NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Abemaciclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy

1 Recommendations

1.1 Abemaciclib plus fulvestrant is recommended as an option for treating hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer in adults who have had endocrine therapy only if:

- exemestane plus everolimus is the most appropriate alternative to a cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitor and
- the company provides abemaciclib according to the commercial arrangement (see section 2).

Why the committee made these recommendations

This appraisal reviews the additional evidence collected as part of the Cancer Drugs Fund managed access agreement for abemaciclib plus fulvestrant for treating hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer after endocrine therapy (NICE technology appraisal guidance 579). The usual treatment for this is exemestane plus everolimus.

Additional clinical trial evidence was collected while abemaciclib plus fulvestrant was in the Cancer Drugs Fund. Some people in the trial had a higher dose of abemaciclib than would normally be used, so it is uncertain how well the drug will work in clinical

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practice. But an indirect comparison suggests that people having abemaciclib plus fulvestrant have longer before their disease progresses and live longer than people having exemestane plus everolimus.

The cost-effectiveness estimates vary. But, even with the uncertainty around the estimates, abemaciclib plus fulvestrant is considered a cost-effective use of NHS resources. Therefore, abemaciclib plus fulvestrant is recommended.

2 Information about abemaciclib with fulvestrant

Marketing authorisation indication

2.1 Abemaciclib (Verzenios, Eli Lilly) is indicated 'for the treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist'.

Dosage in the marketing authorisation

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

Price

2.3 The list price for abemaciclib is £2,950 per 28-day cycle (excluding VAT; BNF online, accessed January 2021):

- for 150 mg tablets: £1,475 per 28-tablet pack or £2,950 per 56-tablet pack
- for 100 mg tablets: £1,475 per 28-tablet pack or £2,950 per 56-tablet pack
- for 50 mg tablets: £1,475 per 28-tablet pack or £2,950 per 56-tablet pack of 50 mg tablets.

2.4 The list price for fulvestrant is £522.41 for two 250 mg/5 ml prefilled syringes of solution for injection (excluding VAT; BNF online, accessed January 2021). This equates to £1,044.82 for the first cycle, and £522.41 for subsequent cycles.

2.5 The company has a commercial arrangement (simple discount patient access scheme). This makes abemaciclib 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 considered evidence submitted by Eli Lilly, a review of this submission by the evidence review group (ERG) and responses from stakeholders. See the committee papers for full details of the evidence.

Clinical pathway

There is a population who could benefit from abemaciclib plus fulvestrant

3.1 Advanced breast cancer is an incurable condition and the aim of treatment is to delay progression and extend survival. Most people who do not need urgent treatment with chemotherapy are offered endocrine therapy as initial treatment, in line with NICE's guideline on advanced breast cancer. After initial endocrine therapy, people can have exemestane plus everolimus before progressing to chemotherapy, though adverse events limit the use of everolimus. People who have had endocrine therapy and are eligible for exemestane plus everolimus as their next treatment may instead have a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor (that is, abemaciclib, palbociclib or ribociclib) with fulvestrant. Ribociclib is recommended for routine use (see NICE's technology appraisal guidance on ribociclib) and palbociclib is available through the Cancer Drugs Fund (see NICE's technology appraisal

guidance on palbociclib). In NICE's original technology appraisal guidance on abemaciclib for advanced disease after endocrine therapy, the clinical experts explained that CDK4/6 inhibitors would not be used twice in the treatment pathway. This is because of the potential for tumours becoming resistant. The clinical experts said that the main groups of people who could benefit from abemaciclib plus fulvestrant after previous endocrine treatment for advanced disease are those whose:

- disease has progressed on or within 12 months of neoadjuvant or adjuvant endocrine therapy (because they are not eligible for CDK4/6 inhibitors with aromatase inhibitors in the NHS)
- advanced disease is progressing slowly on endocrine therapy.

They noted that, through the Cancer Drugs Fund, abemaciclib plus fulvestrant could also be offered later in the treatment pathway, after chemotherapy. The patient experts explained that it would be a backwards step if abemaciclib plus fulvestrant was not recommended for routine commissioning. The committee concluded that there is a population who could benefit from abemaciclib plus fulvestrant being routinely available.

People with advanced breast cancer value the option of a CDK4/6 inhibitor after endocrine therapy

3.2 The patient and clinical experts explained that CDK4/6 inhibitors were welcomed by patients because they can delay disease progression and so delay or avoid the need for chemotherapy. This is desirable because chemotherapy side effects can substantially reduce quality of life. Extending survival can give people valuable extra time with family and friends. The patient experts explained that exemestane plus everolimus, the comparator, was poorly tolerated and used for only a small number of people, because it has similar effects to chemotherapy on quality of life. They also noted that although abemaciclib plus fulvestrant can cause debilitating diarrhoea and other side effects, these can usually be

managed and are preferable to having chemotherapy. The committee concluded that having a choice of treatments that extend how long people live before their disease progresses and delay chemotherapy is valued by people who have already had endocrine therapy.

Having multiple CDK4/6 inhibitor options allows side effects to be managed, which is of value to patients

3.3 The patient and clinical experts explained that they would prefer having a choice of CDK4/6 inhibitors. This is because they have different side-effect profiles so it would give people the option to change to a different treatment if needed. The patient experts stated that managing side effects through having different CDK4/6 inhibitor options is crucial to maintaining quality of life and is of great importance to patients. One clinical expert further noted that ribociclib and palbociclib can cause dose-limiting neutropenia. This means that people having treatment need a week off treatment after 3 weeks, and need up-to-date blood counts to continue treatment. Abemaciclib is continuously dosed, is associated with less neutropenia and there is less of a need for up-to-date blood counts. However, it may cause diarrhoea that needs treatment. The clinical expert said that timing of treatment and managing adverse effects are factors to consider when choosing between CDK4/6 inhibitors. The committee concluded that having multiple CDK4/6 inhibitors allows adverse effects to be managed, which is of value to patients.

Clinical evidence

Data from the group starting on the licensed dose is the most relevant

3.4 MONARCH 2 is a phase 3, multinational, placebo-controlled, double-blind trial. It enrolled women with hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer whose disease had progressed on neoadjuvant or adjuvant endocrine therapy, either:

- 12 months or less from the end of adjuvant endocrine therapy or
- while having first-line endocrine therapy for metastatic disease.

Because of adverse events (diarrhoea), a protocol amendment was made after 26.6% of patients were enrolled. This changed the starting dose of abemaciclib from 200 mg to 150 mg, both twice per day. At the time of the protocol amendment anyone still on 200 mg had their dose reduced to 150 mg. In total, 446 patients were enrolled to have abemaciclib plus fulvestrant (pre-amendment: n=121, postamendment: n=325) and 223 to have placebo plus fulvestrant (pre-amendment: n=57, postamendment: n=166). The company considered it appropriate for the committee to use data from the full trial population in its decision making, rather than from separate pre- and postamendment groups, which the ERG preferred. The overall survival estimate in the full trial population differed from those for the separate pre- and postamendment groups (see section 3.5). The company provided:

- the median dose for the pre- and postamendment groups
- the median time to dose reduction and
- results from an interaction test after adjustments for multiplicity and baseline confounding factors.

These were marked confidential and cannot be reported here. The company did not believe that the outcomes in the subgroups could reasonably be attributed to the starting dose used. It stated that starting dose is not a treatment effect modifier. The company further explained that worldwide regulators have used data that included all patients. Also, clinical advice to the company was that it would be inappropriate to analyse the groups separately, or exclude patients recruited before the amendment. The clinical experts said that they would not expect abemaciclib's efficacy to differ between the 150 mg and 200 mg doses, and clinical outcomes with the 2 doses were similar in practice. A larger study of 150 mg abemaciclib plus an aromatase inhibitor, which is now

routinely commissioned, showed clear efficacy at that dosage. They also explained that a higher dose for a short time at the start of treatment was not likely to confer a long-term advantage, because CDK4/6 inhibitors work through long-term suppression of tumour growth. The ERG noted that the 150 mg starting dose is in the marketing authorisation and will be used in clinical practice. The ERG acknowledged that the sample size calculations for the postamendment population were based on safety outcomes rather than progression-free survival. However, the ERG maintained that the postamendment population was sufficiently powered to detect differences in clinical outcomes and provided methodologically robust results. The committee did not consider that the company's interaction test was sufficient evidence to support using the full trial population. It also noted that the patient baseline characteristics provided by the company were not likely to account for the difference in efficacy reported, but that not all characteristics were provided. The committee considered that the ERG had made a coherent case that the postamendment group was methodologically robust. It discussed whether there was a genuine dose effect, or whether differences between the groups were because of chance or baseline imbalances. It considered whether the differences might be greater in the placebo arm than in the treatment arm, but this was difficult to determine. The committee understood the challenges of interpreting the MONARCH 2 clinical data given the protocol amendment. It preferred to use the postamendment group data to estimate the clinical effectiveness of abemaciclib plus fulvestrant because:

- this group included only people who had the licensed dose of abemaciclib
- the trial was redesigned and adequately powered to detect a treatment effect for progression-free survival in this group.

The committee considered that excluding data from the 26.6% of people who were recruited before the amendment was justified. It concluded that

data from those recruited after the amendment, who started on the licensed dose, was more relevant than data for the full trial population

Clinical effectiveness

Abemaciclib plus fulvestrant improves progression-free survival but the improvement in overall survival is less certain

3.5 In the original NICE technology appraisal guidance for abemaciclib plus fulvestrant, abemaciclib plus fulvestrant statistically significantly improved progression-free survival compared with placebo plus fulvestrant in the full trial population. The effect of abemaciclib plus fulvestrant on overall survival was not statistically significant. It was concluded that more mature data from MONARCH 2 could resolve uncertainty around this outcome. More data from MONARCH 2 has now been collected and was analysed in June 2019. This analysis included an additional 28 months of data compared with the original appraisal:

- Median follow up was 47.70 months.
- Median progression-free survival was 16.87 months with abemaciclib plus fulvestrant compared with 9.27 months with placebo plus fulvestrant.
- Median overall survival was 46.72 months for abemaciclib plus fulvestrant and 37.25 months for placebo plus fulvestrant.

This analysis confirmed the previous progression-free survival results for the full trial population. The progression-free survival data for the pre- and postamendment groups was marked academic in confidence and cannot be reported here. The updated data from MONARCH 2 also showed that abemaciclib plus fulvestrant statistically significantly improved overall survival compared with placebo plus fulvestrant (hazard ratio 0.757, 95% confidence interval 0.606 to 0.945). The improvement in overall survival was smaller in the postamendment group than in the pre-amendment group. The company explained that it was likely that any differences in

outcomes seen when comparing subgroups were the result of differences in baseline characteristics between subgroups, and random variation. The committee agreed that the explanation for the different clinical results between the pre- and postamendment groups was uncertain. This was because it could not be determined if the differences were because of a genuine dose effect, or because of chance or baseline imbalances. It concluded that abemaciclib plus fulvestrant improved progression-free survival compared with placebo plus fulvestrant. But the improvement in overall survival was less certain in the postamendment group data, which the committee preferred (see section 3.4).

Clinical-effectiveness data from the SACT dataset is less relevant than the updated MONARCH 2 data for decision making

3.6 The company presented observational data from the systemic anticancer therapy (SACT) dataset for 876 people who had abemaciclib plus fulvestrant through the Cancer Drugs Fund:

- Median follow up was only 4.4 months, because more mature MONARCH 2 data became available, which was suitable for decision making.
- Median treatment duration was 10.2 months and the median overall survival was not reached.
- Fewer people were alive at 12 months after having abemaciclib plus fulvestrant compared with those who had treatment in MONARCH 2.

The SACT data was not included in the company's economic analysis. The company explained that the difference in the number of people alive at 12 months may be because people having treatment through the Cancer Drugs Fund were generally older and frailer than those in MONARCH 2. Also, they may have had treatment later in the pathway or when disease was more advanced. The company also highlighted that people with visceral disease may be offered abemaciclib plus fulvestrant over other CDK4/6 inhibitors because there is evidence of efficacy for this

group. The company noted that the data was immature, and since there was no comparator arm, the relative efficacy was unknown. The ERG agreed with most points and considered that MONARCH 2 was the more robust evidence source. The clinical experts agreed that the relative efficacy from MONARCH 2 was generalisable and provided the most robust clinical evidence for decision making. The committee concluded that the SACT data was too immature and that clinical-effectiveness data from MONARCH 2 was more appropriate for decision making.

Indirect treatment comparison

Data from the postamendment group from MONARCH 2 should be used to estimate the clinical effectiveness of abemaciclib plus fulvestrant

3.7 There were no trials directly comparing abemaciclib plus fulvestrant with exemestane plus everolimus. So, the company presented fractional polynomial network meta-analyses in line with the committee's preferred assumptions. These meta-analyses incorporated the updated MONARCH 2 data for progression-free and overall survival for the full trial population. The results were based on the postamendment group at technical engagement, at the ERG's request. The fractional polynomial network meta-analyses for progression-free and overall survival showed that abemaciclib plus fulvestrant improved progression-free and overall survival compared with exemestane plus everolimus for the full trial population. The ERG highlighted that progression-free and overall survival with abemaciclib plus fulvestrant were shorter in the postamendment group than for the full trial population. Considering the heterogeneity and uncertainty across the network, the size of these benefits was uncertain. The committee recalled its preference to use the postamendment group data to estimate the clinical effectiveness of abemaciclib with fulvestrant (see section 3.4). It concluded that data from the postamendment group from MONARCH 2 should be used to estimate the clinical effectiveness of abemaciclib plus fulvestrant compared with exemestane plus everolimus.

The company's economic model

Data from the postamendment group from MONARCH 2 should be used to estimate the cost effectiveness of abemaciclib plus fulvestrant

3.8 In its original submission, the company used fractional polynomial network meta-analysis data that used the full trial population from MONARCH 2 in its economic model for progression-free and overall survival (see section 3.7). The ERG was concerned that this may have overestimated the treatment effects compared with clinical practice. It emphasised that this did not fully reflect the licensed dose that would be used in clinical practice. The ERG preferred to use fractional polynomial network meta-analysis data that used the postamendment group from MONARCH 2 in the economic model. The committee was aware that the results of the model were highly sensitive to the choice of clinical-effectiveness data for abemaciclib plus fulvestrant. Also, using only the postamendment group data gave a much lower estimate of abemaciclib's clinical effectiveness compared with using the full trial population data. The committee was not persuaded that the company's approach was more appropriate, since the trial was redesigned and powered to detect an effect in progression-free survival in the postamendment group (see section 3.4). After consultation, the company used the committee's preferred postamendment data in its network meta-analysis and revised base case to estimate the clinical- and cost effectiveness of abemaciclib plus fulvestrant compared with exemestane plus everolimus. Although the company used the postamendment data in its revised base case, it maintained the view that the full trial population was also relevant when considering the efficacy of abemaciclib plus fulvestrant. The committee concluded that the postamendment group data should be used in the economic model. But it recognised that the cost-effectiveness results were highly sensitive to the choice of clinical-effectiveness data for abemaciclib plus fulvestrant. It further concluded that the uncertainty surrounding why the clinical-

effectiveness estimates differed in the postamendment and full trial population should be considered in its decision making.

The estimates of time to treatment discontinuation for abemaciclib from the MONARCH trial period and over 10 years are plausible

3.9 In the original NICE technology appraisal guidance for abemaciclib with fulvestrant there was uncertainty around how long people had treatment with abemaciclib plus fulvestrant (time to treatment discontinuation). Also, the company's model underestimated the treatment duration and therefore the treatment costs of abemaciclib plus fulvestrant. This was because the company used data from the full trial population, including those who were enrolled before the protocol amendment. Also, people on the lower dose stopped treatment less often because they had fewer adverse events. During that appraisal, the committee suggested that discontinuation should be estimated using the postamendment group data. This was because it used the lower licensed dose with fewer side effects, and more data could be collected on this outcome. In the current appraisal, the company used updated discontinuation data from the postamendment group as requested. It calculated a hazard ratio to apply to the progression-free survival curve for abemaciclib with fulvestrant to extrapolate the time on treatment beyond the available trial data from MONARCH 2. This hazard ratio was estimated by comparing the area under the extrapolated time to treatment discontinuation and progression-free survival curves from MONARCH 2 (a restricted means analysis). It presented hazard ratios estimated at 3 time points: the period covering the trial, 10 years (which it used in its base case) and over a person's lifetime. These hazard ratios are commercial in confidence and cannot be reported here. The ERG preferred the hazard ratio estimated over the trial period but considered the 10-year estimate was plausible. The committee concluded that both the company's and ERG's preferred hazard ratio estimates were plausible and took these into account in its decision making.

The time to stopping everolimus is likely to lie between that based on clinical opinion and that based on BOLERO-2 data in the modelling

3.10 In the original NICE technology appraisal guidance for abemaciclib with fulvestrant, the company estimated a hazard ratio for the time to treatment discontinuation for exemestane plus everolimus compared with progression-free survival. To do this, it used the median progression-free survival and median time to treatment discontinuation from BOLERO-2, a phase 3 randomised controlled trial comparing exemestane plus everolimus with exemestane alone. The hazard ratio was applied to the progression-free survival curve for exemestane plus everolimus generated by the fractional polynomial network meta-analysis, which was used in the model. The company's original model was not set up to model time to treatment discontinuation for exemestane and everolimus separately. This was a limitation because people tended to stop treatment with everolimus because of adverse events but continued to have exemestane. This affected cost effectiveness because everolimus is considerably more expensive than exemestane. In this appraisal, the ERG preferred to use a different approach. It calculated a hazard ratio and applied it to the fractional polynomial network meta-analysis progression-free survival curve to estimate the exemestane plus everolimus time to treatment discontinuation curve in the model. Three approaches to estimate the hazard ratio were presented by the company:

- An estimate based on the clinical opinion from the Cancer Drugs Fund review of NICE's technology appraisal guidance on ribociclib with fulvestrant for hormone receptor-positive, HER2-negative, advanced breast cancer – this assumed that 20% of people stopped everolimus after 6 months, and 70% of those remaining on treatment had a dose reduction (10 mg to 5 mg) but continued exemestane until disease progression.
- An approach using median data from BOLERO-2, which resulted in a hazard ratio of 1.58: the committee noted that the same approach had

also been presented in the Cancer Drugs Fund review of ribociclib plus fulvestrant.

- A restricted mean analysis of BOLERO-2 data to determine the progression-free survival and time to treatment discontinuation relationship: This assumed that progression-free survival and time to treatment discontinuation could be fitted on an exponential curve. The hazard ratio is commercial in confidence and cannot be reported here but the company stated that it was between the estimated hazard ratios for the other approaches.

The committee noted that the committee for the ribociclib plus fulvestrant appraisal stated its preference for the time to stopping everolimus hazard ratio as likely lying between clinical expert opinion and the BOLERO-2 scenario. The clinical experts for the current appraisal noted that the change at 6 months seemed implausible because people would be more likely to stop gradually throughout the first 6 months. The committee said that BOLERO-2 data, even if not based on individual patient data from the trial, was preferable to the opinion of 1 clinician. It also noted, however, that BOLERO-2 is an old trial in which many had pretreatment with chemotherapy. So, a shorter treatment duration may be expected for people having exemestane plus everolimus in current clinical practice. The committee noted the ERG's concerns that the company's third restricted means approach was flawed because it assumed that the data could be fitted on an exponential curve and could underestimate the hazard ratio. The committee was aware that the results of the economic model were highly sensitive to the assumption used to estimate the time to treatment discontinuation for exemestane plus everolimus. It concluded that time on treatment was likely to be between that estimated by the clinicians and that estimated by median data from BOLERO-2.

Fulvestrant administration costs can be reduced in primary care but it is not appropriate to assume this

3.11 The company's base case used administration costs for fulvestrant based on costs used in NICE's technology appraisal guidance on ribociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer. The company also did a scenario analysis in which it assumed that fulvestrant injections are administered by community nurse specialists at a lower cost rather than in secondary care. It also excluded the initial loading dose. The clinical experts agreed that this does not happen in clinical practice, and people have fulvestrant in secondary care. The committee concluded that the company's base-case assumptions on fulvestrant administration cost were appropriate.

Cost-effectiveness results

Abemaciclib plus fulvestrant is likely to be cost effective

3.12 The cost-effectiveness estimates included patient access scheme discounts for abemaciclib and everolimus, and the NHS England price for generic fulvestrant. The exact incremental cost-effectiveness ratio (ICER) cannot be reported here because of the confidential prices. The committee noted that there were a range of ICERs presented, which reflected the range of assumptions about time on treatment with abemaciclib plus fulvestrant and exemestane plus everolimus. It considered these plausible. The range included estimates that were above and below £30,000 quality-adjusted life years (QALYs) gained. Also, the ICER was primarily driven by assumptions about time on treatment with exemestane plus everolimus. The committee noted:

- There were ICERs within the range that NICE considers a cost-effective use of NHS resources, although there were uncertainties in the cost-effectiveness estimates.

- The patient and clinical expert statements that abemaciclib plus fulvestrant is needed as an alternative to the other available CDK4/6 inhibitors, ribociclib and palbociclib, to allow management of adverse effects.
- The scope of the Cancer Drugs Fund review was to compare abemaciclib plus fulvestrant with exemestane plus everolimus in practice. However, since the availability of CDK4/6 inhibitors, the use of exemestane plus everolimus is decreasing, and abemaciclib will be largely used as an alternative to ribociclib and palbociclib. Therefore, the overall cost to the NHS was not expected to increase if abemaciclib were recommended.
- The postamendment data was appropriate for decision making. However, there was unresolved uncertainty as to why the estimates of overall survival were lower using postamendment data to those using data from the full trial population from MONARCH 2. If the full trial data had been used to estimate overall survival in the economic model, the ICER would have been expected to be lower.

The committee concluded that, taking into account the uncertainty around the ICER estimates, it was plausible that abemaciclib plus fulvestrant could be a cost-effective use of NHS resources. It also concluded that the treatment met a need for an alternative CDK4/6 inhibitor treatment.

Other factors

3.13 NICE's advice about life-extending treatments for people with a short life expectancy did not apply.

Conclusion

Abemaciclib plus fulvestrant is recommended for routine use

3.14 The committee noted that some combinations of plausible assumptions gave ICERs over £30,000 per QALY gained. However, these combinations did not take into account the difference in survival between

the whole trial and postamendment populations. Taking into account the whole trial population, survival estimates would have lowered the ICERs. Noting the uncertainty introduced by this issue, the committee concluded that it was likely that abemaciclib plus fulvestrant was a cost-effective use of NHS resources. It also concluded that it met a need for an alternative CDK4/6 inhibitor treatment. It therefore recommended abemaciclib plus fulvestrant for treating hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer in adults who have had endocrine therapy, only if exemestane plus everolimus is the most appropriate alternative to a CDK4/6 inhibitor.

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 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 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 fast track appraisal), at which point funding will switch to routine commissioning budgets. The NHS England and NHS Improvement 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 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.

4.4 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 hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer after endocrine therapy and the doctor responsible for their care thinks that abemaciclib with fulvestrant is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Review of guidance

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

Jane Adam
Chair, appraisal committee
July 2021

6 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 A. The names of the members who attended are in the minutes of the appraisal committee meeting, which are posted on the NICE website.

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.

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.

Sue Harnan, Summaya Mohammad
Technical leads

Emily Eaton Turner, Mary Hughes
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