

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Talazoparib with enzalutamide for untreated 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 talazoparib with enzalutamide in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

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

The evaluation 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 age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

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- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using talazoparib in the NHS in England.

For further details, see [NICE's manual on health technology evaluation](#).

The key dates for this evaluation are:

- Closing date for comments: 18 September 2025
- Second evaluation committee meeting: 08 October 2025
- Details of membership of the evaluation committee are given in section 4

1 Recommendations

- 1.1 Talazoparib with enzalutamide should not be used for untreated hormone-relapsed metastatic prostate cancer in adults when chemotherapy is not clinically indicated.
- 1.2 This recommendation is not intended to affect treatment with talazoparib with enzalutamide 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 healthcare professional consider it appropriate to stop.

What this means in practice

Talazoparib with enzalutamide is not required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because the available evidence does not suggest that talazoparib with enzalutamide is value for money in this population.

Why the committee made these recommendations

Usual treatment for untreated hormone-relapsed metastatic prostate cancer is abiraterone plus prednisolone, enzalutamide alone, or olaparib plus abiraterone and prednisolone.

Clinical trial evidence shows that talazoparib plus enzalutamide increases how long people have before their condition gets worse and how long people live compared with enzalutamide plus placebo.

Talazoparib plus enzalutamide has only been compared indirectly with abiraterone plus prednisolone, and olaparib plus abiraterone and prednisolone. The results are uncertain, so it is unclear how well it works compared with these treatments.

There are also uncertainties in the economic model because it does not include all the usual treatments.

Because of the uncertainties in the economic model and the indirect comparisons it is not possible to determine the most likely cost-effectiveness estimates for talazoparib plus enzalutamide. So, it should not be used.

2 Information about talazoparib

Marketing authorisation indication

- 2.1 Talazoparib (Talzenna, Pfizer) is indicated 'in combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated'.

Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for talazoparib](#).

Price

- 2.3 The list price of talazoparib is £1,655 for a 30-pack of 0.25 mg capsules (excluding VAT; BNF online accessed July 2025).
- 2.4 The company has a commercial arrangement. This makes talazoparib available to the NHS with a discount and it would have also applied to this indication if talazoparib had been recommended. The size of the discount is commercial in confidence.

Carbon Reduction Plan

- 2.5 Information on the Carbon Reduction Plan for UK carbon emissions for Pfizer will be included here when guidance is published.

3 Committee discussion

The [evaluation committee](#) considered evidence submitted by Pfizer, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

The condition

Details of condition

- 3.1 Hormone-relapsed metastatic prostate cancer (also known as metastatic castration-resistant prostate cancer) has spread beyond the prostate. The patient organisation submissions explained that for many it is a debilitating and life-changing condition. People may experience pain, anaemia, fatigue and bone damage. The patient expert agreed and explained that people have usually had several treatments before the metastatic stage. Some are still having side effects of previous treatments. The fear of living with the non-curative nature of this condition adds to a person's psychological burden and impacts their quality of life. The risk of prostate cancer increases with age. Prostate cancer is more common in people from Black African ethnic backgrounds, people with a family history of prostate cancer and people with a homologous recombination repair (HRR) mutation. People from an Ashkenazi Jewish ethnic background have a higher risk of having a breast cancer gene (BRCA) mutation and so a higher risk of prostate cancer.

Clinical management

Treatment options

- 3.2 First-line treatment options for hormone-relapsed metastatic prostate cancer when chemotherapy is not yet indicated include:
- olaparib plus abiraterone and prednisolone (from now, olaparib plus abiraterone) for people who cannot have or do not want chemotherapy (see [NICE's technology appraisal guidance on olaparib with abiraterone for untreated hormone-relapsed metastatic prostate cancer \[TA951\]](#))
 - androgen receptor pathway inhibitor (ARPi) monotherapies, if neither have been previously used:
 - abiraterone with prednisolone (from now, abiraterone; see [NICE's technology appraisal guidance on abiraterone for treating hormone-relapsed metastatic prostate cancer before chemotherapy is indicated \[TA387\]](#))
 - enzalutamide (see [NICE's technology appraisal guidance on enzalutamide for treating hormone-relapsed metastatic prostate cancer before chemotherapy is indicated \[TA377\]](#))
 - 'watchful waiting'.

Comparators

- 3.3 The company submission positioned talazoparib plus enzalutamide as a treatment for:
- untreated hormone-relapsed metastatic prostate cancer when chemotherapy is not clinically indicated and
 - when olaparib plus abiraterone would otherwise be offered.

The company proposed olaparib plus abiraterone as the main comparator. It believed there is a distinct population eligible for olaparib plus

abiraterone but not for abiraterone or enzalutamide monotherapies. It noted that abiraterone may be contraindicated for some people. The EAG believed abiraterone and enzalutamide to be equally relevant comparators because both treatments are used in clinical practice ([see section 3.2](#)). The NHS England Cancer Drugs Fund (CDF) clinical lead explained that abiraterone and enzalutamide are relevant comparators. They are used by people with an Eastern Cooperative Oncology Group performance score (ECOG PS) of 0 to 2 whereas olaparib plus abiraterone is used by people with an ECOG PS of 0 or 1. But they said that all 3 treatments are options for people with ECOG PS scores of 1 and 2. The clinical experts explained that combination treatments like olaparib plus abiraterone would be offered to people who can tolerate the side effects. The ARPi monotherapies would be offered to most others, although they acknowledged that abiraterone is associated with tolerability issues and may not be suitable for everyone. They also said that despite olaparib plus abiraterone having a marketing authorisation for the ‘all-comers’ population in its clinical trials, healthcare professionals would prefer to offer it for HRR-deficient cancer. The NHS England CDF clinical lead explained that it is not possible to define a specific subgroup that would have olaparib plus abiraterone and not the abiraterone or enzalutamide monotherapies. They noted that the treatment pathway was driven by healthcare professional and patient choice. The clinical experts agreed with this. The committee took all the evidence and viewpoints into consideration. It acknowledged the nuances with tolerability of abiraterone and preference for combination treatments when the side effects can be tolerated. But it could not identify a definable population for whom abiraterone or enzalutamide monotherapy would not be an option. It concluded that abiraterone, enzalutamide monotherapy and olaparib plus abiraterone were all relevant comparators for the population being evaluated.

Unmet need

- 3.4 The patient expert submissions stated that there is a high unmet need for first-line treatments for hormone-relapsed metastatic prostate cancer. They explained that, for people with the condition and their carers, ease of administration is a key factor in choosing a treatment. More treatment options are needed because of the non-curative nature of the cancer and to delay chemotherapy. The patient expert noted that talazoparib plus enzalutamide provides a steroid-free option compared with treatments that include abiraterone, which is always used with prednisolone (a type of steroid). The clinical experts explained that, because abiraterone is associated with tolerability issues (see [section 3.3](#)), an alternative poly-ADP ribose polymerase inhibitor (PARPi) and ARPi combination is needed. The clinical expert said that steroid exposure should be taken into consideration because some people are unable to tolerate steroids. The committee understood the unmet need in this population and took this into consideration for its decision making.

Clinical effectiveness

TALAPRO-2

- 3.5 The clinical evidence for talazoparib plus enzalutamide came from TALAPRO-2, a randomised, double-blind, placebo controlled, phase 3 trial. The trial started enrolment with cohort 1 (805 people), an 'all-comers' population that included all participants irrespective of HRR mutation status. The trial compared talazoparib plus enzalutamide (402 people, 21% HRR deficient) with enzalutamide plus placebo (403 people, 21% HRR deficient) as first-line treatment of hormone-relapsed metastatic prostate cancer in adults in whom chemotherapy is not clinically indicated. The primary outcome was radiographic progression-free survival (rPFS) assessed by blinded independent central review. Secondary outcomes included overall survival (OS), adverse events, health-related quality of

life, time to starting cytotoxic chemotherapy, time to starting subsequent antineoplastic treatment and time to first symptomatic skeletal-related event. After cohort 1 enrolment completion, only people with HRR mutations were recruited into cohort 2 of the trial. Cohort 2 included 399 people (200 people having talazoparib plus enzalutamide and 199 people having enzalutamide plus placebo).

TALAPRO-2 results

- 3.6 The company presented results from cohort 1 in its base case. Talazoparib plus enzalutamide showed a statistically significant improvement in OS compared with enzalutamide plus placebo (hazard ratio [HR] 0.796; 95% confidence interval [CI] 0.661, 0.958; 2-sided $p=0.0155$). The median OS was 45.8 months (95% CI 39.4, 50.8) in the talazoparib plus enzalutamide arm and 37.0 months (95% CI 34.1, 40.4) in the enzalutamide plus placebo arm. For rPFS, talazoparib plus enzalutamide showed a statistically significant improvement in OS compared with enzalutamide plus placebo (HR 0.667; 95% CI 0.551, 0.807; 2-sided $p<0.0001$). The median rPFS was 33.1 months (95% CI 27.4, 39.0) in the talazoparib plus enzalutamide arm and 19.5 months (95% CI 16.6, 24.7) in the enzalutamide plus placebo arm. The committee concluded that talazoparib plus enzalutamide improved OS and rPFS compared with enzalutamide plus placebo.

HRR mutation subgroup

- 3.7 TALAPRO-2 prespecified subgroup analysis by HRR mutation. The EAG noted that this analysis was not provided in the company submission and was published in Agarwal et al. (2023). For rPFS, HRR status was a treatment effect modifier because the efficacy was reduced in HRR non-deficient or unknown tumours. For OS, talazoparib plus enzalutamide had a statistically significant benefit over enzalutamide plus placebo in HRR-deficient cancer, but the benefit was not statistically significant in HRR

non-deficient or unknown tumours. At clarification, upon the EAG's request, the company provided TALAPRO-2 clinical efficacy results from cohort 2 (in which 100% had HRR-deficient tumours). The company noted that it was not seeking NICE recommendations for cohort 2 and the marketing authorisation was based on cohort 1 data. The EAG concluded that the treatment effect estimates for rPFS and OS were similar in the talazoparib plus enzalutamide arm for cohort 1 and cohort 2. The placebo plus enzalutamide arm outcomes were worse for cohort 2 compared with cohort 1. This suggested that enzalutamide did not work as well in cohort 2 compared with cohort 1. The EAG suggested that a separate subgroup analysis for the HRR-deficient population may be needed. The clinical experts explained that HRR deficiency is not part of national routine genetic testing in the NHS. There is lack of capacity with HRR testing and it is unlikely to be resolved soon. The committee understood that talazoparib plus enzalutamide was effective in the 'all-comers' group but showed additional benefit in the HRR-deficient group. It noted the HRR was not currently part of routine testing and this subgroup would be difficult to identify in the NHS. So, it concluded that this subgroup did not need to be considered separately.

Indirect treatment comparisons

- 3.8 There were no clinical trials comparing talazoparib plus enzalutamide with olaparib plus abiraterone. So, the company did a network meta-analysis (NMA) to estimate the comparative efficacy of talazoparib plus enzalutamide against olaparib plus abiraterone for rPFS, OS and time to prostate-specific antigen progression. The network included 8 studies (TALAPRO-2, PROpel, BRCAAway, COU-AA-301 and COU-AA-302, NCT01591122, NCT02294461, Hu et al. 2020, PREVAIL) and 5 interventions (talazoparib plus enzalutamide, abiraterone, best supportive care, enzalutamide, olaparib plus abiraterone). The company used a Cox proportional hazards model within a Bayesian framework. The

company used a random effects model in its base case. The results of the proportional hazards NMA are confidential and cannot be reported here. The EAG commented that there were no common comparators linking the network. The network lacked direct evidence, with 4 comparisons across 5 studies linking talazoparib plus enzalutamide with olaparib plus abiraterone. The EAG preferred the fixed effects model over the random effects model. This was because the network was a straight line, and the random effects estimate was based on 1 comparator and 2 studies. Also, the fixed effect model was a better fit for both rPFS and OS outcomes. It highlighted that the proportional hazards assumption was not met for the input data in both the rPFS and OS NMAs and this was checked for the PROpel trial (from [TA951](#) that compared olaparib plus abiraterone with abiraterone). This meant that results could be biased, leading to inaccurate conclusions. The EAG proposed that an unanchored matching-adjusted indirect comparison (MAIC) or fractional polynomials NMA might be more suitable.

The company then presented an unanchored MAIC comparing talazoparib plus enzalutamide with olaparib plus abiraterone. The individual patient level TALAPRO-2 data was matched with the PROpel olaparib plus abiraterone trial data. TALAPRO-2 data was reweighted to ensure that the underlying populations were similar. The company noted some differences between the trial populations but concluded that an unanchored MAIC was feasible. The EAG flagged that because of the differences in trial eligibility criteria, baseline pain scores were higher in PROpel than in TALAPRO-2 and it was not feasible to adjust for these. The EAG's clinical experts explained that pain is a prognostic factor and should be adjusted. The EAG concluded that the PROpel population's condition would be harder to treat and this favoured talazoparib and enzalutamide and caused uncertainty in the MAIC outcomes.

At clarification, the company provided a fractional polynomials NMA. It was based on a network including 4 studies (TALAPRO-2, PROpel, NCT02294461 and COU-AA-302) and 5 interventions (talazoparib plus enzalutamide, abiraterone, best supportive care, enzalutamide, olaparib plus abiraterone). The OS analysis had convergence issues which meant a stable model fit was not identified and OS outcomes were not thought reliable. For rPFS, several plausible model fits were identified. Based on visual fit and low deviance information, the criterion 1 model fit was considered best. The EAG considered the fractional polynomials NMA to be well conducted. It agreed that the OS outcomes from the fractional polynomials NMA were unreliable. The EAG questioned the extent of the validation done for the selection of the rPFS model fit.

The EAG and company's preferred indirect treatment comparison was the unanchored MAIC. This showed a statistically significant benefit for rPFS and a numerical benefit for OS for talazoparib plus enzalutamide compared with olaparib plus abiraterone. Compared with the proportional hazards NMA the rPFS benefit was smaller and the OS benefit was similar.

The committee acknowledged the issues with the indirectness of the evidence base but was not satisfied with any of the indirect treatment comparisons done because:

- The MAIC:
 - was unanchored, despite a network being available
 - could not adjust for all prognostic factors
 - had uncertain outcomes
 - only included a pairwise comparison so excluded abiraterone and enzalutamide monotherapies.

- The NMA had non-proportionality in the network, but did allow for all treatments to be included and for randomisation to be preserved.
- The fractional polynomial NMA relaxed the proportional hazards assumption but did not converge for OS so did not provide usable outcomes.

The committee wanted to see further analysis using methods that preserve randomisation and can model flexible hazards over time to overcome the non-proportional hazards issue in the NMA. These approaches should allow for all comparators to be included within 1 analysis. The committee suggested considering alternative approaches (see [NICE's Decision Support Unit technical support document 18 on methods for population-adjusted indirect comparisons](#)) such as multilevel network meta-regressions. The committee concluded that further analysis is required to determine the relative effect of each treatment option.

Economic model

Company's modelling approach

- 3.9 The company presented two 3-state partitioned survival models. The first estimated the cost effectiveness of talazoparib plus enzalutamide compared with olaparib plus abiraterone using the unanchored MAIC weighted rPFS and OS outcomes from TALAPRO-2 and PROpel. The second estimated the cost effectiveness of talazoparib plus enzalutamide compared with enzalutamide monotherapy using unadjusted data from TALAPRO-2 for both treatment arms (see [section 3.6](#) and [section 3.8](#)). In both models the 3 health states were progression free, progressed disease and death. In the progressed disease health state, the cohort progresses onto palliative care after 1 line of subsequent treatment. The EAG explained that making this assumption meant that most time in the

post-progression health state is spent in palliative care. This may not apply to a cohort having a fixed treatment duration and does not take account of multiple lines of subsequent treatment. The EAG did scenario analyses varying the time spent in palliative care and these made small differences to the incremental cost-effectiveness ratio (ICER). The committee acknowledged the palliative care modelling issue and noted the scenario analysis did not make a large difference to the outcomes. The committee concluded that the model structure was appropriate for decision making. It said that the comparison of outcomes from an unanchored MAIC-adjusted cost-utility model with an unadjusted cost-utility model causes a high level of uncertainty. It recalled that the current indirect comparison was deemed unsuitable (see [section 3.8](#)). The committee wanted to see relative treatment effect derived from an indirect treatment comparison that includes all comparators in a single model that can generate fully incremental cost-effectiveness ratios.

Abiraterone and enzalutamide clinical equivalence

3.10 The EAG considered abiraterone to be a relevant comparator (see [section 3.3](#)). So it provided a separate analysis using the cost-utility model comparing talazoparib plus enzalutamide with enzalutamide monotherapy (see [section 3.9](#)). The EAG replaced the enzalutamide monotherapy cost with abiraterone's cost and assumed abiraterone and enzalutamide were clinically equivalent in the economic model (HR for OS and rPFS, 1.00). This was based on [TA951](#) in which the committee concluded that it was reasonable to assume clinical equivalence to inform the economic modelling. The EAG also did scenario analysis applying alternative hazard ratios to OS and rPFS from TA951 (OS HR of 1.19 [95% credible interval: 1.10 to 1.30] also applied to rPFS) and the proportional hazards NMA from this evaluation (see [section 3.8](#)). These scenarios modelled the reduced clinical effectiveness of abiraterone compared with enzalutamide. All other inputs in the model, for example, the adverse event rates, were

the same for abiraterone and enzalutamide monotherapies. The committee acknowledged the alternative EAG analysis presented for abiraterone as a comparator. But the committee concluded that it wanted all comparators in a single cost-utility model with the respective treatment-specific costs, utilities and disutilities incorporated in line with NICE's reference case.

rPFS and OS extrapolations

3.11 In the company's economic model, independent parametric curves were fitted to the OS and rPFS data. The selections were based on visual and statistical fit, and external validation using TALAPRO-2 and [TA951](#):

- Talazoparib plus enzalutamide compared with olaparib plus abiraterone: For both treatment arms, the company fit generalised gamma distributions to the OS curves and log-normal distributions to rPFS. The EAG agreed with this and said this aligned with the OS curve selection in [TA951](#). For rPFS, the EAG noted that log-logistic distribution also provided a good fit but agreed that log-normal provided reasonable estimates.
- Talazoparib plus enzalutamide compared with enzalutamide monotherapy: For both treatment arms, the company fit log-normal distributions to OS and rPFS. Log-normal was specifically chosen because it did not exhibit any kinks in the extrapolations. The EAG disagreed with the enzalutamide monotherapy curve selections. It noted for OS, log-normal provided a poor statistical and visual fit. The EAG preferred the generalised gamma distribution fit for OS. For rPFS, the EAG agreed with the company's choice of log-normal but noted that the rPFS and OS curves crossed. It preferred the gamma distribution for rPFS because it did not result in the curves crossing. During the committee meeting the company agreed with the EAG's preferred base case.

The committee considered the available data and views, and concluded that the generalised gamma was the most appropriate parametric curve for extrapolating OS for both comparisons. It concluded that, for rPFS, the plausible choices were log-normal distribution for the comparison with olaparib plus abiraterone and gamma distribution for the comparison with enzalutamide monotherapy. However, it noted that if the model was updated for all comparators using a new indirect treatment comparison then these assumptions may need to be reassessed.

Time on treatment assumptions

- 3.12 In the company's model, independent parametric curves were fitted to time to treatment discontinuation Kaplan–Meier data from TALAPRO-2. Log-logistic distribution was selected for talazoparib, enzalutamide (when used in combination) and enzalutamide monotherapy based on statistical and visual fit. Time to treatment discontinuation data was not publicly available for olaparib plus abiraterone. So the company assumed time to treatment discontinuation was the same as rPFS for this treatment arm. The company said this was based on similar assumptions made in the Canadian Drug Agency (CADTH) submission for olaparib plus abiraterone. For the talazoparib plus enzalutamide treatment arm the company did not provide MAIC-adjusted values; only rPFS and OS were included as outcomes in the MAIC (see [section 3.8](#)). The EAG agreed with the log-logistic distribution fitted for the talazoparib, enzalutamide and enzalutamide monotherapy arms of the TALAPRO-2 Kaplan–Meier data. The EAG had concerns with the assumptions in the comparison with olaparib plus abiraterone. The EAG flagged that the CADTH submission assumed that time to treatment discontinuation was lower than rPFS. Since rPFS was shorter for olaparib plus abiraterone compared with talazoparib plus enzalutamide, it would expect the same relationship for time to treatment discontinuation. So, using unadjusted data for the talazoparib plus enzalutamide treatment arm resulted in implausible

outcomes. The results are marked confidential and cannot be reported here. The EAG's clinical experts noted that they would expect time to treatment discontinuation for each treatment to be similar to rPFS for that treatment. So, the EAG's preferred base case assumed that the observed relationship between time to treatment discontinuation and rPFS for talazoparib plus enzalutamide applied to olaparib plus abiraterone. For the EAG's separate analysis that compared talazoparib plus enzalutamide with abiraterone (see [section 3.10](#)), the relationship between time to treatment discontinuation and rPFS for enzalutamide was applied to abiraterone. The EAG also did a scenario analysis in which time to treatment discontinuation was equal to rPFS across all treatment arms. The clinical experts explained that some people stop treatment because of toxicity. So, time to treatment discontinuation would be shorter than rPFS, but others may continue treatment after progression if they have no progression symptoms. The company confirmed that in TALAPRO-2 people could continue treatment beyond progression. The experts said that, on balance, they would expect the 2 outcomes to be similar. The committee said there was no strong justification to assume that time to treatment discontinuation and rPFS would be different for each individual treatment. The committee considered the evidence presented and that time to treatment discontinuation data was not available for all treatments. It concluded that assuming time to treatment discontinuation was equal to rPFS for each treatment was the most plausible assumption.

Skeletal-related events

- 3.13 The costs and disutility associated with skeletal-related events per treatment arm were included by the company in its base case. TALAPRO-2 data was used for talazoparib plus enzalutamide. For olaparib plus abiraterone, data was used from [NICE's technology appraisal guidance on olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer](#) (pooled data from the ALSYMPCA, COU-AA-

301 and AFFIRM trials) and [TA951](#) (PROpel trial). Based on the trial event rates, the company assumed higher skeletal-related events for olaparib plus abiraterone compared with talazoparib plus enzalutamide. The EAG explained that the sources used for the olaparib plus abiraterone arm were 10 years old and that the patient population and bone health management has changed since then. It flagged that in TA951 treatment-specific differences in skeletal-related events were not assumed and event rates were dependent on disease progression. The EAG's clinical experts agreed that most events are related to disease progression but some events like fractures are related to androgen-deprivation treatment. They also did not agree with the higher event rates in the olaparib plus abiraterone arm. The EAG did not include skeletal-related events in the base case. The committee asked clinical experts if they would expect to see a difference in the events between treatment arms. The experts said they did not have experience with talazoparib plus enzalutamide and would have to rely on the TALAPRO-2 trial. They noted that radiotherapy to bone and spinal cord compression, which are associated with the highest event rates for olaparib plus abiraterone, are disease progression related. They flagged that skeletal-related events have a substantial cost and quality of life burden. The committee understood that the most skeletal-related events are related to disease progression. It was concerned that the company analysis was a naive comparison associated with substantial uncertainty and that no attempt was made to link skeletal-related events to rPFS. It noted that excluding them from the base case did not make a big difference to the final outcomes. It concluded that, in the absence of a more robust comparison, it was satisfied with the EAG's assumption of excluding skeletal-related events from the base case. It decided to consider these as a potential uncaptured benefit related to improvements in disease control.

Utility values

3.14 The company used EQ-5D-5L data from TALAPRO-2 and mapped this to ED-5D-3L to inform the utility value in the progression-free health state, using the same value for all treatment arms. The utility value is confidential and cannot be reported here. TALAPRO-2 health-related quality of life data could not be used for the progressed health state because of the small sample size and missing data issues. The company used the following separate utility values for time in the post-progression and palliative care health states from [TA377](#):

- post-progression (0.658), first-line post-progression weighted mean utility from Wolff et al. (2012) and Diels et al. (2015)
- palliative care (0.5), quality of life data from a Swedish prostate cancer cohort (Sandblom et al. 2004).

The EAG reported that most of the time in the progressed health state was spent with the palliative care utility (see [section 3.9](#)). It also noted that higher post-progression utility values ranging between 0.65 and 0.775 have been reported in [TA951](#) and a recent literature review (Castro et al. 2025). The sources used by the company are old, so do not account for the treatment options available in the NHS today, and do not reflect NICE's reference case. In the absence of more recent and NHS-relevant utility data for palliative care, the EAG preferred using a post-progression utility value of 0.775 from [TA951](#) for the entire health state. The committee was concerned that in the company's model, the low palliative care utility value was applied for too long. The committee concluded that in the absence of a plausible approach using post-progression and palliative care utility values it preferred the EAG's approach of using a single value for the full post-progression health state. But, it would consider alternative scenarios if these were generalisable to current NHS practice.

Costs

Drug wastage costs

- 3.15 The company assumed drug wastage costs for intravenous drugs because some of the drugs may be wasted if vial sharing practices are not in place. But no wastage costs were assumed for oral treatments and the costs for the exact number of tablets or capsules needed for treatment were included in the model. The company did provide a scenario in which drug wastage costs were assumed for both intravenous and oral treatments. The EAG preferred this approach in its base case. The committee concluded that full drug wastage costs should be included in the base case.

Post-progression costs

- 3.16 For the progressed health state in the model, the company applied end of life care costs from [TA951](#) and palliative care costs from a UK-specific prostate cancer source (Round et al. 2015). The EAG believed applying both end of life care and palliative care costs to be double counting and preferred to only include the palliative care cost from Round et al. (2015) in its base case. The committee noted this and concluded that it was satisfied with the EAG's assumption of only applying the palliative care costs.

Severity

- 3.17 NICE's methods on conditions with a high degree of severity did not apply.

Other factors

Equality

- 3.18 The committee noted that some people with untreated hormone-relapsed metastatic prostate cancer may be older and from a Black African, Black

Caribbean, or any other Black or Black British ethnic background. People from an Ashkenazi Jewish ethnic background have a higher risk of having a BRCA mutation, and so have a higher risk of prostate cancer. Some people with hormone-relapsed metastatic prostate cancer are trans. Age, race and gender reassignment are protected under the Equality Act 2010. The committee noted that differences in incidence and prevalence cannot be addressed in a technology appraisal. Because its recommendation does not restrict access to treatment for some people over others, the committee concluded that these were no potential equalities issues.

Uncaptured benefits

- 3.19 The committee considered whether there were any uncaptured benefits of talazoparib plus enzalutamide. The committee asked clinical experts if steroid exposure is a key concern for this population. The clinical experts recalled that steroid exposure can impact some people because they are unable to tolerate steroids (see [section 3.4](#)). The committee acknowledged that lack of steroid exposure was an additional benefit of talazoparib plus enzalutamide that is not captured in the economic modelling. As discussed in [section 3.13](#), the committee agreed to exclude the cost and disutility associated with skeletal-related events from the economic model base case. This was because it considered these as a potential uncaptured benefit of talazoparib plus enzalutamide. So the committee took these into consideration for its decision making.

Cost-effectiveness estimates

Acceptable ICER

- 3.20 [NICE's manual on health technology evaluations](#) notes that, above a most plausible ICER of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a

technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the high level of uncertainty, specifically that:

- all comparators have not been modelled in the same population and a fully incremental analysis was not provided (see [section 3.3](#) and [section 3.9](#))
- none of the indirect treatment comparison approaches were deemed suitable; specifically, the unanchored MAIC used in the base case was very uncertain (see [section 3.8](#))
- inconsistent modelling of time on treatment across the treatment arms (see [section 3.12](#))
- the post-progression utility values in the company's base case were not considered generalisable to NHS practice and add further uncertainty to the model outcomes (see [section 3.14](#)).

But the committee also noted:

- the unmet need for first-line treatments for untreated hormone-relapsed metastatic prostate cancer because of the lack of treatment options with multiple mechanisms of action (see [section 3.4](#))
- talazoparib plus enzalutamide provides a steroid-free treatment option in this population (see [section 3.4](#) and [section 3.19](#)).

So, the committee concluded that an acceptable ICER would be towards the lower end of the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained). But that it would reconsider this once further analyses have been provided (see [section 3.21](#)).

Cost-effectiveness estimates and further analyses

3.21 Because of confidential commercial arrangements for talazoparib, the comparators and other treatments in the model, the exact cost-

effectiveness estimates are confidential and cannot be reported here. Neither the company's nor the EAG's base-case ICERs included all the committee's preferred assumptions, so the ICERs based on the committee's preferred assumptions are unknown. The committee requested the following further analyses:

- modelling abiraterone and enzalutamide monotherapies as comparators in the same population as olaparib plus abiraterone (see [section 3.3](#) and [section 3.9](#))
- exploring alternative indirect comparison methods that preserve randomisation, include all the comparators and allow for flexible hazards over time (see [section 3.8](#))
- exploring alternative post-progression utility analysis reflective of NHS practice (see [section 3.14](#)).

The committee's preferred assumptions were to:

- assume time to treatment discontinuation is equal to rPFS for each treatment (see [section 3.12](#))
- exclude skeletal-related events for all treatment arms and consider it as an uncaptured benefit (see [section 3.13](#))
- fully apply drug wastage costs (see [section 3.15](#))
- exclude end of life care costs and only include palliative care costs (see [section 3.16](#)).

Conclusion

Recommendation

3.22 The committee recognised that talazoparib plus enzalutamide is an effective treatment in terms of rPFS and OS compared with enzalutamide monotherapy. But, the indirect comparison evidence is highly uncertain and the available evidence does not suggest that talazoparib plus enzalutamide is value for money. The committee requested further

analyses to inform its decision making. So, talazoparib plus enzalutamide should not be used for untreated hormone-relapsed metastatic prostate cancer in adults.

4 Evaluation committee members and NICE project team

Evaluation 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 being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

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

Chair

Dr Charles Crawley

Chair, technology appraisal committee B

NICE project team

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

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Draft guidance consultation talazoparib with enzalutamide for untreated hormone-relapsed metastatic prostate cancer

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ISBN: [to be added at publication]