NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Olaparib for previously treated BRCA-mutation positive hormone-relapsed metastatic prostate cancer

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using olaparib 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?

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 olaparib in the NHS in England.

Issue date: October 2021

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

The key dates for this appraisal are:

Closing date for comments: 31 January 2021

Third appraisal committee meeting: TBC

Details of membership of the appraisal committee are given in section 5.

1 Recommendations

1.1 Olaparib is not recommended, within its marketing authorisation, for treating hormone-relapsed metastatic prostate cancer with BRCA1 or BRCA2 mutations that has progressed after abiraterone or enzalutamide in adults.

1.2 This recommendation is not intended to affect treatment with olaparib 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

Treatments for BRCA-mutation positive hormone-relapsed metastatic prostate cancer that has progressed after enzalutamide or abiraterone include docetaxel, cabazitaxel and radium-223 dichloride. In its initial evidence submission, the company restricted the treatment population to people who have already had a taxane (mainly docetaxel). This is narrower than olaparib's marketing authorisation. In its response to consultation, the company provided exploratory analyses for people who have not had a taxane.

Clinical trial evidence shows that people taking olaparib have more time before their disease progresses, and live longer overall, than people having retreatment with abiraterone or enzalutamide. However, this retreatment is not considered effective and is not standard care in the NHS.

It is uncertain how effective olaparib is compared with docetaxel, cabazitaxel or radium-223 dichloride because there is no evidence directly comparing them. An indirect comparison suggests that olaparib increases how long people who have had docetaxel live compared with cabazitaxel, but this is uncertain.

The cost-effectiveness estimates for olaparib are higher than what NICE normally considers an acceptable use of NHS resources. Therefore, olaparib is not recommended.

2 Information about olaparib

Marketing authorisation indication

2.1 Olaparib (Lynparza, AstraZeneca) is indicated 'as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and BRCA1/2-mutations (germline and/or somatic) who have progressed following prior therapy that included a new hormonal agent'.

Dosage in the marketing authorisation

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

Price

2.3 The price for olaparib is £2,317.50 per pack of 56 tablets, each containing 100 mg or 150 mg of the active ingredient (excluding VAT; BNF online, February 2021). The company has a commercial arrangement. This makes olaparib available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. 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 AstraZeneca, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence.

Treatment pathway

There is an unmet need for new treatments for hormone-relapsed metastatic prostate cancer

3.1 People with newly diagnosed hormone-sensitive non-metastatic prostate cancer are normally offered androgen deprivation therapy (ADT) or radical therapy such as surgery or radiotherapy. If the disease progresses with ADT, it is known as hormone-relapsed prostate cancer but treatment with ADT continues, either alone or with darolutamide. People with newly diagnosed hormone-sensitive metastatic prostate cancer are usually offered ADT alone, ADT with docetaxel with or without prednisone or prednisolone (from now, referred to as docetaxel), or ADT with enzalutamide. NHS England's interim guidance on treatment options during the COVID-19 pandemic allows use of abiraterone with prednisone or prednisolone (from now, referred to as abiraterone) with ADT, if enzalutamide is contraindicated or not tolerated, although this guidance is temporary. Darolutamide, enzalutamide and abiraterone are new hormonal agents. Olaparib is a poly-ADP-ribose polymerase (PARP) inhibitor. For people with hormone-relapsed metastatic prostate cancer for which chemotherapy is not yet indicated, treatment options include abiraterone or enzalutamide if neither has been used before (see NICE's technology appraisal guidance on enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated and abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated), or 'watchful waiting'. The clinical experts confirmed that people would have either abiraterone or enzalutamide only once. So, people who have had a new hormonal agent when their cancer was hormone sensitive or non-metastatic would not have it again when their cancer is hormone relapsed. After this, treatment options include:

- docetaxel

- retreatment with docetaxel for people who had docetaxel when their disease was hormone sensitive
- cabazitaxel with prednisone or prednisolone (from now, referred to as cabazitaxel) for people who have already had docetaxel
- radium-223 dichloride for people with symptomatic bone metastases and no visceral metastases, and who have already had docetaxel or cannot have it.

The patient experts explained that hormone-relapsed metastatic prostate cancer affects all aspects of their lives and is difficult for them, their families and their friends. They highlighted the need for treatments that can extend survival and help them maintain or improve their quality of life because there is no cure. They also explained that they would like more treatment options so they can delay chemotherapy (docetaxel and cabazitaxel) and its adverse effects. This is because the adverse effects, especially those of docetaxel, can be debilitating, even up to 1 year after people have stopped having it. The committee concluded that there is an unmet need for new treatments for hormone-relapsed metastatic prostate cancer.

The company's approach of considering people who have had or have not had a taxane separately is acceptable

3.2 The marketing authorisation for olaparib states that it is indicated 'as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and BRCA1/2-mutations (germline and/or somatic) who have progressed following prior therapy that included a new hormonal agent'. The company limited the population in its initial submission to people who have already had a taxane (mainly docetaxel). It chose cabazitaxel as the comparator (see section 3.3), which requires previous treatment with docetaxel. The company explained that it did this because its clinical advisers suggested that in the NHS around 75% of people have docetaxel while their disease is hormone sensitive. The ERG

agreed that most people who have abiraterone or enzalutamide will have already had treatment with docetaxel, but that this proportion is likely to be less than 75%. The clinical experts explained that having previous treatment with docetaxel is not specified in olaparib's marketing authorisation and should not be a factor when deciding who would have olaparib in NHS practice. The Cancer Drugs Fund clinical lead was disappointed with the company's initial decision to limit the population. The clinical lead explained that many people who do not choose docetaxel early in the pathway might then be unable to have it after developing hormone-relapsed metastatic disease, for example if they become too ill. At the company's initial proposed position, olaparib would never be suitable for them. The clinical and patient experts explained that they are keen to have olaparib available as early in the treatment pathway as possible, but to have it at some point is most important. The committee appreciated that limiting olaparib to people who had had docetaxel would exclude people who cannot or should not have docetaxel but who could benefit from olaparib. It was aware that these people are likely to be older and more likely to have a poorer disease performance status, comorbidities, peripheral sensory neuropathy, poor bone marrow function, poor cognition or chemotherapy contraindications (see NICE's technology appraisal guidance on abiraterone for treating newly diagnosed high-risk hormone-sensitive metastatic prostate cancer). The committee also noted that NICE's recent recommendations for darolutamide with androgen deprivation therapy for treating hormone-relapsed non-metastatic prostate cancer and enzalutamide for treating hormone-sensitive metastatic prostate cancer mean that more people would choose a new hormonal agent before docetaxel. In response to consultation, the company submitted clinical-effectiveness data and exploratory cost-effectiveness analyses for the population who had not had a taxane (see section 3.6 and section 3.22). NICE's process requires a committee to appraise a drug across its marketing authorisation rather than by subgroups. However, the committee noted there are unlikely to be common

comparator treatments for the whole licensed population (see section 3.3). Also, it noted, that the treatment options, and so the comparators, are different for people who can and cannot have, or have already had, taxanes (see section 3.3 and section 3.22). People who have not had a taxane, but can have it, would have docetaxel. People who have not had a taxane, but cannot or should not have it, would have ADT or, if suitable, radium-223 dichloride. People who have had a taxane would then have cabazitaxel, retreatment with docetaxel or, if suitable, radium-223 dichloride. Therefore, the committee concluded that the company's approach of considering these groups of people separately is acceptable.

When a taxane has been used, cabazitaxel, radium-223 dichloride, and retreatment with docetaxel are all relevant comparators

3.3 NICE's scope for this appraisal lists docetaxel, cabazitaxel and radium-223 dichloride as comparators. But the company included only cabazitaxel as a comparator for people who had had treatment with a taxane. It considered that there was not enough evidence for docetaxel and radium-223 dichloride. The ERG agreed that there is limited evidence for both docetaxel and radium-223 dichloride. The company stated that its clinical advice and data from a recent UK national audit suggested that radium-223 dichloride is often used later in the treatment pathway, once options such as cabazitaxel are exhausted. The committee recognised that this would include radium-223 dichloride as a relevant comparator because it could be used at the same position as olaparib for some people. The company highlighted that NICE's guideline on the diagnosis and management of prostate cancer does not recommend repeat cycles of treatment with docetaxel if the disease recurs after the planned course of chemotherapy is completed. It also pointed out that cabazitaxel is more likely to be used instead of docetaxel retreatment because response rates to docetaxel may decline over time. The committee was aware that retreatment with docetaxel happens in NHS practice, as documented in NICE's technology appraisal guidance on abiraterone, and as noted by stakeholders in this appraisal (see section 3.1). The clinical experts noted

that people who had already had both docetaxel and abiraterone or enzalutamide may currently be offered docetaxel again or cabazitaxel. They may also be offered radium-223 dichloride if they have symptomatic bone metastases and no visceral metastases. The committee appreciated that, in the subgroup who had had a taxane, docetaxel retreatment, cabazitaxel and radium-223 dichloride would all be alternatives to olaparib. It noted that patients and their doctor would decide which treatment is best. The committee concluded that cabazitaxel is likely to be the main, but not the only, comparator for olaparib in people who have had a taxane. It would have preferred to see exploratory analyses with radium-223 dichloride and retreatment with docetaxel because they are also relevant comparators.

In the PROfound trial, the baseline characteristics of people are generalisable to NHS practice, but the comparator treatment is not

3.4 PROfound was a phase 3, randomised, open-label, multicentre trial of olaparib compared with investigator's choice of enzalutamide or abiraterone in people with hormone-relapsed metastatic prostate cancer that had progressed on abiraterone, enzalutamide or both. The trial enrolled people with homologous recombination repair gene mutations, including BRCA1, BRCA2, ataxia-telangiectasia mutation and other mutations. It stratified them according to whether they had had taxane treatment before. The primary end point was time to disease progression determined radiographically. Overall survival was among the secondary end points. The company presented clinical evidence for the population who had BRCA mutations in line with the marketing authorisation (the licensed population). It also presented it for the subgroup of this population who had had taxane treatment before (see section 3.2; from now, referred to as the 'BRCA-mutation, prior-taxane subgroup'). The committee was satisfied that baseline characteristics from the BRCA-mutation prior-taxane subgroup, including age, Eastern Cooperative Oncology Group performance status and prostate-specific antigen level, are generalisable to people in the NHS. However, it noted that some

treatment regimens that people had had before entering the trial, such as having had both abiraterone and enzalutamide, did not reflect NHS practice. The clinical experts did not expect this to modify the treatment effect of olaparib in the trial. Clinical experts explained that retreating with abiraterone or enzalutamide has no clinical benefit and could effectively be considered a placebo. The company acknowledged that the comparator in its trial does not reflect current NHS practice. The committee concluded that baseline characteristics in PROfound were generalisable to NHS practice with the exception of some people having had both enzalutamide and abiraterone before starting the trial. It further concluded that the comparator, that is, retreating with abiraterone or enzalutamide, is not offered in the NHS.

Olaparib is more effective than retreating with enzalutamide or abiraterone but this comparison does not reflect NHS practice

3.5 In the licensed population and BRCA-mutation prior-taxane subgroup of PROfound, olaparib increased both progression-free survival and overall survival compared with investigator's choice of abiraterone or enzalutamide. The results cannot be reported here because the company considers them confidential. The committee recalled that retreating with abiraterone or enzalutamide is not expected to have a clinical benefit (see section 3.4). The committee concluded that olaparib was effective compared with enzalutamide or abiraterone in PROfound. However, it thought that the results should be interpreted with caution because the comparator arm in the trial does not reflect NHS care. The committee also concluded that any comparison of olaparib with cabazitaxel or other relevant comparators (see section 3.3) would need to use other sources of data and an indirect treatment comparison.

Previous treatment with a taxane does not appear to affect the effectiveness of olaparib in PROfound

3.6 In its response to consultation, the company submitted results from PROfound for a subgroup of people who had not had treatment with

docetaxel (see section 3.2). The results cannot be reported here because the company considers them confidential. The committee noted that, because of the inclusion and exclusion criteria in PROfound, the trial likely excluded many people who cannot or should not have docetaxel in NHS practice. The committee noted that subgroup analyses by prior taxane status for people who have BRCA mutations were not prespecified in the clinical study protocol, and therefore constitute post-hoc analysis. It also noted the small size of the subgroup of people who had not had treatment with docetaxel, and the immaturity of overall survival data in this group. It concluded that these results were highly uncertain. The committee noted that it did not see any formal testing of interaction when this group was compared with the subgroup who had had docetaxel. But it acknowledged that the clinical efficacy of olaparib in PROfound did not seem to have been affected by previous treatment with a taxane.

The company's method for adjusting for treatment switching in PROfound is appropriate, including using recensoring

3.7 The company explained that, in PROfound, most people switched from abiraterone or enzalutamide to olaparib after radiographic disease progression. The number of people who switched cannot be reported here because the company considers it confidential. The committee recognised that treatment switching biased the treatment effect for overall survival. This was because people in the control arm who switched to olaparib may have benefited from the treatment effect of olaparib and likely lived longer than if they had not switched. The company considered several different methods to adjust for treatment switching. These included the rank preserving structural failure time model (RPSFTM), inverse probability of censoring weights and 2-stage estimation. The company chose the RPSFTM because it did not depend on time-varying covariates to predict switching, did not reduce the effective sample size, and did not assume that there are no unmeasured confounders. The ERG agreed that the RPSFTM was the most appropriate method. The company did sensitivity analyses to explore and validate the assumption of a common treatment

effect in the overall trial population, but not in the BRCA-mutation prior-taxane subgroup. The company further explained that it had applied recensoring to remove any censoring bias from the treatment switching-adjusted results. Recensoring involves censoring data before the end of the trial follow-up period. This is to avoid informative censoring related to the association between prognostic factors and treatment switching. Informative censoring can happen when adjusting survival times if some people who switch treatments do not die during the trial. The committee was aware that the main limitation of recensoring is losing longer-term survival information. The ERG preferred to consider results with and without recensoring because both can bias results. One approach tends to overestimate the effect of treatment, and the other tends to underestimate it. The committee noted that, towards the end of the trial follow-up period, data from very few people contributed towards the estimates of overall survival. Therefore, in this case, recensoring did not lose a large amount of data, but avoided informative censoring. The committee concluded that the company's method for adjusting for treatment switching was appropriate, including using recensoring.

The indirect comparison of olaparib with cabazitaxel is uncertain because of differences between PROfound and CARD

3.8 The company did not find direct clinical trial evidence comparing olaparib and cabazitaxel so it did an indirect treatment comparison for progression-free survival and overall survival. It used evidence from the CARD trial, a phase 3, randomised, open-label, multicentre trial. The trial compared cabazitaxel and prednisone (from now, referred to as cabazitaxel) with enzalutamide or abiraterone in people with hormone-relapsed metastatic prostate cancer previously treated with docetaxel and either enzalutamide or abiraterone. The primary end point was radiographic progression-free survival. Secondary end points included overall survival and skeletal-related events. Clinical experts explained that the comparator in CARD was similar to PROfound, that is, people who had already had abiraterone were offered enzalutamide, and vice versa. In the company's indirect

treatment comparison, olaparib increased progression-free survival and overall survival compared with cabazitaxel. The results cannot be reported here because the company considers them confidential. The ERG highlighted several differences between the trials. It explained that all people in the subgroup of PROfound with a BRCA-mutation and prior-taxane treatment had BRCA mutations, but mutation status in CARD was unknown. A proportion of people in PROfound had had cabazitaxel (the company considers the proportion to be confidential so it cannot be reported). The ERG explained that people in CARD had not had cabazitaxel before. Also, the central review of radiographic disease progression imaging was blinded in PROfound, but open-label in CARD. The clinical experts explained that BRCA-mutation status does not affect how well cabazitaxel works. They also noted that previous cabazitaxel is unlikely to affect how well olaparib works because its mode of action is different. The ERG explained that some studies suggested BRCA-mutation status could modify treatment effect, and some suggested it does not. In NICE's technology appraisal guidance on cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel, the committee considered the TROPIC trial. This compared cabazitaxel plus prednisone with mitoxantrone plus prednisone in people with hormone-relapsed metastatic prostate cancer whose disease had progressed after docetaxel treatment. In that appraisal, the committee considered that mitoxantrone plus prednisolone was unlikely to have clinical benefits. Therefore, in this appraisal, the committee noted that mitoxantrone was similar to the control arms of PROfound and CARD. In response to consultation, the company explored if it could include TROPIC in its indirect treatment comparison. It argued that the population in TROPIC was not comparable to the population in PROfound. This was because people enrolled in TROPIC had not had treatment with abiraterone or enzalutamide, as in PROfound or CARD. It was also because there were differences in the inclusion and exclusion criteria, and comparator arms between TROPIC and PROfound. However, it did present a scenario

analysis including TROPIC, which had a small effect on cost-effectiveness estimates. The ERG agreed that TROPIC should be excluded from the indirect comparison. The committee concluded that there were differences between PROfound and CARD, which led to uncertainty in the company's indirect treatment comparison, and that the population in TROPIC was unlikely to reduce this uncertainty.

It is inappropriate to adjust for treatment switching in CARD

3.9 The company did not adjust for treatment switching in CARD as it did in PROfound. It explained that this was because it did not have access to individual patient data from CARD. In its first meeting, the committee considered that overall survival in the cabazitaxel arm in CARD may have been underestimated. This was because 33% of people in the abiraterone or enzalutamide arm switched to cabazitaxel after disease progression. The clinical experts explained that treatment switching was included in the trial protocol in PROfound, but not in CARD. The committee appreciated that this may explain why more people switched treatments in PROfound than in CARD but did not remove the risk of bias. In response to consultation, the company explained that cabazitaxel is available in the NHS and that it was inappropriate to adjust for treatment switching because the trial did not deviate from NHS practice. Adjusting would also cause an imbalance in the abiraterone or enzalutamide arms between CARD and PROfound, which would undermine the anchored indirect treatment comparison. The committee recognised that the need to adjust would also depend on whether the proportion of treatment switching in the trial reflected NHS practice. It concluded that it was inappropriate to adjust for treatment switching in CARD. However, it acknowledged that there was still some uncertainty in the size of the effect estimate comparing olaparib with cabazitaxel.

Differences between postprogression treatments in the trials and those used in the NHS affect generalisability of the trial results to NHS practice

3.10 The committee discussed treatments offered in PROfound and CARD after disease progression. It noted that these treatments did not reflect NHS practice, and that this would affect both costs of treatment (see section 3.18) and its outcomes. The company considers that the distribution of postprogression treatments in PROfound are confidential so cannot be reported here. The committee noted that life-extending treatments could have affected the hazard ratios for overall survival seen in PROfound and CARD. If these treatments were offered differently to how they are in the NHS, then the trial results (and costs) would not apply to the NHS. The committee noted that most people in PROfound and CARD had abiraterone or enzalutamide (of those people who had a postprogression treatment after cabazitaxel in CARD, 37% had abiraterone and 37% had enzalutamide). It recalled that these treatments would not offer any clinical benefit and would not be used in NHS practice (see section 3.4). Instead, people in the NHS would have access to life-extending treatments such as radium-223 dichloride. The committee noted that using radium-223 dichloride after disease progression on olaparib in PROfound was limited (the proportion is considered confidential and cannot be reported here). However, 15% of people in CARD had radium-223 dichloride after disease progression on cabazitaxel. In response to consultation, the company excluded abiraterone and enzalutamide from postprogression treatments to align with NHS practice. The company stated that it could not adjust for differences in overall survival because it did not have the data. Instead, it did scenario analyses to explore the effect that differences in postprogression treatments may have had by improving or worsening the hazard ratio for overall survival for olaparib compared with cabazitaxel by 5% and 10%. The committee noted the differences in postprogression treatments between the 2 trials and the NHS. It concluded that this further

affected the validity of company's indirect treatment comparison and its generalisability to NHS practice.

Economic model

Hazard ratios from the subgroup with BRCA-mutation and prior-taxane treatment of PROfound should be used to model outcomes on cabazitaxel

3.11 In its initial submission, the company used patient-level data from the subgroup with BRCA-mutation and prior-taxane treatment of PROfound to model the absolute rates of progression-free survival and overall survival for people having olaparib. It then applied hazard ratios for progression-free survival and overall survival from the indirect treatment comparison to that data to model the efficacy for people having cabazitaxel. However, it used hazard ratios from the licensed population, rather than from the prior-taxane subgroup. The company explained that it did this because olaparib's efficacy in the licensed population and prior-taxane populations were similar, and the former group had larger patient numbers. The committee disagreed with the company's approach in comparing a subgroup with the whole group. The committee would have preferred the company to use hazard ratios from the subgroup with BRCA-mutation and prior-taxane treatment to model comparative effectiveness with cabazitaxel. The committee considered the company's approach to be inconsistent. This was because the company had used data from the PROfound subgroup with BRCA-mutation and prior-taxane treatment for other model inputs, for example, survival, adverse events and baseline characteristics for olaparib. The committee considered it appropriate to match data used in the model to the population under consideration when possible. In its response to consultation, the company agreed with the committee and used the hazard ratios from the subgroup with BRCA-mutation and prior-taxane treatment to model survival on cabazitaxel in the prior-taxane group. The committee concluded that the revised company approach was appropriate.

The ERG's approach to extrapolating overall survival for both treatments is appropriate

3.12 PROfound reported results based on a prespecified analysis in June 2019 for the primary end point of radiological progression-free survival. At the latest data cut-off (March 2020) available for overall survival, the trial was still collecting data as planned (the exact number of events is considered confidential by the company and cannot be reported here). The company used parametric survival curves to fit the trial data and extrapolate it beyond the trial duration because the model used a lifetime horizon. The company and the ERG both considered the Gompertz curve to be appropriate to extrapolate progression-free survival and time to treatment discontinuation for olaparib. This was based on the best statistical fit to the olaparib PROfound observed data. The company originally selected the log-logistic curve to model overall survival for olaparib. The ERG emphasised that the company had applied a time-constant hazard ratio to the log-logistic model to estimate overall survival for cabazitaxel. The ERG explained that it considered this approach to be inappropriate because log-logistic models do not support proportional hazards assumptions. It thought that the resulting estimates may have overestimated survival gain with olaparib. The committee agreed with the ERG that the company had inappropriately applied a hazard ratio to a log-logistic model. The ERG explained that it had explored other models and had chosen the Rayleigh distribution for treatment with olaparib for its base case, based on the best statistical and visual fit. The committee noted that none of the parametric curves fitted the observed hazard rates for the olaparib arm from the trial well. It noted that Rayleigh, Weibull and exponential hazard function curves appeared reasonable although possibly pessimistic. In its first committee meeting, the committee asked the company to explore more flexible models to account for changes in hazard rates. In response to this, the company explored spline-based models. However, these had a poorer statistical fit than the exponential model. The company then selected the exponential curve to model overall

survival for olaparib, noting it supported the proportional hazards assumption. The ERG confirmed that spline-based models had a poorer fit than some parametric models. It also explained that these models were implausible because they have decreasing hazard rates up to and beyond 20 years when usually hazard rates increase as the population ages. The committee preferred the Rayleigh hazard function for modelling overall survival of olaparib. This was based on a better visual and statistical fit to the observed Kaplan–Meier data from PROfound. The committee concluded that the ERG's approach was appropriate.

The company's clinical survey has limitations and should not inform the plausibility of survival extrapolations for olaparib or cabazitaxel

3.13 To inform the clinical plausibility of long-term overall survival estimates for people who had olaparib or comparators, the company selected and surveyed 6 NHS clinical experts. In its original submission, the company selected the log-logistic curve to model overall survival because it reflected clinical opinion from its survey. This was despite the exponential curve having the best overall fit to the observed data. The ERG highlighted concerns with the company's survey. It explained that 3-year survival with olaparib predicted by the surveyed experts was higher than the observed survival in PROfound at 2 years. The ERG thought this was unreasonable. It also pointed out the highly varied responses between experts, indicating problems with the survey or with the clinical experts predicting survival with olaparib. The committee appreciated that because olaparib is not available in the NHS, clinicians will not have seen people who are taking olaparib, making estimating survival very difficult. The committee noted that predicted survival for cabazitaxel chosen by the company was much lower than the survival predictions for cabazitaxel suggested by the experts surveyed. It noted that the survey did not ask for survival predictions specifically for people with BRCA-mutated disease. It also noted that the company's survey of clinical experts was of limited value in terms of absolute estimates of survival. However, it thought that it may help to estimate the likely relative difference in survival between

olaparib and cabazitaxel. The committee agreed that the log-logistic curve overestimated this relative difference in survival compared with the survey results. Also, it recognised the challenges in asking clinicians to estimate survival for a drug they are not yet able to prescribe. The committee concluded that the survey had limitations and limited value in informing long-term survival estimates.

Additional evidence presented by the company is inconclusive for validating the extrapolation of overall survival

3.14 In its first committee meeting, the committee discussed the TROPIC trial (see section 3.8). It was aware that the trial did not require people to have had treatment with abiraterone or enzalutamide as in PROfound or CARD. But the committee considered that the TROPIC trial could help validate survival extrapolations because of the maturity of the overall survival data. In its response to consultation, the company did not think it was appropriate to use TROPIC to validate survival extrapolations because it enrolled people who had not yet had abiraterone or enzalutamide. The company instead used 2 sources of external data for people with hormone-relapsed metastatic prostate cancer, the Ontario Cancer Registry and the US FLATIRON database, to support its choice of the exponential curve. The company compared the mean and median survival for people who had had abiraterone or enzalutamide and a taxane from the Ontario Cancer Registry with the mean and median survival predicted for cabazitaxel by its model using different parametric survival extrapolations of olaparib data. The company also compared the percentage of overall survival at different time points (3, 6, 12 and 24 months) for people who had had treatment with abiraterone or enzalutamide followed by docetaxel, then cabazitaxel, from the FLATIRON database with the modelled overall survival rates for cabazitaxel at the same time points. The company considers the results of both analyses confidential so they cannot be reported here. The committee noted limitations with both analyses presented by the company. The main limitation was that the company selected people after

a specific treatment sequence, rather than all sequences after which olaparib would be suitable. Also, BRCA-mutation status was not available from these sources. The committee noted that the results from the Ontario Cancer Registry and FLATIRON database were relatively consistent with model estimates for cabazitaxel from all extrapolations. That is, the registry data did not support an exponential model over any other parametric models. The committee concluded that additional evidence provided by company was inconclusive for validating extrapolations of overall survival.

Treatment costs

Data on time to treatment discontinuation should be used to model olaparib treatment duration and costs

3.15 Olaparib has a confidential discount agreed between the NHS and the company. In its initial submission, the company assumed that people have olaparib until their disease progresses. It used the progression-free survival data from PROfound to model olaparib costs, even though PROfound included time to treatment discontinuation data. The company explained that it did this because the cabazitaxel trial provided only data on progression-free survival. The company explained that the estimates of median progression-free survival and median time to treatment discontinuation from PROfound were similar. The committee noted that people may stop olaparib for reasons other than disease progression, for example, adverse effects or personal choice. The ERG preferred to use the time to treatment discontinuation data from PROfound. It explained that the curve for time to treatment discontinuation was above the curve for progression-free survival, so the company may have underestimated olaparib's costs. The ERG considered that using the curve for time to treatment discontinuation aligned with the relative dose-intensity calculation (see section 3.16). The ERG explained that cabazitaxel is administered in hospital every 3 weeks. Therefore, time to treatment discontinuation and progression-free survival are likely more aligned for

cabazitaxel than for olaparib, which is taken as a daily tablet. Also, because cabazitaxel is less expensive than olaparib, the bias of using progression-free survival to estimate its costs would be lower than for olaparib. In its response to consultation, the company agreed with the committee's conclusion, notably, that time to treatment discontinuation better estimates treatment duration and costs of olaparib than progression-free survival.

The cost of olaparib should be estimated using individual patient data from PROfound

3.16 To estimate the cost of olaparib in its original submission to NICE, the company used the mean relative dose intensity from PROfound. The relative dose intensity is the proportion of the planned dose of a drug a person takes over a given period of time. The ERG explained that the mean relative dose intensity did not account well for how much of a planned dose of a drug people had over time. So, it did not accurately estimate the mean per-patient cost of olaparib during the trial, and was also not suitable for extrapolation. The ERG preferred to use the median relative dose intensity. The company agreed with this approach during technical engagement. However, the committee was concerned with both the company's initial approach and the ERG's approach. It noted that generally the mean is the preferred metric to estimate costs, but agreed with ERG's concerns. The committee would have preferred that the company had calculated the costs of olaparib for each person based on their individual dose and treatment duration, and used these estimates to inform the mean per-patient cost of olaparib. The ERG clarified that, unless the company provides it with the individual patient data, it cannot calculate or validate these costs. The ERG suggested an alternative approach of presenting the mean monthly relative dose intensity over time for people remaining on treatment, and the number of observations for each time point. This would illustrate how the mean relative dose-intensity changes throughout the model time horizon and how it affects model results. In its response to consultation, the company argued that the costs

of olaparib were appropriately reflected in the model because time to treatment discontinuation is based on individual patient data. It explained that it did not do an additional analysis based on individual dose because the model was not sensitive to relative dose intensity. It suggested that this was shown in its scenario analysis, in which assuming a full dose for the entire duration of treatment (that is, 100% relative dose intensity) had minimal effect on cost-effectiveness estimates. The ERG questioned whether the cost of olaparib in the model should be based on the number of tablets consumed or the number of packs prescribed, because the NHS pays for whole packs, not individual tablets. It argued that, if the costs were based on the number of packs prescribed, a relative dose intensity of 100% might be the most reasonable estimate. The ERG highlighted that this concern would not apply to cabazitaxel because it is administered as an intravenous therapy in hospital. The Cancer Drugs Fund clinical lead explained that they expect minimal drug wastage with olaparib. This is because clinicians implement dose adjustments quickly when determining the right dose for an individual person. The committee was satisfied that it was appropriate for the company to exclude drug wastage in its model. It would have preferred the company to use individual patient data from PROfound to calculate the per-patient cost of olaparib, but acknowledged this was likely to have had a small effect on cost-effectiveness results. It concluded that the company's approach is acceptable for decision making.

The ERG's estimate of the costs of prophylactic granulocyte colony-stimulating factor in the cabazitaxel arm is appropriate

3.17 People having cabazitaxel may have prophylactic granulocyte colony-stimulating factor (G-CSF) to prevent neutropenia. The company and the ERG added the costs of G-CSF to the costs of having cabazitaxel. In its initial submission, the company assumed that all people having cabazitaxel had prophylactic G-CSF for 14 days. This was to align with CARD and cabazitaxel's marketing authorisation, which recommends treatment with G-CSF 'usually for up to 14 days'. The ERG explained that

the company's approach overestimated the use of G-CSF. In its base case, the ERG assumed that a lower proportion of people have G-CSF, based on the results of the company's survey with clinical experts (the company considered the exact estimate confidential so it cannot be reported here). The ERG also assumed that treatment would typically last for 7 days, based on clinical opinion. The clinical experts and the Cancer Drugs Fund clinical lead explained that people would be unlikely to have G-CSF for more than 7 days, and considered the ERG's estimate to be reasonable. In its response to consultation, the company agreed with the ERG's approach. The committee concluded that the ERG's estimate of the costs of prophylactic G-CSF in the cabazitaxel arm was appropriate. It also acknowledged that the company had followed this approach in its revised cost-effectiveness modelling.

The company's and ERG's estimates of postprogression treatment costs do not reflect NHS practice

3.18 Both the company and the ERG incorporated the costs of treatments after disease progression on olaparib and cabazitaxel. The company explained that its model allowed people to have only 1 active treatment after disease progression. The ERG noted that people in PROfound had more than 1 active treatment on average after disease progression. The clinical experts confirmed that people can have multiple treatments after disease progression in NHS practice. After technical engagement, both the company and the ERG assumed that the same proportion of people whose disease progressed on olaparib or cabazitaxel would have an active treatment. The company considers the exact proportions of people having each treatment after disease progression on olaparib to be confidential so they cannot be reported here. People who do not have active treatment would have best supportive care after progression. The company assumed that the treatments offered would differ depending on whether the disease progressed on olaparib or cabazitaxel, and that disease could be retreated with abiraterone or enzalutamide. The ERG acknowledged that, in the NHS, people are likely to have different

treatments after progression, depending on their first treatment. However, it noted that there was no reliable data to inform this. It reminded the committee that PROfound and CARD had important differences (see section 3.8) and that using the trials' proportions of postprogression treatments does not reflect NHS practice. The committee again noted that retreatment with abiraterone or enzalutamide would not happen in NHS practice, which was confirmed by the clinical experts. They considered that the company's estimate for the number of people having radium-223 dichloride in the olaparib arm was too low. They also considered that the ERG's estimate that 55% of people in both arms would have radium-223 dichloride was too high. In its response to consultation, the company excluded abiraterone and enzalutamide from postprogression treatments. However, it continued to assume people would have different treatment after progression depending on whether they initially had olaparib or cabazitaxel. The company explained that this was because the proportions of postprogression treatments used in the model were based on the clinical trial data from PROfound and CARD. It claimed that the data reflects that people who take olaparib can then have chemotherapy as a subsequent therapy before radium-223 dichloride. It also claimed that the data reflects that people whose disease progresses on cabazitaxel may have exhausted their treatment options apart from radium-223 dichloride. So, a higher proportion of people having radium-223 dichloride is likely. The company highlighted that, after it excluded abiraterone and enzalutamide from its model, using other subsequent treatments increased in proportion. The company provided 2 scenario analyses to explore the effect of the cost of postprogression treatment, in which it:

- excluded retreatment with cabazitaxel from postprogression treatment options
- excluded all costs related to postprogression treatments.

Both had a minimal effect on cost-effectiveness estimates. The committee agreed that both the company's and ERG's estimates of

postprogression treatment costs did not reflect NHS practice. However, it acknowledged adequate adjustment for these differences may not be possible, and that it was likely to have a minimal effect on cost-effectiveness results. Therefore, it concluded that both approaches were not ideal, but were acceptable for decision making.

The ERG's approach to costing best supportive care is appropriate

3.19 In its initial submission, the company assumed that the costs of best supportive care differed for people who:

- had had and stopped an active treatment after their disease had progressed on either olaparib or cabazitaxel
- did not have an active treatment after progression, that is, had best supportive care directly after olaparib or cabazitaxel.

The company explained that this avoided double counting the costs of best supportive care. It also explained that the model structure did not allow estimation of the costs of best supportive care after active treatment. The ERG disagreed with the company's approach and instead assumed the same best supportive care costs were incurred regardless of whether a person had an active treatment after disease progression. The clinical and patient experts explained that everyone would move to palliative care after active treatments had stopped, and that this would be the same for everyone. In its response to consultation, the company agreed with the ERG's approach, and followed it in its revised cost-effectiveness modelling. The committee accepted this approach to costing best supportive care.

The costs of testing for BRCA mutations should be included in the cost-effectiveness estimates

3.20 Before starting treatment with olaparib, people must have a BRCA mutation confirmed using a validated test. The NICE guide to the methods of technology appraisal states that 'if a diagnostic test to establish the

presence or absence of this biomarker is carried out solely to support the treatment decision for the specific technology, the associated costs of the diagnostic test should be incorporated into the assessments of clinical and cost effectiveness'. The company excluded the costs of testing for BRCA mutations in its initial base case. It explained that this was because the NHS Genomic Test Directory includes this test, so it is likely part of standard NHS practice. The company included the costs of testing in a scenario analysis, using costs from the testing service for ovarian cancer that the company currently funds (the cost per test is confidential and cannot be reported here). The ERG included the testing costs in its base case because its clinical advice suggested the NHS does not currently test for BRCA mutation. One clinical expert noted that they do not routinely test for BRCA mutations unless there is a family history. Another clinical expert explained that they do genomic testing for all people with hormone-relapsed metastatic prostate cancer, and that many oncologists want testing in the NHS. The Cancer Drugs Fund clinical lead explained that the Genomic Test Directory includes testing for BRCA mutations. However, he said that testing is not standard NHS care, and the cost of olaparib to the NHS should include testing costs. The ERG explained that it calculated the cost to identify 1 person with BRCA mutations by applying the company's cost per test to the expected prevalence of BRCA mutations in people with hormone-relapsed metastatic prostate cancer. It based this on the prevalence of BRCA mutations in people who entered screening for PROfound (the company considers the value to be confidential and so it cannot be reported here). The clinical experts advised that the prevalence of BRCA mutations in people with hormone-relapsed metastatic prostate cancer in clinical practice approximates 10%. In its response to consultation, the company agreed with the ERG's approach and included the cost of testing for BRCA mutations in its revised base case. The committee acknowledged that the revised company approach was appropriate.

Utility values

The company's utility values based on PROfound are appropriate

3.21 The company and the ERG used utility values from PROfound for the progression-free and postprogression health states. The utility values are considered confidential by the company so cannot be reported here. The company mapped EQ-5D-5L values from PROfound to generate EQ-5D-3L values. The company modelled worse quality of life with cabazitaxel and prednisone than with olaparib. Cabazitaxel treatment was associated with an additional decrement of -0.023 (Matza et al. 2013) because it is administered intravenously. Once people stopped having cabazitaxel, their utility reverted to the same as olaparib. The company sourced mean utility decrements associated with adverse events and the mean duration of adverse events from NICE's technology appraisal guidance on cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel and the literature. The committee concluded that the company's utility values were appropriate.

People who have not had treatment with a taxane

Exploratory analyses for people who have not had treatment with a taxane are highly uncertain

3.22 The company did exploratory cost-effectiveness analyses for the population who had not had a taxane. The committee recalled its remit to look at a technology across its marketing indication. However, it appreciated that no single comparator would be relevant both for people who had or had not had treatment with docetaxel (see section 3.2). For people who have not had treatment with a taxane, the company chose the following comparators:

- docetaxel and best supportive care (ADT and monitoring) for the group of people who had not had docetaxel but for whom docetaxel is appropriate

- best supportive care only for the group who had not had docetaxel and for whom docetaxel is unsuitable.

The committee agreed that these comparators are broadly appropriate, but noted that radium-223 dichloride is also a relevant comparator for people for whom docetaxel is unsuitable. It also recalled its concerns that people in PROfound who had not had treatment with a taxane were unlikely to represent people who cannot or should not have docetaxel in clinical practice (see section 3.6). The company believed that a robust indirect treatment comparison for olaparib compared with docetaxel was not feasible. This was because of a lack of evidence for docetaxel in the relevant population. The company's exploratory analysis comparing olaparib with docetaxel used results from the TAX327 randomised trial for docetaxel plus prednisone. This trial was done before abiraterone and enzalutamide were available. The control arm in TAX327 was mitoxantrone plus prednisone. TAX327 did not report progression-free survival data, so the company assumed that the size of relative effectiveness of docetaxel on progression-free survival would be the same as that on overall survival. To compare olaparib with best supportive care, the company used the abiraterone or enzalutamide arm from PROfound as a proxy. In addition to limitations noted by the company, the committee also noted that the company's exploratory analyses for the group who have not had treatment with taxanes did not mirror the committee's preferred assumptions for people who have had treatment with taxanes, for example:

- assuming that the same proportion of people whose disease progressed on olaparib or cabazitaxel would have an active treatment (see section 3.18)
- adjusting for differences in postprogression treatments between PROfound and NHS practice (see section 3.18).

The committee noted that the company's modelling assumed people

who cannot or should not have docetaxel could then have docetaxel or cabazitaxel after disease progression, which is implausible. The committee also noted that the company's exploratory analyses for people who have not had treatment with a taxane were not validated by the ERG. The committee concluded that company's exploratory analyses for people who have not had treatment with a taxane were highly uncertain and made inappropriate assumptions.

End of life

Olaparib likely meets NICE's criteria for life-extending treatments at the end of life for people who have had treatment with a taxane

3.23 The committee considered the criteria for 'life-extending treatments at the end of life' outlined in NICE's guide to the methods of technology appraisal, that is:

- a treatment must be indicated for people with a short life expectancy, normally less than 24 months and
- there must be sufficient evidence to indicate that treatment offers an extension to life, normally of at least an additional 3 months, compared with current NHS treatment.

In addition, the appraisal committees will need to be satisfied that:

- the estimates of the extension to life are sufficiently robust and can be shown or reasonably inferred from either progression-free survival or overall survival (taking account of trials in which crossover has occurred and been accounted for in the effectiveness review) and
- the assumptions used in the reference case economic modelling are plausible, objective and robust.

The ERG explained that, for people who have had treatment with a taxane, overall survival with cabazitaxel was less than an average of

24 months when using both the exponential curve (company updated base case) and Rayleigh curve (ERG's base case) to extrapolate overall survival in the model. The company also presented results from other trials in hormone-relapsed metastatic prostate cancer, COU-AA-301 and AFFIRM, in which median overall survival ranged from 16 to 18 months with enzalutamide or abiraterone treatment. The committee was satisfied that olaparib is indicated for people with a short life expectancy. The committee acknowledged that both parametric extrapolations of overall survival predicted at least a 3-month survival benefit with olaparib compared with cabazitaxel in the prior-taxane group. The committee considered the end of life criteria for the people who had not had treatment with a taxane, noting that survival estimates for both olaparib and comparators in in this group were uncertain. This was because of the small subgroup size in PROfound (see section 3.5) and the exploratory nature of the analyses and the lack of verification of the model by the ERG (see section 3.22). The committee also noted that new hormonal agents are now available much earlier in the treatment path (see section 3.1). This would mean that olaparib, which requires pretreatment with a new hormonal agent, would also be offered earlier. This could mean a longer life expectancy than modelled by the company. The committee could not determine if end of life criteria were met for people who had not had treatment with a taxane. It concluded that olaparib likely meets NICE's criteria for life-extending treatments for people with a short life expectancy in people who have had a taxane.

Cost-effectiveness estimate

Olaparib is not a cost-effective treatment option for people who have had treatment with a taxane at the price chosen by the company

3.24 Because of confidential commercial arrangements for olaparib, cabazitaxel and other postprogression therapies, the cost-effectiveness estimates cannot be reported here. The committee noted that the

company addressed a number of its preferences from its first committee meeting, including by:

- using the hazard ratios from the BRCA-mutation prior-taxane subgroup of PROfound to model the efficacy of cabazitaxel in the prior-taxane group (see section 3.11)
- using the time to treatment discontinuation data to model olaparib treatment duration and costs (see section 3.15)
- assuming only a proportion of people having cabazitaxel have prophylactic G-CSF, and have it for an average of 7 days (see section 3.17)
- assuming treatments available to people after progression on olaparib or cabazitaxel do not include retreatment with abiraterone or enzalutamide (see section 3.18)
- assuming the cost of best supportive care is the same regardless of whether people had active treatment after progression (see section 3.19)
- including the cost of testing for BRCA mutations (see section 3.20).

The committee also acknowledged that the company explored some of its preferences from its first meeting in scenario analyses, and that they had a minor impact on cost-effectiveness estimates. Namely, the company explored:

- whether TROPIC could be included in the indirect treatment comparison (see section 3.8)
- uncertainty around the effect of postprogression treatments on postprogression survival (see section 3.10)
- more flexible approaches for extrapolating survival (see section 3.12)
- uncertainty around dosing of olaparib (see section 3.16)
- uncertainty around the cost of postprogression treatments in the NHS (see section 3.18).

The committee noted that the company did not provide cost-effectiveness results against all relevant comparators, including radium-223 dichloride and retreatment with docetaxel (see section 3.3). It also noted several differences between the ERG's and company's base-case models. It preferred the ERG's analysis, without adjusting for switching in CARD, because it is aligned with its preferences:

- not adjusting for switching in CARD (see section 3.9)
- using the Rayleigh model to extrapolate overall survival data (see section 3.12)
- using the ERG model, which applied the committee's preferences for other minor differences between the company's and the ERG's models, such as assumptions related to bone and CT scans while on treatment, or costs of ADT.

Applying confidential discounts for cabazitaxel and radium-223 dichloride, and considering its preferences, the committee noted the cost-effectiveness estimates for olaparib compared with cabazitaxel were higher than what NICE normally considers an acceptable use of NHS resources for people who have had treatment with a taxane. This was the case even when considering end of life criteria. The committee noted that olaparib was not cost effective even in the company's own base case. Because of these confidential discounts, the cost-effectiveness results cannot be reported here. The committee could not address the cost effectiveness of olaparib compared with docetaxel retreatment or radium-223 dichloride. This was because neither the company nor the ERG presented the committee with incremental analyses including these comparators. So, the committee could not recommend olaparib for use in the NHS for treating hormone-relapsed metastatic prostate cancer with BRCA1 or BRCA2 mutations that has progressed after abiraterone or enzalutamide in adults who have had treatment with docetaxel.

The cost-effectiveness estimates for people who have not had treatment with a taxane are uncertain but suggest olaparib is not cost effective

3.25 The committee recalled high uncertainty in the results from the company's cost-effectiveness modelling for people who have not had treatment with a taxane (see section 3.22) and for estimates on the end of life criteria (see section 3.23). It noted that it had seen no modelling specifically for people who cannot or should not have a taxane in NHS practice. It also noted that the existing model made inappropriate assumptions and had not been validated by the ERG (see section 3.22). Based on the estimates it did see, it anticipated that the most likely cost-effectiveness estimates compared with docetaxel or best supportive care were higher than what NICE normally considers an acceptable use of NHS resources. This was regardless of whether or not end of life criteria were applied, and even in the company's own analyses. Because of confidential discounts for cabazitaxel and radium-223 dichloride, the cost-effectiveness results cannot be reported here. So, the committee could not recommend olaparib for use in the NHS for people who have not had docetaxel regardless of whether they cannot, should not, or chose not to have it.

Other considerations

There are some equalities considerations

3.26 The committee recalled its recent appraisal of abiraterone for treating newly diagnosed high-risk hormone-sensitive metastatic prostate cancer (see NICE's technology appraisal guidance on abiraterone). It noted that, in this appraisal, the company initially limited its submission to people who have already had a taxane, which would be docetaxel in the NHS. It agreed that people who cannot or should not have docetaxel are likely to be older than those who can have docetaxel. The committee also noted that some people with prostate cancer may not identify as men. Age, sex, and gender reassignment are protected characteristics under the Equality Act 2010.

Olaparib is not innovative because it does not offer benefits not already included in the modelling

3.27 The Cancer Drugs Fund clinical lead explained that, if recommended, olaparib would change the treatment pathway and may help to promote BRCA-mutation testing in prostate cancer in the NHS. The committee acknowledged these potential advantages. It also noted that treatment with corticosteroids given with cabazitaxel has associated adverse effects and that this could possibly be delayed. However, the committee noted that the company had modelled a relative increase in utility for treatment with olaparib compared with cabazitaxel, so it did not consider there to be benefits not adequately captured in the economic analysis. The committee understood that to consider a technology innovative, a substantial change in management of a condition and benefits not adequately captured in the economic analysis were both needed. It concluded olaparib is not innovative because it does not offer benefits not already included in the modelling.

4 Proposed date for review of guidance

4.1 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.

Amanda Adler

Chair, appraisal committee

October 2021

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

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.

Rebecca Thomas and Hannah Nicholas
Technical leads

Ewa Rupniewska
Technical adviser

Shonagh D'Sylva and Jeremy Powell
Project managers

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