

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Talazoparib with enzalutamide for untreated hormone-relapsed metastatic prostate cancer

Final scope

**Remit/evaluation objective**

To appraise the clinical and cost effectiveness of talazoparib with enzalutamide within its marketing authorisation for treating hormone-relapsed metastatic prostate cancer in adults for whom chemotherapy is not clinically indicated.

**Background**

Prostate cancer is a condition in which tumours develop in the prostate, a gland in the male reproductive system. The exact cause is unknown but environmental and genetic factors are associated with an increased risk of developing prostate cancer.<sup>1,2</sup>

Prostate cancer is the most common cancer in men<sup>3</sup>, and the incidence increases with age. It is more common in those who have a family history of prostate cancer, in black African men compared to white men, and is least common in Asian men.<sup>1</sup>

In England and Wales, around 45,885 people were newly diagnosed with prostate cancer between 2019 and 2020.<sup>4</sup> Of this, 13% had metastatic disease, that is, disease that has spread to other parts of the body (such as the bones).<sup>4</sup> In 2019, around 12,000 people died from prostate cancer.<sup>5</sup>

[NICE clinical guideline 131](#) recommends radical treatment (surgery and radiotherapy) and androgen deprivation therapy (ADT) for the treatment of local and locally advanced prostate cancer. The aim of ADT is to suppress androgen levels and cause prostate cancer cell death. This can be achieved by orchidectomy (surgical removal of the testes) or by hormonal treatments such as luteinising hormone-releasing hormone agonist (e.g., goserelin) and antagonist (e.g., degarelix), and androgen receptor inhibitor (e.g., bicalutamide). For newly diagnosed metastatic prostate cancer cases, docetaxel (chemotherapy) can be offered within 12 weeks of starting ADT. In other metastatic cases, ADT is recommended initially.

Prostate cancer may initially be responsive to hormone therapy but eventually become resistant to it. This is known as hormone-relapsed prostate cancer (also known as hormone-resistant, hormone-refractory, and castration-resistant) and refers to prostate cancer which has progressed following ADT. Hormone-relapsed prostate cancer is characterised by a rise in prostate-specific antigen (PSA) despite ADT.

New hormonal agents (NHAs) refer to recently developed medicines which decrease androgen levels. These include apalutamide, enzalutamide, darolutamide and abiraterone. Two treatments are currently recommended for hormone-relapsed metastatic prostate cancer before chemotherapy. Enzalutamide is recommended for treating hormone-relapsed metastatic prostate cancer after ADT has failed, and before chemotherapy is indicated ([TA377](#)). Similarly, abiraterone in combination with prednisone or prednisolone is recommended for treating hormone-relapsed

metastatic prostate cancer in people who have no or mild symptoms after ADT has failed, and before chemotherapy is indicated ([TA387](#)).

Olaparib is recommended for treating hormone-relapsed metastatic prostate cancer with BRCA1 or BRCA2 mutations that has progressed after a newer hormonal treatment such as abiraterone or enzalutamide ([TA887](#)). Olaparib with abiraterone and prednisone or prednisolone is recommended as an option for untreated hormone-relapsed metastatic prostate cancer in adults who cannot have or do not want chemotherapy ([TA951](#)).

Chemotherapy docetaxel is recommended for people with hormone-relapsed metastatic prostate cancer with a Karnofsky Performance Status Score of 60% or more ([NICE clinical guideline 131](#) and [TA101](#)).

Abiraterone in combination with prednisone or prednisolone is recommended for the treatment of hormone-relapsed metastatic prostate cancer if the disease has progressed on or after one course of docetaxel-containing regimen ([TA259](#)). Enzalutamide is also recommended for treating hormone-relapsed metastatic prostate cancer in adults whose disease has progressed during or after docetaxel-containing chemotherapy ([TA316](#)).

Cabazitaxel in combination with prednisone or prednisolone is recommended for treating hormone-relapsed metastatic prostate cancer in people whose disease has progressed during or after docetaxel chemotherapy ([TA391](#)). Radium-223 dichloride is recommended as an option for treating hormone-relapsed prostate cancer in people with symptomatic bone metastases and no known visceral metastases if they have already had docetaxel or if docetaxel is contraindicated or unsuitable ([TA412](#)).

### The technology

Talazoparib (Talzenna, Pfizer) with enzalutamide (Xtandi, Astellas Pharma) has a marketing authorisation in the UK for 'the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC) in whom chemotherapy is not clinically indicated'.

Enzalutamide has a marketing authorisation in the UK for treating adult men with:

- Hormone-sensitive metastatic prostate cancer in combination with ADT
- High-risk hormone-relapsed non-metastatic prostate cancer
- Hormone-relapsed metastatic prostate cancer, whose disease is asymptomatic or mildly symptomatic after failure of ADT and for whom chemotherapy is not yet clinically indicated
- Hormone-relapsed metastatic prostate cancer, whose disease has progressed on or after docetaxel therapy.

<b>Interventions</b>	Talazoparib in combination with enzalutamide
<b>Population</b>	Adults with hormone-relapsed metastatic prostate cancer for whom chemotherapy is not clinically indicated
<b>Subgroup</b>	<p>If the evidence allows, the following subgroup will be considered:</p> <ul style="list-style-type: none"> <li>• homologous recombination repair (HRR) status including: <ul style="list-style-type: none"> <li>○ breast cancer gene (BRCA1 and BRCA2)</li> <li>○ ataxia-telangiectasia mutated (ATM) gene.</li> </ul> </li> </ul> <p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Olaparib with abiraterone (and prednisone or prednisolone)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

<p><b>Economic analysis</b></p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The economic modelling should include the cost associated with diagnostic testing for people with hormone-relapsed metastatic prostate cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: <a href="https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation">https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation</a>).</p>
<p><b>Related NICE recommendations</b></p>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">Olaparib with abiraterone for untreated hormone-relapsed metastatic prostate cancer</a> (2024). NICE technology appraisal guidance 951. No current plans to review this guidance.</p> <p><a href="#">Lu vipivotide tetraxetan for treating PSMA-positive hormone-relapsed metastatic prostate cancer after 2 or more therapies</a> (2023). NICE technology appraisal guidance 930. No current plans to review this guidance.</p> <p><a href="#">Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer</a> (2023). NICE technology appraisal guidance 887. No current plans to review this guidance.</p> <p><a href="#">Enzalutamide for treating hormone-sensitive metastatic prostate cancer</a> (2021). NICE technology appraisal guidance 712. Review date 2024.</p> <p><a href="#">Enzalutamide for hormone-relapsed non-metastatic prostate cancer</a> (2019). NICE technology appraisal guidance 580. Review date 2022.</p> <p><a href="#">Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases</a> (2016). NICE technology appraisal guidance 412. Review date to be confirmed.</p>

	<p><a href="#">Cabazitaxel for hormone-relapsed metastatic prostate cancer treated with docetaxel</a> (2016). NICE technology appraisal guidance 391. No current plans to review this guidance.</p> <p><a href="#">Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated</a> (2016). NICE technology appraisal guidance 387. No current plans to review this guidance.</p> <p><a href="#">Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated</a> (2016). NICE technology appraisal guidance 377. No current plans to review this guidance.</p> <p><a href="#">Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen</a> (2014). NICE technology appraisal guidance 316. No current plans to review this guidance.</p> <p><a href="#">Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen</a> (2016). NICE technology appraisal guidance 259. No current plans to review this guidance.</p> <p><a href="#">Docetaxel for the treatment of hormone-refractory metastatic prostate cancer</a> (2006). NICE technology appraisal guidance 101. No current plans to review this guidance.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">Prostate cancer: diagnosis and management</a> (2021). NICE guideline 131. No current plans to review this.</p> <p><b>Related Quality Standards:</b></p> <p>'<a href="#">Prostate cancer</a>' (2021). NICE quality standard 91. No current plans to review this.</p>
<p><b>Related National Policy</b></p>	<p>The NHS Long Term Plan (2019) <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2023) <a href="#">Manual for prescribed specialist services (2023/2024)</a> Chapter 105: Specialist cancer services (adults)</p> <p>Department of Health (2016) <a href="#">Department of Health and Social Care, NHS Outcomes Framework 2016-2017</a> Domains 1-5.</p> <p>NHS England (2013) <a href="#">NHS England B14/S/a 2013/14 NHS standard contract for cancer: specialised kidney, bladder and prostate cancer services (adult)</a>.</p> <p>NHS England (2016) <a href="#">Clinical Commissioning Policy Statement: Docetaxel in combination with androgen deprivation therapy for the treatment of hormone naïve metastatic prostate cancer</a></p>

### References

1. Cancer Research UK (2022) [Prostate cancer risks and causes](#). Accessed May 2024.
2. Macmillan Cancer Support (2021) [Potential causes of prostate cancer](#). Accessed May 2024.
3. Cancer Research UK (2018) [Prostate cancer incidence statistics](#). Accessed May 2024.
4. National Prostate Cancer Audit (2022) [Annual Report 2021](#). Accessed May 2024.
5. Cancer Research UK (2019) [Prostate cancer mortality statistics](#). Accessed May 2024.