

**NATIONAL INSTITUTE FOR HEALTH AND CARE  
EXCELLENCE**

**Final appraisal determination**

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

**1 Recommendations**

1.1 Niraparib is recommended for use within the Cancer Drugs Fund as an option for treating relapsed, platinum-sensitive high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer that has responded to the most recent course of platinum-based chemotherapy in adults, only if:

- they have a germline BRCA mutation and have had 2 courses of platinum-based chemotherapy or
- they do not have a germline BRCA mutation and have had 2 or more courses of platinum-based chemotherapy  
and
- the conditions in the managed access agreement for niraparib are followed.

1.2 This recommendation is not intended to affect treatment with niraparib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

## Why the committee made these recommendations

People with relapsed, platinum-sensitive high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer have a high unmet clinical need because the disease has a poor prognosis and chemotherapy is the only available treatment for many people. Niraparib appears to be a promising treatment for this disease. Olaparib may be another treatment option, but it is only recommended for people with a BRCA mutation who have had 3 or more courses of platinum-based chemotherapy.

A clinical trial shows that niraparib extends progression-free survival compared with routine surveillance, but the final results on overall survival are not available yet. Therefore, it's not clear whether niraparib will increase the length of time people live. Because of the uncertainty in the clinical evidence, the estimates of cost effectiveness are very uncertain. Therefore niraparib cannot be recommended for routine use in the NHS.

If niraparib increases the length of time people live, it may have the potential to be cost effective in 2 groups: people with a germline BRCA mutation who have had 2 courses of platinum-based chemotherapy, or people who do not have a germline BRCA mutation and have had 2 or more courses of platinum-based chemotherapy. More evidence is needed to address the uncertainties in the clinical and cost effectiveness for these groups. Niraparib is therefore recommended for use within the Cancer Drugs Fund as an option for treating relapsed, platinum-sensitive ovarian cancer in these 2 groups while further data are collected.

## 2 Information about niraparib

<b>Marketing authorisation indication</b>	Niraparib (Zejula, Tesaro) has a marketing authorisation in the UK 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'.
<b>Dosage in the marketing authorisation</b>	300 mg, taken orally, once daily until disease progression.
<b>Price</b>	£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 March 2018).  The pricing arrangement considered during guidance development was that the company had agreed a patient access scheme with the Department of Health and Social Care. This scheme would provide a simple discount to the list price of niraparib with the discount applied at the point of purchase or invoice. The level of the discount was updated during the appraisal and is commercial in confidence. The Department of Health and Social Care considered that this patient access scheme would not constitute an excessive administrative burden on the NHS. The managed access agreement agreed between the company and NHS England will replace this patient access scheme.

## 3 Committee discussion

The appraisal committee (section 7) considered evidence submitted by Tesaro and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

### ***Clinical need and current management***

#### **People with ovarian cancer have a high unmet clinical need**

- 3.1 The patient expert explained that relapsed ovarian, fallopian tube or peritoneal cancer is a devastating condition with a poor prognosis. It is of great importance to patients and their families that new and innovative treatments that extend and improve quality of life are available. The patient expert emphasised that any extension to life is incredibly precious.

The clinical and patient experts also explained that UK survival rates for ovarian cancer are among the worst in western Europe. Possible reasons for this include late diagnosis of ovarian cancer in the UK and a tendency for more radical surgical techniques and greater access to other drug treatments in other countries. The committee concluded that patients with ovarian cancer have a high unmet clinical need.

**People with ovarian cancer will welcome a new treatment option that extends periods of remission and improves quality of life**

3.2 The committee noted that olaparib, a poly-ADP-ribose polymerase (PARP) inhibitor, is another maintenance treatment for relapsed platinum-sensitive ovarian cancer, but that NICE found this to be cost effective only for [people with BRCA 1 or BRCA 2 mutations who have had 3 or more courses of platinum-based chemotherapy](#). For people who have had fewer than 3 courses of platinum-based chemotherapy, or who have had 3 or more courses but do not have BRCA 1 or BRCA 2 mutations, chemotherapy is the only available active treatment. The clinical and patient experts explained that the chemotherapy regimens used have multiple and debilitating side effects which are a huge burden to patients and diminish their quality of life. Also, with each course of chemotherapy, there is an increased risk of resistance. Patients and clinicians therefore welcome any treatment that extends the period between courses of chemotherapy because this means longer periods in which people can lead a normal life. The clinical experts explained that PARP inhibitors such as niraparib are considered to be extremely promising and innovative new treatments. The patient expert emphasised that it would be most beneficial to patients to have niraparib as a treatment option after 2 courses of chemotherapy when they still feel relatively well, rather than after 3 courses of chemotherapy as is the case with olaparib. The committee concluded that a new treatment that extends periods of remission and improves quality of life for patients with ovarian cancer would be greatly valued by patients and their families.

### **The evidence on clinical effectiveness is relevant to clinical practice in England**

3.3 The clinical evidence came from NOVA, which was a double-blind randomised placebo-controlled trial. NOVA assessed the clinical effectiveness of niraparib in people who have relapsed, platinum-sensitive ovarian cancer, with and without a germline BRCA mutation. Patients had previously had 2 or more platinum-based chemotherapy regimens and their cancer had responded to the last regimen. The committee considered that NOVA was well conducted, and that the baseline characteristics of people in the trial were well balanced between treatment groups and represented patients who would be eligible for niraparib therapy in clinical practice in England.

### **Niraparib improves progression-free survival compared with placebo but the benefit appears to be greatest in people with a germline BRCA mutation**

3.4 Progression-free survival was the primary endpoint in NOVA. The median progression-free survival in people without a germline BRCA mutation (that is, the germline 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 germline BRCA mutation (that is, the germline 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 niraparib increased progression-free survival compared with placebo in both groups, but the greatest benefit appeared to be in the germline mutation-positive group. The clinical experts advised that having a BRCA mutation is a good predictor of response to a PARP inhibitor. The committee concluded that niraparib improves progression-free survival in people with or without a germline BRCA mutation, but the benefit appears to be greatest in people with a germline BRCA mutation.

**Results suggest progression-free survival is higher in patients with homologous recombination deficiency (HRD) positive tumours, but the HRD test is not considered reliable enough for predicting treatment benefit**

3.5 The company presented data for a germline mutation-negative subgroup of patients who had HRD-positive tumours. The difference in median progression-free survival between niraparib and placebo in the HRD-positive subgroup was 9.1 months (HR 0.38, 95% CI 0.24 to 0.59;  $p < 0.001$ ). The committee noted that this was higher than for the overall germline mutation-negative group (see section 3.4). The clinical experts explained that the results for the HRD-positive subgroup are unreliable because the 2 available tests for HRD do not reliably identify patients who would and would not benefit from therapy. HRD testing is therefore considered to be experimental and so is not routinely available within the NHS. The committee concluded that HRD testing is not reliable as a means of identifying patients who would and would not benefit from niraparib treatment, and therefore it decided against making a specific recommendation for this group.

**Overall survival data from NOVA are immature**

3.6 Fewer than 20% of patients in the intention-to-treat population of NOVA had died at the latest analysis, and median overall survival had not been reached. The committee considered whether treatment with niraparib is likely to lead to an increase in overall survival and the size of any benefit. The clinical experts advised that the progression-free survival benefit shown for niraparib would be expected to translate into an overall survival benefit, but the magnitude of this is difficult to establish. They referred to analyses from NOVA showing the time between progression after niraparib or placebo maintenance therapy, and progression after the next subsequent anti-cancer therapy. The time between the 2 points was not statistically significantly different between niraparib and placebo, indicating that the next line of treatment worked equally well regardless of whether patients had had niraparib or placebo. The clinical experts explained that there are multiple factors that could confound the overall

survival results, including the use of subsequent therapies and crossover in the trial. They also highlighted that there is a small subgroup of exceptional survivors (about 15% of patients) who are still in remission and disease-free for over 5 years with a PARP inhibitor. However, there are no methods currently available to identify these people in advance. The committee concluded that there is no reason to suppose that the overall survival benefit will be less than the progression-free survival benefit, but it is uncertain whether the overall survival benefit will be equal to or exceed the progression-free survival benefit.

**Niraparib extends the chemotherapy-free interval, but it is not known whether this influences response to subsequent platinum-based chemotherapy**

3.7 In both the germline mutation-positive and germline mutation-negative groups, there was a statistically significant increase in the chemotherapy-free interval for niraparib compared with placebo. The committee recalled that this is an important outcome for patients because of the debilitating effects of chemotherapy (see section 3.1). For the germline mutation-positive group, the median chemotherapy-free interval for niraparib was 22.8 months compared with 9.4 months for placebo (HR 0.26, 95% CI 0.17 to 0.41;  $p < 0.001$ ). For the germline mutation-negative group, the median chemotherapy-free interval for niraparib was 12.7 months compared with 8.6 months for placebo (HR 0.50, 95% CI 0.37 to 0.67;  $p < 0.001$ ). The committee considered whether prolonging the chemotherapy-free interval through maintenance treatment with niraparib could affect response to the subsequent course of platinum-based chemotherapy. The clinical experts explained that this is currently unknown and is difficult to predict with the available data. The committee concluded that niraparib extends the chemotherapy-free interval compared with placebo, but it is not known whether this influences response to subsequent platinum-based therapy. However prolonging the progression-free interval may mean that more patients would be eligible for further platinum, which is considered to be the most effective chemotherapy for this group of patients.

### ***Relative efficacy of niraparib and olaparib***

**Niraparib has not been shown to be more effective than olaparib in patients with a germline BRCA mutation, including patients who have had 3 or more courses of chemotherapy**

3.8 There is no direct trial evidence comparing niraparib and olaparib. The company therefore carried out a naive side-by-side comparison of progression-free survival for niraparib (from the NOVA trial) and olaparib (from study 19) in people with a germline BRCA mutation. The ERG considered that a naive comparison ignored the benefits of randomisation and had the same biases as a comparison of independent cohort studies. It therefore asked the company to carry out an indirect comparison of niraparib and olaparib, using placebo as the common comparator, to estimate their relative efficacy in people with BRCA mutation-positive ovarian cancer who have had 3 or more courses of chemotherapy (for whom [olaparib](#) is recommended by NICE). The company's indirect comparison included people who had had 2 or more courses of chemotherapy because it considered that this was more statistically valid. The results showed no statistically significant differences in progression-free survival between the 2 treatments, although the point estimates favoured olaparib. The committee noted that the ERG had made some adjustments to the analysis but this also showed no statistically significant differences. The committee considered that the indirect comparison provided a more robust estimate of the relative efficacy of niraparib and olaparib than the naive comparison. It concluded that niraparib has not been shown to be more effective than olaparib in people with BRCA mutation-positive ovarian cancer, including people who have had 3 or more courses of chemotherapy.

**Assumptions about the effectiveness of niraparib based on the results from study 19 are highly uncertain**

3.9 Because of the immature overall survival data for niraparib (see section 3.6), the committee understood that the company had used data



on olaparib from study 19 to make inferences about the long-term efficacy of niraparib, and it discussed whether this was appropriate. Following consultation, the committee heard from the manufacturer of olaparib that there are differences in the molecular mechanism of action between olaparib and niraparib, although both are PARP inhibitors, and differences in the safety and tolerability of the treatments. It commented that there are also differences in the design and populations of NOVA and study 19. It questioned the appropriateness of using olaparib trial data to extrapolate long-term clinical effectiveness for niraparib, particularly for post-progression survival. The manufacturer of niraparib accepted that the 2 trials did not have the same design and did not include identical populations, and that it would not expect to see exactly the same results if niraparib had been used in study 19 or if olaparib had been used in NOVA. However, the company maintained that study 19 provides the best available evidence to inform estimates of progression-free and overall survival for niraparib and that there is no rationale for considering that niraparib would be less effective than olaparib. The committee agreed with the company that study 19 is the only currently available evidence for a PARP inhibitor, but noted that direct evidence on the effectiveness of niraparib from NOVA is likely to be available in 2020. This will provide much more robust estimates of the long-term benefit of niraparib, rather than using data from a different drug in a non-identical trial. The committee considered that niraparib may prove to have similar effectiveness to olaparib, but this was as yet unproven because of the immaturity of the data. The committee concluded that assumptions about the effectiveness of niraparib based on study 19 are highly uncertain because it is not known whether the NOVA results will be similar to those from study 19.

## ***Adverse events***

### **Niraparib has a manageable adverse-event profile**

3.10 The most common adverse events with niraparib in NOVA were nausea, loss of appetite, fatigue, headache, constipation, thrombocytopenia, anaemia and neutropenia. In the niraparib arm, 74.1% of patients had a grade 3 or higher adverse event compared with 22.9% in the placebo arm. In the niraparib arm 14.7% of patients stopped treatment because of adverse events (2.2% in the placebo arm). The clinical and patient experts explained that niraparib is extremely well tolerated and adverse events tend to be manageable and short lived. Most of the haematological adverse events were identified through routine blood tests, and the patients were unaware of them. The committee concluded that niraparib has a manageable adverse-event profile.

## ***The company's economic model***

### **The choice of model structure is not critical to the decision-making**

3.11 The company presented a 3-state decision analytic model to estimate the cost effectiveness of niraparib in 3 groups of patients:

- people without a germline BRCA mutation who have had 2 or more courses of platinum-based chemotherapy (that is, the germline mutation-negative-2L+ group) compared with routine surveillance
- people with a germline BRCA mutation who have had 2 courses of platinum-based chemotherapy (that is, the germline mutation-positive-2L group) compared with routine surveillance
- people with a germline BRCA mutation who have had 3 or more courses of platinum-based chemotherapy (that is, the germline mutation-positive-3L+ group) compared with olaparib.

The model used mean progression-free survival and overall survival for each treatment, rather than modelling transitions between health states.

The costs and quality-adjusted life years (QALYs) for each treatment were

accumulated based on the mean time spent in the progression-free and progressed-disease health states. The ERG considered that the company's model structure was inappropriate and preferred a partitioned survival model approach. The committee heard that the company had explored other model structures, including a partitioned survival model, and found that the cost-effectiveness results differed by no more than £1,000 per QALY gained, as long as the same assumptions for survival were used, which was a key driver of the results. The committee accepted that the model was adequate for decision-making and that the choice of model structure was not critical.

### **The modelling of progression-free survival is very uncertain**

3.12 The choice of survival curves to model progression-free survival had a major impact on the cost-effectiveness results for the germline mutation-negative-2L+ and the germline mutation-positive-2L groups. The company and the ERG disagreed about the selection of curves and used different curves to inform their respective base-case analyses. The ERG considered that the company relied too heavily on the statistical fit of the curves, rather than clinical validity. This resulted in a curve that showed people still alive, without progression, at 20 years. The company therefore applied a 20-year cap to the curves to overcome the implausibly long tails produced by the selected distributions. The ERG preferred the choice of curves to be based on a distribution that predicted no patients remained alive and progression-free by 10 years for niraparib, and by 5 years for routine surveillance, combined with visual fit to the observed Kaplan–Meier data. However, the committee heard from the clinical experts that it is biologically plausible that patients on niraparib could survive longer than 10 years, and therefore the ERG's assumption of a cut-off at 10 years was potentially pessimistic. The committee also heard from the company that, based on a comparison with data on olaparib from study 19, the ERG's distributions underestimated the number of patients on niraparib that would be expected to be progression-free at 5 years. Also, in the company's opinion, the ERG's distributions showed a worse statistical fit.

During consultation, the company presented a scenario with alternative modelling assumptions using flexible spline models, which they considered to be a more clinically realistic view of the plausible range of cost-effectiveness estimates for niraparib. The committee welcomed this more conservative analysis but noted that the scenario did not decrease the general uncertainty around the validity of any of the extrapolations. The committee concluded that there is a progression-free survival benefit with niraparib. However the best way to model this benefit long-term, beyond the available data from the trial, is very uncertain.

### **The overall survival estimates in the model are highly uncertain**

3.13 The company estimated overall survival in the model by assuming a 2:1 ratio for overall survival and progression-free survival gain. The company explained that this was based on the relationship between overall survival and progression-free survival gain in a trial of olaparib (study 19), using mature data from a subgroup of people with a BRCA mutation. The ERG considered that the 2:1 ratio was unreliable and needed further validation. It preferred to assume that all patients, regardless of treatment, have the same post-progression risk of death (ratio of overall survival to progression-free survival of 1:1). This ratio resulted in much higher incremental cost-effectiveness ratios (ICERs) for niraparib. The clinical experts considered that the company's assumption that overall survival benefit is twice the progression-free survival benefit was likely to be optimistic, but that the size of any survival benefit was not yet known. The committee accepted that study 19 was the only currently available evidence on overall survival benefit after treatment with a PARP inhibitor. However this does not mean that NOVA will ultimately yield the same result for niraparib (see section 3.9), particularly as the subgroup from study 19 included people with a BRCA mutation, so the results may not apply to people without a BRCA mutation. Following consultation, the committee noted that the ERG had tested the validity of the company's ratio calculation using the reported medians for the BRCA mutation and wildtype-mutation subgroups. The ERG's results suggested that overall

survival benefit could actually be less than the progression-free survival benefit in the BRCA wildtype-mutation subgroup. The committee acknowledged the ERG's comments that the overall survival and progression-free survival relationship appears not to be stable between different populations and, in the absence of direct evidence, is highly uncertain. It also acknowledged that use of a ratio between overall and progression-free survival meant that the estimate of overall survival benefit was entirely dependent on the size of the modelled progression-free survival benefit, which was subject to considerable uncertainty. During consultation, the company presented a scenario analysis that assumed a 1.5:1 ratio for overall survival and progression-free survival gain, which they considered to be the minimum likely ratio. The committee welcomed the company's more conservative analysis but it noted that the scenario did not decrease the uncertainty around the overall survival estimates. Therefore the committee concluded that it is not possible to resolve the uncertainty about the overall survival benefit with niraparib until mature data from NOVA become available.

**Time to treatment discontinuation, as measured in the NOVA trial, is a better indicator of treatment length in clinical practice than progression-free survival**

3.14 The company and the ERG had different approaches to modelling time to treatment discontinuation. The assumptions used had a major impact on the cost-effectiveness results for the germline mutation-negative-2L+ group and to a lesser extent the germline mutation-positive-2L group. The company applied log-logistic and lognormal distributions for the germline mutation-negative-2L+ and the germline mutation-positive-2L groups respectively. The ERG explained that progression-free survival in the model was based on independent review-committee evaluation but time to treatment discontinuation was based on investigator assessment. Time to treatment discontinuation in the model was shorter than progression-free survival because patients could be clinically assessed to have progressed before the independent review committee reviewed the evidence. The ERG preferred to assume that time to treatment discontinuation was equal

to progression-free survival because niraparib is only stopped on disease progression or because of unacceptable toxicity. The clinical experts explained that time to treatment discontinuation in the trial would more closely reflect treatment discontinuation in clinical practice than independent retrospective assessment of progression-free survival. The committee concluded that the company's estimation of time to treatment discontinuation was more reflective of real life clinical practice and therefore the most appropriate.

### **Niraparib has not been shown to be cost effective compared with routine surveillance**

3.15 For the germline mutation-negative-2L+ group, the estimated ICERs incorporating the updated patient access scheme ranged from £23,795 (company) to £81,674 (ERG) per QALY gained. For the germline mutation-positive-2L group, the ICERs ranged from £20,694 (company's base case) to £54,632 (ERG's base case) per QALY gained. The committee considered that the results for both groups were associated with considerable uncertainty because of the immaturity of the overall survival data and uncertainty about the best way to model progression-free survival. It also considered that the ERG's estimates were likely to represent worst-case scenarios, being based on less favourable assumptions for time to treatment discontinuation, progression-free and overall survival. The committee concluded that these uncertainties could only be resolved with the availability of more mature data from NOVA. Therefore, the committee was not confident that niraparib represented a cost-effective use of NHS resources and could not recommend it for routine commissioning. However, if the company's projection of progression-free and overall survival benefit, and the company's projected ratio between them, does prove to be correct when further evidence becomes available then niraparib would have the potential to be considered cost effective.

**Niraparib is not cost effective compared with olaparib in patients with a germline BRCA mutation who have had 3 or more previous courses of therapy**

3.16 The committee recalled that niraparib has not been shown to be more effective than olaparib in people with BRCA mutation-positive ovarian cancer, including people who have had 3 or more courses of chemotherapy (see section 3.8). Therefore, the committee considered that niraparib could only be considered cost effective at the same or a lower overall cost than olaparib for this patient group. The committee noted that the total costs for niraparib estimated by the company were lower than olaparib, while the ERG estimated them to be higher. The committee recognised that the costs were uncertain because of the limited data on progression-free survival, dose received and length of treatment (see sections 3.14 and 3.15). The committee was therefore not confident that niraparib would have the same cost as or a lower overall cost than olaparib, particularly when olaparib is supplied free of charge after 15 months because the company had suggested that people could remain progression-free on niraparib for many years. The committee concluded that it could not recommend niraparib as a cost-effective use of NHS resources for people with a germline BRCA mutation who have had 3 or more previous lines of chemotherapy.

***End of life***

**End-of-life criteria for people without a germline BRCA mutation are not met**

3.17 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 germline BRCA mutation. The committee acknowledged that there are various sources of evidence that provide different estimates for life expectancy without niraparib for people without a germline BRCA mutation, and that the precise figure is uncertain. It was aware that no data on overall survival were available directly from NOVA because the

data were too immature and the median overall survival had not been reached in either arm of the trial. The committee had accepted that the company's model was suitable for decision-making (see section 3.11), and it noted that the estimated life expectancy with routine surveillance in the model was 2.87 years. The committee was therefore not persuaded that the average life expectancy for people without a germline BRCA mutation had been shown to be less than 24 months without niraparib treatment, and it concluded that the end-of-life criteria were not met.

## ***Cancer Drugs Fund***

### **Niraparib is an innovative treatment for relapsed ovarian cancer**

3.18 Having concluded that niraparib could not be recommended for routine use, the committee then considered whether it could be recommended for treating relapsed platinum-sensitive ovarian cancer within the Cancer Drugs Fund. The committee discussed the new arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting the [addendum to the NICE process and methods guides](#). The committee recognised that niraparib is an innovative treatment for relapsed ovarian cancer. It therefore considered whether clinical uncertainty associated with niraparib could be addressed through collection of additional data and maturing evidence from the NOVA trial. It agreed that:

- mature data on overall survival and progression-free survival would be a valuable addition to the clinical evidence base and likely to resolve the major uncertainties identified
- with further evidence, it may be possible to gain a more complete understanding of who would benefit most from treatment using somatic and other testing
- use in the NHS would allow collection of data on the duration of treatment in clinical practice.



## **Niraparib meets the criteria for inclusion in the Cancer Drugs Fund for treating relapsed platinum-sensitive ovarian cancer in certain groups of patients**

3.19 The committee recalled that the base-case ICERs estimated by the company for the germline mutation-positive-2L group and the germline mutation-negative-2L+ group were £20,694 and £23,795 per QALY gained respectively, compared with routine surveillance (see section 3.15). It noted that the ICERs remained within the range normally considered a cost-effective use of NHS resources (that is, £20,000 to £30,000 per QALY gained) when the company incorporated more conservative assumptions for progression-free survival and overall survival. The committee acknowledged that, despite the high uncertainty associated with the ICERs (see section 3.15), there was the plausible potential that it would be cost effective in routine use, pending the results on overall survival from NOVA. However, for the germline mutation-positive-3L+ group, the committee considered that niraparib only had the plausible potential to be cost effective in routine use at the same cost as or a lower overall cost than olaparib (see section 3.8) and therefore could not be considered for inclusion in the Cancer Drugs Fund for this population. The committee was also aware that, if niraparib was available through the Cancer Drugs Fund for patients with a germline BRCA mutation who had had 2 previous courses of chemotherapy, the small number of patients eligible for a PARP inhibitor after 3 courses of chemotherapy would have access to olaparib. The committee concluded that niraparib meets the criteria for inclusion in the Cancer Drugs Fund for treating relapsed platinum-sensitive ovarian cancer only in the germline mutation-positive-2L and the germline mutation-negative-2L+ populations.

## **4 Implementation**

4.1 When NICE recommends a treatment as an option for use within the Cancer Drugs Fund, NHS England will make it available according to the conditions in the managed access agreement. This means that, if a patient has relapsed, platinum-sensitive high-grade serous epithelial

ovarian, fallopian tube or primary 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 and the Cancer Drugs Fund criteria in the managed access agreement. Further information can be found in NHS England's [Appraisal and funding of cancer drugs from July 2016 \(including the new Cancer Drugs Fund\) – A new deal for patients, taxpayers and industry](#).

- 4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance when the drug or treatment, or other technology, is approved for use within the Cancer Drugs Fund. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, for use within the Cancer Drugs Fund, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal determination or agreement of a managed access agreement by the NHS in Wales, whichever is the latter.
- 4.3 Niraparib has been recommended according to the conditions in the managed access agreement. The Department of Health and Social Care and Tesaro have agreed that niraparib will be available to the NHS with a patient access scheme which makes it available with a discount. The patient access scheme has been incorporated into the managed access agreement. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to [NICE to add details at time of publication].

## 5 Recommendations for data collection

As a condition of the positive recommendation and the managed access agreement, the company is required to collect efficacy data from the NOVA trial.

## 6 Review of guidance

- 6.1 The data collection period is expected to end in 2020, when the final analysis of the NOVA trial is available. The process for exiting the Cancer Drugs Fund will begin at this point and the review of the NICE guidance will start.
- 6.2 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the data collection period has ended and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the standard timelines described in the [addendum](#) to NICE's methods and processes when appraising cancer technologies.

Jane Adam  
Chair, appraisal committee  
May 2018

## 7 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.

**Irina Voicechovskaja and Marcela Haasova**

Technical Leads

**Zoe Charles**

Technical Adviser

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