

Midostaurin for untreated acute myeloid leukaemia

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 are 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.

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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.

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1 Recommendations

- 1.1 Midostaurin is recommended, within its marketing authorisation, as an option in adults for treating newly diagnosed acute FLT3-mutation-positive myeloid leukaemia with standard daunorubicin and cytarabine as induction therapy, with high-dose cytarabine as consolidation therapy, and alone after complete response as maintenance therapy. It is recommended only if the company provides midostaurin with the discount agreed in the [patient access scheme](#).

Why the committee made these recommendations

Treatment for acute myeloid leukaemia is chemotherapy. Evidence from a randomised controlled trial shows that people taking midostaurin with chemotherapy live longer than people taking chemotherapy alone.

There is uncertainty about the cost effectiveness of midostaurin because of problems with the economic model. But with the most plausible model assumptions and the discounted price, the cost-effectiveness estimates of midostaurin plus chemotherapy compared with chemotherapy alone are within the range that NICE normally considers a cost-effective use of NHS resources, so midostaurin is recommended.

2 Information about midostaurin

Marketing authorisation indication

- 2.1 Midostaurin (Rydapt, Novartis) is indicated 'in combination with standard daunorubicin and cytarabine induction and high-dose cytarabine consolidation chemotherapy, and for patients in complete response followed by midostaurin single agent maintenance therapy, for adult patients with newly diagnosed acute myeloid leukaemia who are FLT3 mutation-positive'.

Dosage in the marketing authorisation

- 2.2 The dose of midostaurin is 50 mg orally twice daily on days 8–21 of induction and consolidation chemotherapy cycles. For patients who have a complete response midostaurin is continued every day as single agent maintenance therapy until relapse, for up to 12 cycles of 28 days each.

Price

- 2.3 The company stated that the list price of midostaurin is £5,609.94 for 56 capsules. The company has a [commercial arrangement](#). This makes midostaurin available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee ([section 5](#)) considered evidence submitted by Novartis and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

New treatment option

People with FLT3-mutation-positive acute myeloid leukaemia would welcome a new treatment option

3.1 Acute myeloid leukaemia is a rapidly progressing form of leukaemia, often diagnosed following an emergency admission to hospital. The clinical experts explained that there are 2 main types of FLT3 mutation; ITD and TKD. The FLT3-ITD mutation is associated with poorer outcomes. The committee understood that the marketing authorisation for midostaurin is for adults with any type of FLT3-mutation-positive acute myeloid leukaemia. A patient expert stated that people with the disease have fatigue, weakness or breathlessness, memory loss, bruising, bleeding and frequent infections. Also, the diagnosis has a big emotional impact on them and their families and carers. The clinical experts explained that if the disease progresses, outcomes are likely to be poor. New treatments that could improve the chance of successfully inducing first remission would be welcomed. The committee concluded that people with untreated disease would welcome any new treatment that could improve survival and quality of life and induce remission, especially one that can be taken orally.

Clinical management

Treatment for acute myeloid leukaemia is chemotherapy

3.2 Current treatment for newly diagnosed acute myeloid leukaemia is intensive chemotherapy, for people who are well enough to have it. The clinical experts explained that the aim of intensive chemotherapy is to induce complete remission, after which people would either have consolidation chemotherapy or a stem cell transplant. The committee understood that midostaurin would be used to treat FLT3-positive acute myeloid leukaemia when given with induction

and consolidation chemotherapy, and then as maintenance monotherapy for up to 12 months. The committee concluded that established clinical management is chemotherapy (without midostaurin), and this is the relevant comparator for this appraisal.

Clinical evidence

The mean age of people in the trial is lower than in NHS clinical practice in England

3.3 The evidence for midostaurin came from RATIFY, a phase 3, multicentre, double-blind, randomised, placebo-controlled trial that included 717 patients with FLT3-positive acute myeloid leukaemia. It compared midostaurin plus intensive chemotherapy (daunorubicin plus cytarabine), followed by midostaurin monotherapy (n=360) with chemotherapy alone (n=357). The ERG noted that RATIFY only included people aged 18 to 60 years, but that a significant proportion of people with acute myeloid leukaemia are over 60. The clinical experts explained that a large proportion of patients aged 60 to 70 are eligible for treatment with intensive chemotherapy, which would increasingly be used for those over 70 as well. A clinical expert said that it would not be unreasonable to assume that the results seen in the trial would be similar for people over 60. The committee understood that the marketing authorisation for midostaurin (see section 2) is not restricted to a particular age group. It concluded that RATIFY was relevant to clinical practice in England, but that the mean age of people likely to have midostaurin in England is higher than the mean age of people in the trial.

Clinical effectiveness results

Midostaurin increases overall and event-free survival compared with chemotherapy alone

3.4 The primary outcome measure in RATIFY was overall survival. Treatment with midostaurin plus chemotherapy increased median overall survival compared with chemotherapy alone from 25.6 months to 74.7 months (hazard ratio [HR] 0.77; 95% confidence interval [CI] 0.63 to 0.95, p=0.0078). The increase in mean overall survival was smaller. The committee understood that this was because of the plateau in the Kaplan–Meier curves and the effect of stem cell transplant on

survival. Event-free survival was a secondary end point in RATIFY; the company defined an event as not achieving complete remission within 60 days of starting treatment, relapse from complete remission or death from any cause. Treatment with midostaurin plus chemotherapy increased median event-free survival compared with chemotherapy alone from 3.0 months to 8.2 months (HR 0.78; 95% CI 0.66 to 0.93, $p=0.002$). The committee concluded that midostaurin plus chemotherapy was clinically effective compared with chemotherapy alone.

Adverse effects

Midostaurin is well tolerated

- 3.5 The committee noted that, although there was an increase in exfoliative dermatitis in the midostaurin group compared with the standard care group in RATIFY, the numbers of people who had other adverse effects were similar between the 2 groups. It concluded that midostaurin was generally well tolerated.

The company's economic model

The model does not reflect clinical practice because people do not move from the relapsed state to remission

- 3.6 The company used a partitioned survival economic model with 5 health states: acute myeloid leukaemia diagnosis and induction, complete remission, relapse, stem cell transplant and death. The complete remission health state was split into 3 further substates (consolidation, monotherapy and complete remission after stopping first-line treatment). The stem cell transplant state was split into 3 tunnel states (treatment, recovery and post-stem cell transplant recovery). The company used RATIFY data in the model, and assumed that after a period equal to the length of the trial, or 80 cycles (about 6.2 years), people surviving would be cured. The ERG noted that the model did not allow for the possibility of relapsed or refractory disease responding to subsequent therapy other than stem cell transplant. People in the relapsed state did not move into the complete remission state, so they either moved into the stem cell transplant state or stayed in the relapsed state for a long time. The ERG noted that after about 10 years in the model, 15% of the people in the midostaurin group were in the relapsed health state, which was associated with high costs (about £60,000 per

year) and low quality of life (utility value of 0.53). The clinical experts stated that they would expect about 10% to 15% of people whose disease relapsed to be in complete remission after subsequent therapy. People whose disease did not respond to subsequent therapy were likely to live for only a few months. The committee agreed that in RATIFY, people whose disease relapsed after initial therapy lived for much longer than the clinical experts suggested they would in NHS clinical practice. In its exploratory analysis, the ERG added a new cured health state to the model, in which it assumed the same costs and benefits (utility value of 0.83) as the complete remission after first-line therapy health state. The ERG explored 3 analyses in which all people who were still alive entered the cured state after 80 cycles (about 6.2 years), after 3 years or when they stopped initial therapy. The committee considered that neither the company's base case nor the ERG's exploratory analyses reflected the clinical experts' description of what they would see in clinical practice. The committee concluded that, of the analyses presented by the company and the ERG, surviving patients with relapsed disease entering a cured health state after 3 years was the most appropriate to overcome the model's restriction on people in the relapsed state and to better reflect clinical practice in England.

The most plausible utility value for the relapsed health state is 0.78

3.7 In response to consultation, the company presented evidence from a study by Leunis et al. (2014). The study reported a utility value of 0.78 for people who had a relapse after initial treatment but survived for a long time afterwards. The company argued that the utility value for the relapsed health state should be no more than 0.78, and implemented a utility value of 0.655, as a midpoint between 0.78 and the company's original value of 0.53 (see [section 3.6](#)). The committee understood that this health state included people with relapsed or refractory disease and also people whose disease was in remission after subsequent treatment. It agreed that the utility value for this health state should be lower than the utility value for people whose disease was in remission after initial treatment. However, the committee considered that in the long term some people in the relapsed health state would be in remission after subsequent treatment. For example in the committee's preferred model, surviving patients with relapsed disease entered a cured health state, perhaps as a result of salvage treatment, after 3 years (see [section 3.6](#)). Therefore it concluded that 0.78 was the most plausible utility value for people in this health state.

However, the committee agreed that changing the utility value did not resolve its concerns that the model did not reflect clinical reality in England.

The costs associated with complete remission after initial therapy and stem cell transplant recovery are implausible

3.8 In its base-case model, the company used the same routine care costs as used in the [NICE technology appraisal for azacitidine for people in complete remission after first-line therapy and stem cell transplant recovery](#). The ERG noted that people in the equivalent health states in the azacitidine appraisal had poorer health than the people expected to be in these health states in the current model, and it therefore considered that the costs in the current model (about £8,000 per year) were too high. The ERG explored 3 analyses in which it assumed there were no routine care costs in the first-line therapy and stem cell transplant recovery health states after the cure point (80 cycles or about 6.2 years), after 3 years, or after patients stopped treatment. The clinical experts stated that people whose disease was in complete remission would still need to attend hospital appointments for monitoring. They also stated that the main treatment goal was to enable a stem cell transplant. People whose disease was in complete remission after stem cell transplant were likely to be seen in hospital frequently, although this would lessen over time. The committee noted that in RATIFY, 59.4% of people in the midostaurin group and 55.2% of people in the standard care group had a stem cell transplant. The clinical experts explained that they would expect more people to have a stem cell transplant in clinical practice because its use is increasing with the better health of older patients. The committee agreed that the routine care costs applied in the company's base-case model for people in the complete remission after first-line therapy and stem cell transplant recovery health states were too high. However, it considered that it was implausible that there would be no costs associated with monitoring these groups of people after a certain point, as in the ERG's exploratory analyses. The committee agreed that its preferred model was the ERG's exploratory analysis in which no health state costs were applied after the cure point either for people in complete remission after first-line therapy or for post-stem cell transplant recovery. It concluded that, of the options presented, this was the best one to overcome the model's overestimation of long-term costs following successful treatment and to better reflect clinical practice in England.

There is uncertainty about the management costs used in the relapsed health state

3.9 In the company's original model, the relapsed health state was associated with ongoing management costs of £4,884 per cycle. The committee considered that these costs were too high to be applied for the rest of a person's life in the model. The committee's preferred model structure included surviving patients with relapsed disease entering a cured health state after 3 years (see [section 3.6](#)) with the same costs as the complete remission after first-line treatment state (£659 per cycle), and zero costs applied after the cure point (see [section 3.8](#)). In response to consultation, the company amended its original base-case model by implementing management costs of £2,000 per cycle for the relapsed health state, for the rest of the person's life in the model. This cost was derived from an economic model for acute myeloid leukaemia by Wang et al. (2014). The committee understood that the relapsed health state included people with relapsed or refractory disease and also people whose disease was in remission after subsequent treatment, and that the proportion of each group would change over time. Therefore it did not agree with applying a constant figure for management costs in the relapsed health state for life. The committee understood that in its preferred model (see [section 3.6](#)), the management costs would apply for 3 years for people who had a relapse after initial treatment, until they entered the new cured health state. The committee concluded that it was plausible that management costs would be closer to £2,000 than £4,884 per cycle for the 3 years before people moved into the cured health state. However, it noted that there was uncertainty about the management costs used for the relapsed health state in the model, because the structure of the model, particularly the duration of the relapsed state, did not accurately reflect clinical practice in England.

Survival after the cure point

The survival rate after the cure point is lower than in the general population but there is uncertainty about how much lower

3.10 In the model, the company assumed that people who were alive after cycle 80 (about 6.2 years) were cured and applied the same mortality rate that would be expected in the general population, adjusted for age and sex. The ERG noted a study by Martin et al. (2011), which suggested that the mortality rate for people

who had a stem cell transplant was 4 to 9 times higher than for the general population for at least 25 years after the transplant. The clinical experts stated that they would expect mortality risk to increase following stem cell transplant, but that an overall 4-fold increase in mortality rate seemed high. The committee also noted that some people's disease may be cured by chemotherapy alone and they might be expected to have lower mortality after the cure point than people who have had a stem cell transplant. In response to consultation, the company presented analyses using a 2-fold increase in mortality rate, based on the opinions of 7 clinical experts. The committee was concerned that a standardised mortality rate was difficult for a clinical expert to estimate. This is because they would need to compare survival in people with acute myeloid leukaemia with an age-matched general population, who they may not have direct experience of treating. However, the committee was also aware that a 4-fold increase in mortality rate had been used after stem cell transplant in the NICE appraisal of inotuzumab ozogamicin for a population with a different disease (acute lymphoblastic leukaemia) and in poorer health. The committee agreed that the mortality rate for people whose disease had been 'cured', and especially for people who had a stem cell transplant, would likely be higher than the general population mortality rate. It concluded that although a 2-fold increase in mortality rate after the cure point was plausible, there was uncertainty and the true increase in mortality could be higher.

Duration of treatment

The length of treatment in the model should match the RATIFY trial

- 3.11 In the model, the company assumed that the maximum number of cycles of midostaurin monotherapy was 12, which is consistent with the RATIFY protocol and with the marketing authorisation. The ERG noted that a small number of people in RATIFY actually had up to 18 cycles of midostaurin monotherapy. It therefore increased the maximum cycle length in its base case to 18. The committee agreed that the cost data in the model should be consistent with the clinical data. It concluded that the data in the model should be taken from the trial, but noted that because of the small number of people who had more than 12 cycles, increasing the maximum cycle length to 18 had a limited effect on the ICER.

The company's original calculation of time on treatment is the most appropriate

- 3.12 In response to the ERG's clarification questions, the company changed the way it calculated the time on treatment in the model. This reduced the total amount of midostaurin that people had, and increased the amount of treatment taken in the standard care group. In its exploratory analysis, the ERG used the company's original calculation. At the committee meeting, the company stated that its original calculation was more appropriate. Therefore the committee concluded that this original calculation should be used in the model.

Utility values in the model

Age-adjusted utility values are appropriate

- 3.13 The company used utility values from literature sources, because information on health-related quality of life was not collected as part of RATIFY. It used utility values of 0.830 for the complete remission after first-line therapy state and 0.826 for the post-stem cell transplant recovery state. The ERG noted that the company had not adjusted these utility values in the model to account for health-related quality of life decreasing with age. In its base-case model, the ERG adjusted the utility values in these 2 health states for age, which the committee concluded was appropriate. In its response to consultation, the company used a different method of adjusting the utility values for age. The committee concluded that using this different method was appropriate, but it had a limited effect on the ICER.

Including adverse effects of stem cell transplant in the model is appropriate

- 3.14 The company did not reduce the utility values for adverse effects from initial or subsequent treatment, including stem cell transplant. It suggested that because it had used utility values that were specific to treatment stage, the values would already include the impact of any adverse effects. The clinical experts highlighted that graft versus host disease, a potential adverse effect of stem cell transplant, would have a significant impact on quality of life. In its base case, the ERG reduced the utility values and increased costs to account for the effects of graft versus host disease. The committee concluded that the adverse effects of

stem cell transplant should be included in the model.

Cure point

The cure point used in the model is uncertain

- 3.15 The ERG noted that the company had used a cure point of about 6.2 years (80 cycles in the model) based on the length of RATIFY, and extrapolated the survival benefit of midostaurin over standard care at this point over a lifetime. The ERG noted that this was an arbitrary assumption and explored analyses in which it changed the cure point to 5 years, resulting in a similar ICER, and 4 and 7 years, which increased the ICER over the 6.2 year base case. The clinical experts stated that they would expect anyone whose disease was still in relapse after 5 years to be cured. The committee considered that it would prefer to use the latest point at which the data showed a levelling out effect because this was more logically a point of 'cure'. However it noted that at 7 years, the trial data were based on a very small number of people and were therefore unreliable. The committee concluded that there was uncertainty about the most plausible choice of cure point, but noted that moving the cure point either earlier or later increased the ICER.

Mean age of the population in the model

The mean age of the population eligible for midostaurin is higher than the mean age of the population in the model

- 3.16 The mean age of the population entering the company's model was 45 years based on RATIFY, which excluded people over 60. The clinical experts explained that a large and increasing proportion of people aged 60 to 70 with FLT3-positive acute myeloid leukaemia would be eligible for intensive chemotherapy, and therefore eligible for midostaurin. They also suggested that 40% to 60% of people currently having intensive chemotherapy are over 60. The committee agreed that the mean age of people who would be eligible for midostaurin in NHS practice in England would likely be higher than 45 years. In its base case, the ERG used the mean age of 45. However, it presented 3 exploratory analyses in which it changed the mean age of the population entering the model to 50, 55 and 60. Increasing the mean age significantly increased the ERG's base-case ICER. The ERG pointed out that this change only

affected the life expectancy of people in the model and did not change treatment effectiveness. The committee concluded that it was likely the mean age of people eligible for midostaurin in England would be around 60. However, in its response to consultation, the company presented evidence of a lower mean age of people with FLT3-positive acute myeloid leukaemia from the Haematological Malignancy Research Network (HMRN), a large UK registry. The exact figure is academic in confidence and cannot be reported here. The committee considered that this lower mean age was plausible.

The data in the economic model should be based on RATIFY

3.17 In response to the ERG's critique of the mean age of people in RATIFY, the company did a new analysis of a single-arm phase 2 study of midostaurin, which included people with FLT3-positive acute myeloid leukaemia up to the age of 70. In the new analysis, the company used propensity score matching to compare people in the phase 2 study with historical controls. It also selectively used some of the ERG's amendments to the company's original base-case model:

- using complete response data uncensored for stem cell transplant
- reverting to its original calculation of time on treatment
- including adverse effects of stem cell transplant and

- using overall survival data from a later data cut.

The company claimed the new analysis showed that midostaurin was effective in improving overall survival for people over 60 and incorporated the data into its model. The mean age of the population entering the company's new model was 65. The company applied overall survival data from the propensity score-matched analysis of the phase 2 study to people in the model who were over 60, and overall survival data based on RATIFY to people who were 60 or under. The ERG noted that people in the historical control groups had a shorter life expectancy than people in the RATIFY standard care group. The clinical experts stated that survival rates for people with FLT3-positive acute myeloid leukaemia had improved in recent years. The committee noted that midostaurin appeared more effective in this analysis than in RATIFY, but agreed that this was likely because of the poor survival rates of people in the historical control groups. The committee also noted that this analysis was a non-randomised comparison that could be susceptible to confounding. It concluded that it should not be used in preference to the trial-based economic model with a simple and logical age adjustment.

Cost-effectiveness results

The most plausible ICER is below £30,000 per quality-adjusted life year gained

3.18 The company presented the results of deterministic analyses, which included error corrections made by the ERG and the company. It included:

- a cured health state, which people entered after stopping initial treatment (see [section 3.6](#))
- a utility value of 0.655 in the relapsed health state (see [section 3.7](#))
- no health state costs after the cure point either for people in complete remission after first-line therapy or for post-stem cell transplant recovery (see [section 3.8](#))
- management costs of £2,000 per cycle for people in the relapsed health state after stopping initial treatment and until death (see [section 3.9](#))
- a mortality rate 2 times higher than that of the general population after the cure point (see [section 3.10](#))

- a maximum of 18 cycles of maintenance therapy with midostaurin (see [section 3.11](#))
- the company's original calculation of time on treatment (see [section 3.12](#))
- the company's different method of adjusting utility values for age (see [section 3.13](#))
- adverse effects of stem cell transplant (see [section 3.14](#))
- a mean age of 60 years on entering the model (see [section 3.16](#)) and
- a patient access scheme discount.

Including the agreed patient access scheme discount, the ICER was below £30,000 per QALY gained. The exact ICER is confidential and cannot be reported here to prevent back-calculation of the discount. The company also explored the committee's preferred model assumptions in scenario analyses, incorporating:

- a utility value of 0.78 for the relapsed health state (see [section 3.7](#))
- the figure from the HMRN registry for the mean age of the population entering the model (see [section 3.16](#)) and
- a mortality rate 4 times that of the general population after the cure point (see [section 3.10](#)).

When the company incorporated all of these scenarios, the ICER was also below £30,000 per QALY gained. The committee noted that changing the cure point from 80 cycles to 4 or 7 years, which it agreed was plausible (see [section 3.15](#)), did not increase the ICER to above £30,000 per QALY gained. The committee concluded that the ICERs were within the range that NICE usually considers an acceptable use of NHS resources.

End of life

Midostaurin does not qualify as a life-extending treatment for people with a short life expectancy

- 3.19 The committee considered the advice about life-extending treatments for people with a short life expectancy in [NICE's Cancer Drugs Fund technology appraisal process and methods](#). This states that a treatment can be considered as a 'life-extending treatment at the end of life' if it is indicated for patients with

a short life expectancy, normally less than 24 months, and it offers an extension to life, normally of a mean value of at least an additional 3 months compared with current NHS treatment. The committee noted that the results of RATIFY showed that midostaurin increased life expectancy compared with standard care by more than 3 months. Therefore midostaurin met the criterion of extension to life of at least an additional 3 months. However, it noted that all the estimates of mean overall survival for people with acute myeloid leukaemia from the literature were over 24 months, except those in a study by Marnadie et al. (2013). The committee agreed that this study was not likely to be representative of the UK population because it was based on relatively old registry data from 1995 to 2002, and included people from countries where life expectancy is lower than in the UK. The committee noted that the median overall survival of people in the RATIFY standard care group was 26 months, with a higher mean value, and that this was a more relevant population because it included people with FLT3-positive acute myeloid leukaemia. One of the clinical experts highlighted another study in people with FLT3-positive acute myeloid leukaemia (Knapper et al. 2017), which reported that median overall survival for people in the control group was more than 24 months. In response to consultation, the company presented HMRN registry data. The committee considered the mean and median overall survival for people with newly diagnosed acute myeloid leukaemia, and for the subgroup of people with FLT3-positive acute myeloid leukaemia who had intensive chemotherapy. The exact figures are academic in confidence and cannot be reported here. The committee agreed that the mean overall survival better represented the whole population than the median, and that none of the means presented suggested that overall survival was below 24 months. It also noted that the total number of life years that the company's model predicted for the standard care group suggested that life expectancy was more than 24 months. Therefore midostaurin did not meet the short life expectancy criterion of less than 24 months. The committee concluded that midostaurin did not meet both of NICE's criteria and therefore was not considered a life-extending treatment at the end of life.

Innovation

Midostaurin's benefits are captured in the cost-effectiveness analysis

3.20 The company considered midostaurin to be an innovative treatment. It highlighted that induction therapy for treating FLT3-positive acute myeloid leukaemia has not changed much in the past 30 years and that midostaurin is the first targeted tyrosine kinase inhibitor that inhibits FLT3 activity. A patient expert and the clinical experts explained that there was an unmet need for a targeted treatment to improve remission rates and overall survival. The committee concluded that midostaurin would be beneficial for patients, but it had not been presented with evidence of any additional benefits that were not captured in the measurement of QALYs.

Conclusion

Midostaurin is recommended for routine use in the NHS

3.21 The committee acknowledged that there was uncertainty in the cost-effectiveness model particularly about the mean age of the population, the cure point, the mortality rate after the cure point, and the management costs in the relapsed health state. However it concluded that, with the discount agreed in the patient access scheme, midostaurin is a cost-effective use of NHS resources, and recommended it within its marketing authorisation for treating newly diagnosed FLT3-positive acute myeloid leukaemia.

4 Implementation

- 4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- 4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal 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 appraisal document.
- 4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has FLT3-mutation-positive acute myeloid leukaemia and the doctor responsible for their care thinks that midostaurin is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee C](#).

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

The [minutes of each appraisal committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

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

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Accreditation

