NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using niraparib in the NHS in England. The appraisal committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts and patient experts.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the consultees and commentators for this appraisal and the public. This document should be read along with the evidence (see the committee papers).

The appraisal committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: August 2021

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The appraisal committee will meet again to consider the evidence, this appraisal consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final appraisal document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using niraparib in the NHS in England.

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 17 September 2021

Second appraisal committee meeting: 05 October 2021

Details of membership of the appraisal committee are given in section 7

1 Recommendations

1.1 Niraparib is recommended as an option for treating relapsed, platinum-sensitive high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer in adults. It is recommended only if:

- they have a BRCA mutation and
- have had 2 courses of platinum-based chemotherapy and their disease has responded to the most recent one and
- the company provides it according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with niraparib that was funded by the Cancer Drugs Fund before final guidance was published. If this applies, when that funding ends niraparib will be funded by the company until the patient and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

This appraisal reviews the additional evidence collected as part of the Cancer Drugs Fund managed access agreement for niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer (NICE technology appraisal guidance 528).

Niraparib improves how long people with a BRCA mutation live before their disease progresses and new evidence suggests it may also extend how long these people live.

Cost-effectiveness estimates for niraparib in this population are in the range usually considered a cost-effective use of NHS resources. Therefore, niraparib is recommended for people with a BRCA mutation whose disease has responded to 2 courses of platinum-based chemotherapy.

Although niraparib also improves how long people without a BRCA mutation live before their disease progresses, it is uncertain if niraparib increases how long people live in this population. Because it is uncertain if people without a BRCA mutation live

longer than 3 months, niraparib does not meet NICE's criteria for a life-extending treatment at the end of life.

Cost-effectiveness estimates for people without a BRCA mutation are highly uncertain and are higher than what NICE considers cost effective. So, niraparib is not recommended for people without a BRCA mutation.

2 Information about niraparib

Marketing authorisation indication

2.1 Niraparib (Zejula, GSK) has a marketing authorisation for 'the maintenance treatment of adult patients with platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy'.

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 niraparib is £4,500 for a 58-capsule pack of 100 mg capsules; £6,750 for an 84-capsule pack of 100 mg capsules (excluding VAT; British national formulary online, accessed August 2021)

2.4 The company has a commercial arrangement (simple discount patient access scheme). This makes niraparib 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 GSK, 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.

The appraisal committee was aware that it had not been possible to resolve some key issues during the technical engagement stage. It recognised that there were remaining areas of uncertainty associated with the analyses presented and took these into account in its decision making

Treatment pathway and clinical need

There is an unmet clinical need for maintenance treatments in clinical practice, especially for people without a BRCA mutation

3.1 Relapsed ovarian, fallopian tube or peritoneal cancer is a devastating condition with limited treatment options. For people who have had fewer than 3 courses of platinum-based chemotherapy, there are no maintenance treatment available. People have multiple cycles of chemotherapy as the disease responds and relapses. The patient expert explained that chemotherapy side effects can substantially reduce a patient's quality of life and concerns about relapse and the need for repeated courses of treatment is physically and psychologically challenging. NICE recommends olaparib for maintenance treatment of relapsed platinum-sensitive ovarian, fallopian or peritoneal cancer for people with a BRCA1 or BRCA2 mutation who have had 3 or more courses of platinum-based chemotherapy. Niraparib and olaparib are both poly-ADP-ribose polymerase (PARP) inhibitors. The clinical expert explained that maintenance therapy with PARP inhibitors can delay disease progression and extend the time between platinum-based chemotherapies. Delaying disease progression may therefore delay the onset of platinum drug resistance. People with ovarian cancer that becomes platinum resistant have fewer chemotherapy regimen options available when the disease relapses and therefore have a poor prognosis.

So, treatments that avoid the need for chemotherapy are highly valued by patients and their families. Extending survival, even by only a few months can give people valuable extra time with family and friends. The clinical experts explained that several PARP inhibitors are currently available for first-line use through the Cancer Drugs Fund (see technology appraisal guidance 598, technology appraisal guidance 693 and technology appraisal guidance 673) for people with and without a BRCA mutation, but are limited to only niraparib in people without a BRCA mutation. Because PARP inhibitors would not be used more than once in the treatment pathway, the number of people who would have treatment in a relapsed disease setting may be smaller in future clinical practice (subject to the outcome of future Cancer Drug Fund reviews). The committee concluded that there is an unmet need for maintenance treatments in clinical practice, especially for people without a BRCA mutation.

Clinical evidence

Niraparib improves progression-free survival compared with placebo regardless of how it is assessed

3.2 The clinical-effectiveness evidence came from NOVA, a double-blind, randomised, placebo-controlled trial. NOVA assessed the clinical effectiveness of niraparib in people with relapsed, platinum-sensitive ovarian cancer, with and without a BRCA mutation. Patients had previously had 2 or more platinum-based chemotherapy regimens and their cancer had responded to the last regimen. In the original NICE technology appraisal guidance, niraparib showed statistically significantly improved progression-free survival compared with placebo for both subgroups (with and without a BRCA mutation). However, the effect of niraparib on overall survival was uncertain. It was concluded that more mature data from NOVA could resolve this uncertainty and provide more evidence on the relative treatment effect. More data from NOVA has now been collected, and was analysed in October 2020. This analysis included an additional 53 months of data compared with the original appraisal.

There was no updated data on progression-free survival because it was not assessed after the primary analysis. The committee recalled:

- The median progression-free survival in people without a BRCA mutation (that is, the mutation-negative group) was 9.3 months with niraparib and 3.9 months with placebo. The difference in median progression-free survival between niraparib and placebo was 5.4 months (hazard ratio [HR] 0.45, 95% confidence interval [CI] 0.34 to 0.61; p<0.001).
- For patients with a BRCA mutation (that is, the mutation-positive group), median progression-free survival was 21 months with niraparib and 5.5 months with placebo. The difference in median progression-free survival was 15.5 months (HR 0.27, 95% CI 0.17 to 0.41; p<0.001).

The committee noted that progression-free survival results differed based on how they were assessed. The committee were aware that the company model used progression free survival results assessed by an Independent Review Committee (IRC). The committee noted that any difference in benefit accrued could have a significant impact on the cost effectiveness results because time on treatment (and so the related cost) was based on investigator assessment (IA), the preferred assumption from the original appraisal of niraparib. The ERG explained that this could result in costs and benefit not being aligned in the economic modelling. The committee considered the results of the 2 alternative methods of assessing progression free survival (IA or IRC). Results are considered confidential and cannot be reported here. The committee noted niraparib increased progression-free survival compared with placebo in both treatment groups using both assessments. Both assessments showed greater clinical benefit in the mutation-positive group although the size of benefit was smaller for progression-free survival assessed by IA. The clinical expert and Cancer Drugs Fund clinical lead cautioned focusing only on the median results and explained that the hazard ratios of both IA

and IRC assessed progression-free survival were similar. The committee agreed that, because hazards were similar regardless of who assessed, the method of assessment was unlikely to be critical to decision making. However, the committee concluded that, because investigator assessment is more relevant to clinical practice, scenario analyses should explore the effect of using progression free survival assessed by IA on cost-effectiveness results.

Niraparib may improve overall survival compared with placebo for people with a BRCA mutation but survival benefit with niraparib for people without a BRCA mutation is highly uncertain

3.3 The committee recalled that median overall survival had not been reached in the original appraisal of niraparib and that survival benefit with niraparib was the main clinical uncertainty. Updated data from NOVA showed:

- Median overall survival in people without a BRCA mutation was 31.1 months with niraparib and 36.5 months with placebo. The difference in median overall survival between niraparib and placebo was 5.4 months (HR 1.1, 95% CI 0.83 to 1.46).
- Results for people with a BRCA mutation are confidential and cannot be reported.

The committee noted that NOVA was not powered to test for statistical significance for overall survival and the company and ERG explained that the results for the placebo arm are confounded by a high rate of crossover and missing data. Discontinuation from the trial was more than 80% in both niraparib and placebo arms with at least 14% missing data. As a result, only updated survival data from the niraparib arm of NOVA was used for assessment of relative effectiveness. The committee noted that despite high levels of subsequent PARP inhibitor use in NOVA the company had not attempted to adjust for this in their submission using methods such as the inverse probability of censoring weighting adjustment (IPCW). The committee was aware that a recent commentary

from a presentation at the American Society of Clinical Oncology showed this analysis was available for a previous data cut from the NOVA trial. While acknowledging the uncertainty that may be associated with this analysis because of the small sample size and a high proportion of missing data, the committee agreed that additional information about the relative improvement in overall survival which accounted for subsequent PARP use in both subgroups (with and without a BRCA mutation) would be helpful to estimate the survival benefit with niraparib compared with placebo. The clinical expert and Cancer Drugs Fund clinical lead both agreed that the progression-free survival benefit shown for niraparib is likely to translate into an overall survival benefit for people with a BRCA mutation. The evidence was less certain for those without a BRCA mutation. The committee concluded that niraparib may improve overall survival for people with a BRCA mutation but survival benefit with niraparib for people without a BRCA mutation is highly uncertain. Further analyses are needed to show survival results adjusting for cross-over to subsequent treatments.

Estimating relative effectiveness of niraparib compared with routine surveillance based on a naive comparison using Study 19 data is highly uncertain

3.4 Because of limitations in the survival data from the placebo arm of NOVA, the company used alternative data sources to estimate the relative effectiveness of niraparib compared with routine surveillance. In their original Cancer Drug Fund review submission, the company used an assumption of a progression-free survival to overall survival benefit ratio of 1:1 to estimate overall survival for people on routine surveillance as their base case . For this appraisal, they also presented 2 alternative scenario analyses, one using placebo data from the olaparib trial, Study 19, and a second using routine surveillance data from UK real world evidence published by Lord et al. 2020. The ERG preference was to use a naive comparison of niraparib data from NOVA with data from Study 19

for the routine surveillance arm. Study 19 is a double-blind, placebo-controlled, international multicentre randomised controlled trial designed to assess the safety and efficacy of olaparib in people with platinum-sensitive recurrent ovarian or fallopian tube cancer or primary peritoneal cancer with high grade serous features or a serous component. After technical engagement, the company revised its base case to use Study 19 data in alignment with the ERG. The committee noted there were differences in the patient characteristics between the subgroups in NOVA and Study 19 and that no adjustments had been attempted by the company to account for these differences. The committee concluded that the results of the naive comparison with Study 19 to estimate relative effectiveness of niraparib compared with routine surveillance were highly uncertain and agreed they would like to see the results adjusting for differences in baseline characteristics conducted for the subgroups (with and without a BRCA mutation) for the NOVA and Study 19 populations. This analysis could be a matched adjusted indirect treatment comparison or an alternative method. The choice of method should be justified and follow guidance in the NICE decision support unit technical support document 18.

The overall trial population in NOVA is not suitable for decision making

3.5 The ERG noted that the company reported results for the overall trial population, that is, presented combined data for BRCA positive and negative subgroups from NOVA. The company highlighted that the pooled population is aligned with the marketing authorisation for niraparib and that it allows survival outcomes of patients treated with niraparib to be compared with the UK-based, real-world evidence. Lord et al. 2020 published survival outcomes of people treated with standard care across 13 National Health Service trusts. This study included patients who had completed at least 2 lines of platinum-based chemotherapy with evidence of an objective disease response (complete or partial response), similar to people enrolled in NOVA. BRCA mutation status was unknown for most people in the study (84.5%), so results were not available by BRCA

status. The committee noted this was a post-hoc analysis and recalled the population included in the scope of the Cancer Drug Fund review included only people with a BRCA mutation who have had 2 lines of platinum-based chemotherapy and people without a BRCA mutation who have had 2 or more lines of platinum-based chemotherapy. The ERG explained that the median number of previous lines of therapy in Lord et al. 2020 was 3. Including people with a BRCA mutation who had 3 or more courses of chemotherapy (a population outside the scope of this appraisal) in the routine surveillance arm could overestimate the efficacy of niraparib. The clinical expert explained that although both people with and without a BRCA mutation could have niraparib, clinical trial evidence suggests considering these groups separately because prognosis is different for each subgroup. The committee concluded that the overall trial population is not suitable for decision making and that the subgroups of interest in this appraisal are people with a BRCA mutation who have had 2 lines of platinum-based chemotherapy or people without a BRCA mutation who have had 2 or more lines of platinum-based chemotherapy.

Data from the systemic anti-cancer therapy (SACT) database is less relevant than updated data from NOVA

3.6 Observational data for patients in the Cancer Drugs Fund from the SACT dataset was presented by the company but were not originally included in its economic analysis. The December 2019 data cut found that 43% (n=68) of people with a BRCA mutation and 59% (n=509) of people without a BRCA mutation had completed treatment, that is, patients had stopped treatment because of progression, acute toxicity, patient choice, or death, or because the patient did not have a treatment record entered in SACT in at least 3 months. Median follow up for overall survival was 20.3 months and 17.5 months for the BRCA mutation positive and BRCA mutation negative subgroups respectively. Median overall survival was not reached for the BRCA mutation positive subgroup, but the survival rates show that 87% were alive at 12 months, and 64% at 24 months. For the BRCA mutation negative subgroup, median overall survival was

22.6 months. The ERG highlighted that differences seen between SACT and NOVA results are likely to be because of differences between patient populations. The committee was aware that no comparator data is available from the SACT dataset. It considered alternative data sources for the comparator treatment arm such as the Study 19 placebo arm and Lord et al. 2020. The committee recalled that the observational data is not split by BRCA status (see section 3.6) and so did not consider it suitable for decision making. The ERG explained that using Study 19 placebo arm data would be comparing RCT data with non-randomised data which may underestimate the relative efficacy of niraparib because of the high heterogeneity in the patient populations. The committee agreed that although subgroup data from NOVA may not be fully reflective of NHS clinical practice, it is still the source of the most mature and robust data for niraparib. The committee concluded that data from the SACT database is less useful for decision making than updated data from NOVA.

Cost effectiveness

The company's updated model is suitable for decision making

3.7 The committee considered the preferred committee assumptions from the original appraisal of niraparib. It recalled that variation in the cost-effectiveness estimates was largely dependent on choice of survival curves to model progression-free survival and ratio of the progression-free survival to overall survival benefit used to estimate overall survival. The committee in the original appraisal of niraparib had concluded that there was a plausible potential for niraparib to be cost effective, and that updated survival data from NOVA could reduce the uncertainty and produce more reliable cost-effectiveness estimates using the original economic model. It had accepted the company's means-based model, noting that the choice of model structure was not critical to decision making, because the company had explored other model structures such as the partitioned survival model and stated that results did not differ by much. The ERG considered the company's means-based model structure

to be inappropriate now that mature survival data from NOVA is available and considered that a partitioned survival model should be used to validate results of the company model. The committee agreed that a partitioned survival model would be more suitable considering mature overall survival data is available. It would have preferred that the company's original partitioned survival model was validated by the ERG and the impact of model structure on the updated results explored. However, on balance the committee concluded that that the company's updated means-based model was suitable for decision making.

The company's approach to modelling survival is suitable for people with a BRCA mutation

3.8 The committee recalled that the progression-free survival data was unchanged for this Cancer Drug Fund review but that the terms of engagement outline that survival modelling should consider both statistical and visual fit of parametric and flexible spline models for modelling progression-free survival data and for the company to fully investigate the most appropriate overall survival modelling using updated clinical trial data. After technical engagement, for people with a BRCA mutation the ERG and company agreed on using the same survival curves to extrapolate progression-free (a flexible hazard k=1 curve) and overall survival (lognormal distributions) to extrapolate data from Study 19 for the routine surveillance arm and updated overall survival data from NOVA for the niraparib arm.The committee recalled their conclusion that there was progression free survival benefit with niraparib in this subgroup (see section 3.2) and a possible benefit in overall survival (see section 3.3). It agreed that the approach used by the ERG and company to model survival was suitable. The committee noted it would have preferred to see adjustments for cross over and baseline characteristics for people with a BRCA mutation but that these analyses were unlikely to affect the cost effectiveness results significantly. The committee concluded that the company's approach to modelling survival is suitable for people with a BRCA mutation.

The extrapolation of progression-free survival for people without a BRCA mutation is not critical to decision making

3.9 The company used a flexible normal k=1 curve to estimate progression-free survival beyond the trial period for people without a BRCA mutation. The ERG preferred a more conservative curve (flexible hazard k=1) which was considered more clinically plausible. The committee noted that the estimates from the two curves were almost identical but that the company's normal k=1 had a better statistical fit. The committee also noted that the long-term estimates from the hazard k=1 curve were more aligned with the BRCA mutation positive subgroup from 15 years onwards. The committee concluded that the choice between these extrapolations of progression-free survival for people without a BRCA mutation is not critical to decision making.

Estimating overall survival for people without a BRCA mutation will depend on updated data adjusted for cross-over and baseline differences

3.10 The company had agreed with the ERG's preferred approach to estimate overall survival for routine surveillance after technical engagement. They agreed to use overall survival data from Study 19 for the routine surveillance arm and updated overall survival data from NOVA for the niraparib arm. However, the committee recalled that the survival benefit in the BRCA negative group was uncertain and that it would like to see the results of adjusting for differences in baseline characteristics (see section 3.4) and analyses to account for crossover to PARP inhibitors. The committee also noted that, given the uncertainty around survival, a conservative scenario should be presented which assumes no overall survival benefit for those without a BRCA mutation. The committee agreed this would show the highest cost-effectiveness estimate and allow it to understand the range of possible results. The committee concluded that the correct approach to model survival for people without a BRCA mutation will depend on updated data, and that the company should fully investigate the most appropriate overall survival modelling using the updated analyses which adjust for cross-over and baseline differences.

Both treatment specific and health-state based utility values would be considered by committee

3.11 The company used treatment-specific utility values based on mapped EQ-5D-3L data from NOVA in its original submission for niraparib. For the Cancer Drug Fund submission, the company updated the treatment-specific utility values using the later 2020 data cut from NOVA. The company noted that these utilities reflected a higher quality of life on niraparib compared with routine surveillance. The higher utility values may reflect lower symptom burden from previous chemotherapy. The ERG preferred health-state utilities based on progression status because it did not think that niraparib would be associated with better health-related quality of life because the adverse event rate was higher for niraparib compared with placebo. The clinical expert and Cancer Drugs Fund clinical lead noted that utilities may improve on niraparib as it may improve clinical response for people with partial response to treatment. The company explained that niraparib has a positive effect on the mental health of patients having an active treatment that delays progression of disease instead of a "wait and watch" approach. They noted that this benefit was not captured in the trial data because of the double-blind nature of NOVA and was not incorporated in the utilities and economic model. The committee were aware the company had completed a mixed linear regression analysis to explore if niraparib was associated with improved quality of life but had not seen these analyses. Consequently, the committee was unable to take this into account in its decision making and concluded that it would continue to consider both treatment specific and health-state based utility values for the cost-effectiveness analyses.

Niraparib dose in the economic model should reflect prescribed dose

3.12 The company amended the mean cost for niraparib based on updated dose data from the latest NOVA data-cut (the company used the prescribed dose in the original appraisal of niraparib). The dose used by the company in the Cancer Drug Fund review was based on actual dose consumed (dispensed dose minus returned dose per cycle) and reflected

treatment doses returned by patients to the investigator during the trial. In its original appraisal, the committee preferred to use the prescribed dose as a weighted average. The committee considered that prescribed niraparib doses are unlikely to be returned to the NHS and reused. This view was supported by the Cancer Drugs Fund clinical lead, and the committee concluded that using prescribed dose (as used in the ERG preferred base case) reflects natural wastage that will happen in clinical practice and should be used to calculate the cost of niraparib treatment.

Dose used in the model should reflect the dose of niraparib in the summary of product characteristic (SmPC) and NOVA

3.13 The prescribed dose used in NOVA as specified in the SmPC for niraparib is 300 mg. The clinical expert explained that some clinicians favour starting treatment with a lower 200 mg dose of niraparib in clinical practice because it is associated with reduced toxicity and treatment stopping rates. The response to the lower dose is expected to be sustained and similar to the 300 mg higher dose. The committee noted that the company produces 100 mg capsules to account for this change in clinical practice but also noted that the benefits accrued from niraparib should align with the treatment costs from NOVA. It concluded that the dose used in economic model should reflect the dose of niraparib in the SmPC and NOVA.

End of life

Life expectancy for people without a BRCA mutation is uncertain and not shown to be less than 24 months without niraparib

3.14 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. It noted that the company had made a case for applying the end-of-life criteria to the subgroup of people without a BRCA mutation who have had 2 or more lines of platinum-based chemotherapy for people with short life expectancy (normally less than

24 months). The committee considered the alternative sources of evidence which provided estimates for life expectancy without niraparib for people without a BRCA mutation. It considered that the results from these sources were highly uncertain as they contained populations which were heterogenous. The committee recalled that Lord et. al. included people with a BRCA mutation who had 3 or more courses of chemotherapy (see section 3.5) and were likely to have a poorer prognosis than people in earlier stages of treatment. The committee accepted that the company's model was suitable for decision making (see section 3.7) and noted that the estimated life expectancy with routine surveillance in the company's base-case analysis was greater than 2 years. The committee was not persuaded that the average life expectancy for people without a BRCA mutation had been shown to be less than 24 months without niraparib treatment. It concluded that the criterion for short life was not met.

Extension to life by more than 3 months with niraparib for people without a BRCA mutation is uncertain

3.15 The committee recalled that the survival benefit for people without a BRCA mutation was uncertain (see section 3.4). Additional analyses were needed to adjust for subsequent treatment use and differences in base line characteristics. The committee concluded that it is uncertain if niraparib would extend life by more than 3 months compared with routine surveillance. So, it is currently uncertain if niraparib meets the extension to life criteria.

Cost-effectiveness results

The estimates for people with a BRCA mutation are within the range considered a cost-effective use of NHS resources

3.16 The company's incremental cost-effectiveness ratios (ICERs) for people with a BRCA mutation was £22,185 per quality-adjusted life year (QALY) gained. Taking the ERG's preference for health-state utilities and use of

prescribed dose of niraparib into account, the ICER was £27,339 per QALY gained. These ICERs are within the range normally considered to be a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained). The committee concluded that, for people with a BRCA mutation, niraparib could be recommended for routine commissioning for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer.

The estimates for people without a BRCA mutation are uncertain and currently outside the range considered a cost-effective use of NHS resources

3.17 The company's ICER for people with a BRCA mutation was £39,608 per QALY gained. The ERG's base-case ICER considering its preferred choice of different survival curves to estimate progression-free survival and time to treatment discontinuation, preference for health-state utilities and use of prescribed dose of niraparib was £51,684 per QALY gained. NICE's guide to the methods of technology appraisal 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 consider the degree of certainty around the ICER and whether the technology meets the criteria for special consideration as a 'life-extending treatment at the end of life'. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted the high level of uncertainty for people without a BRCA mutation specifically regarding the clinical effectiveness (see section 3.4) and appropriate survival modelling approach (see section 3.10). As the end-of-life criteria were not met for people without a BRCA mutation and the ICERs presented were highly uncertain, the committee concluded that it could not recommend niraparib for routine use in the NHS for people without a BRCA mutation because it was not presented with evidence that showed that niraparib was a cost-effective use of NHS resources.

Cancer Drugs Fund

Niraparib cannot be recommended in the Cancer Drugs Fund

3.18 The aim of a Cancer Drugs Fund guidance review is to decide if the drug can be recommended for routine use. Niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer may not remain in the Cancer Drugs Fund once the guidance review has been completed (see section 6.19 of the guide to the processes of technology appraisal).

Other factors

3.19 The following analyses would help to resolve the uncertainty around the survival benefit of niraparib for people without a BRCA mutation:

- Exploring progression-free survival assessed by investigator and its effect on cost effectiveness results
- Adjusting for the high levels of subsequent PARP inhibitor use in NOVA using methods such as the IPCW
- Adjusting for baseline differences in the NOVA and Study 19 populations using methods outlined in NICE decision support unit technical support document 18, such as an matching-adjusted indirect comparison
- Investigating the most appropriate overall survival modelling using updated analyses adjusting for cross-over and baseline differences
- Modelling the niraparib arm assuming no overall survival benefit compared to routine surveillance.

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 relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer and the doctor responsible for their care thinks that niraparib is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Proposed date for review of guidance

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

Brian Shine
Chair, appraisal committee
August 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.

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.

Sana Khan

Technical lead

Lorna Dunning

Technical adviser

Thomas Feist

Project manager

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