event-free and in remission increases. This means the initial hazard of an event is high and reduces over time. The company said that the Weibull curve did not fit this pattern. The EAG responded that, when estimating event-free survival, the plausibility of the proportion of people who are event-free later in the curve was most important. It said a curve that fitted the data well could produce implausible long-term estimates. The committee concluded that the Weibull distribution produced the most plausible long-term event-free survival estimate.

Modelling complete response with venetoclax plus azacitidine

3.12 The company estimated CR and CRi with venetoclax plus azacitidine using an equation and data from the AGILE trial. The EAG preferred to use the data available from the NMA in its base case, and queried why the company had not done the same. After consultation, the company accepted this and used the NMA data to estimate CR and CRi for venetoclax plus azacitidine.

Costs

3.13 In its original base case, the company included the following assumptions about costs:

- lower blood cell transfusion costs with ivosidenib plus azacitidine than with venetoclax plus azacitidine, based on more time in remission with ivosidenib plus azacitidine
- less time in hospital for ivosidenib plus azacitidine than with venetoclax plus azacitidine (32 days for venetoclax plus azacitidine based on a US study [Rausch et al. 2021]; hospital stay for ivosidenib is considered confidential by the company so cannot be reported here)
- relative dose intensity under 100% for both treatments based on AGILE trial data
- no costs for testing for IDH1 mutation.

The EAG's original base case included the following assumptions:

- a smaller difference in medical resource use costs (including blood cell transfusion costs) between ivosidenib plus azacitidine and venetoclax plus azacitidine because of the EAG's choice of Weibull distribution for long-term event-free survival
- time in hospital for venetoclax plus azacitidine was 14 days based on a UK study (Othman et al. 2021)
- relative dose intensity was 100% for both treatments
- no costs for testing for IDH1 mutation.

At consultation, the company revised its base case to include 100% relative dose intensity and 23 days in hospital for venetoclax plus azacitidine. The 23-day hospital stay was an average of the 2 estimates used for hospital stay from the original company and EAG base cases. The EAG maintained that a 14-day hospital stay was the most appropriate. The company argued that IDH1 mutation testing should not be included in the base case. The committee heard that there may be a need for NHS service redesign to allow for faster testing. The company maintained that it was not appropriate to include testing costs in the base case because it was already a recommended part of AML treatment. The EAG included the cost of testing in its revised base case.

The committee queried whether posaconazole increased the bioavailability of ivosidenib, as it does for venetoclax, and the implication for costs in the NHS. In the NHS, almost everyone with AML also has an azole medicine such as posaconazole as a preventative antifungal treatment. The company confirmed that case studies show that concomitant treatment with posaconazole increases the bioavailability of ivosidenib, so ivosidenib is used at a lower dose. Doses in the company base case were adjusted for concomitant posaconazole use and reduced to 250 mg for ivosidenib (instead of 500 mg) and 100 mg for venetoclax (instead of 400 mg).

The committee concluded that the following assumptions on costs were the

most appropriate:

- including the cost of IDH1 mutation testing
- assuming 14 days in hospital for venetoclax plus azacitidine at the start of treatment.

Cost-effectiveness estimates

3.14 The committee's preferred model assumptions were:

- using NMA point estimates of overall and event-free survival for ivosidenib plus azacitidine compared with venetoclax plus azacitidine (see section 3.6)
- everyone in the event-free survival state in the model with CR or CRi at 3 years is 'cured', with an SMR of 1.2 (see section 3.8)
- using the Weibull distribution to estimate long-term event-free and overall survival (see section 3.10 and section 3.11)
- including the cost of IDH1 mutation testing (see section 3.13)
- a 14-day stay in hospital for people having venetoclax plus azacitidine at the start of treatment (see section 3.13).

These model assumptions resulted in a deterministic ICER under £30,000 per QALY gained.

NICE's health technology evaluations manual 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 it will also take into account other aspects including uncaptured health benefits. The committee noted the high level of uncertainty in the company's clinical evidence and model assumptions. The committee recalled the statements from the clinical and patient experts about the need for targeted treatments for people for whom intensive

induction chemotherapy is unsuitable. It noted that ivosidenib is the first targeted treatment for AML with an IDH1 mutation, and it is administered orally and in an outpatient setting. The committee acknowledged that people with untreated AML who cannot have intensive induction chemotherapy have a poor prognosis. But it also noted the high levels of uncertainty in the evidence. The committee considered that an acceptable ICER would be below £30,000 per QALY gained. So, the committee concluded that the most likely cost-effectiveness estimate for ivosidenib plus azacitidine compared with venetoclax plus azacitidine was within the range that NICE considers a cost-effective use of NHS resources.

Other factors

Innovation

3.15 The committee considered if ivosidenib plus azacitidine was innovative. It did not identify any additional benefits of ivosidenib not captured in the economic modelling.

Severity

3.16 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a greater weight to QALYs (a severity modifier) if technologies are indicated for conditions with a high degree of severity. When taking into account the committee's preferred comparator of venetoclax plus azacitidine, both the absolute and proportional QALY shortfall estimates were not within the range that indicates a severity modifier may be considered. The committee concluded that the severity weighting did not apply.

Equality

3.17 At consultation, an equality issue was raised that, if applied, the severity modifier may disadvantage older people at the end of life. Age is a protected characteristics under the Equality Act 2010. The committee had not applied the severity modifier and was satisfied that its approach had not disadvantaged older people in this appraisal. No other equality issues were identified.

Conclusion

Recommendation

3.18 Having concluded that ivosidenib plus azacitidine is a cost-effective use of NHS resources (see section 3.14), the committee recommended it for routine use in the NHS, for treating newly diagnosed AML with an IDH1 R132 mutation in adults who cannot have standard intensive induction chemotherapy.

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 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 acute myeloid leukaemia with an IDH1 R132 mutation and the healthcare professional responsible for their care thinks that ivosidenib plus azacitidine 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 technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

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

Chair

Richard Nicholas
Vice 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.

Emilene Coventry
Technical lead

Victoria Kelly, Michelle Green
Technical advisers

Leena Issa
Project manager

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