

## Health Technology Briefing December 2022

### Abemaciclib with abiraterone acetate and prednisone for metastatic castration-resistant prostate cancer

Company/Developer

Eli Lilly and Company Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 27805

NICE ID: 11831

UKPS ID: 666915

#### Licensing and Market Availability Plans

Currently in phase II/III clinical development.

#### Summary

Abemaciclib with abiraterone acetate and prednisone (AAP) is in clinical development for patients with prostate cancer which has spread from its original site (metastatic) and is untreatable via testosterone suppression therapy (castration resistant). Prostate cancer is a cancer of the prostate gland (a small organ in a man's pelvis) and is the most common cancer in men in the UK. The symptoms may vary depending on the stage of cancer but can include pain, tiredness, and problems emptying the bladder and the bowels. The castration-resistant form of metastatic prostate cancer is particularly dangerous and leads to a very poor prognosis, hence additional treatment options are needed.

Abemaciclib is a medicinal product taken orally. It works by blocking the activity of certain enzymes known as cyclin-dependant kinases (CDK) 4 and 6, which play a key role in regulating the way cells grow and divide. By blocking these enzymes, abemaciclib slows disease progression. If licensed, abemaciclib combination with AAP will offer an additional treatment option for men with mCRPC.

#### Proposed Indication

For the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC).<sup>1</sup>

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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## Technology

### Description

Abemaciclib (Verzenio, LY2835219) is a potent and selective inhibitor of cyclin-dependent kinases 4 and 6 (CDK4 and CDK6), and most active against Cyclin D1/CDK4 in enzymatic assays. Abemaciclib prevents retinoblastoma protein (Rb) phosphorylation, blocking cell cycle progression from the G1 to the S-phase of cell division, leading to suppression of tumour growth.<sup>2</sup>

Abemaciclib is currently in phase II and III clinical development for the treatment for patients with metastatic castration-resistant prostate cancer. In the phase II/III clinical trial (CYCLONE 2; NCT03706365) abemaciclib is administered orally.<sup>1</sup>

### Key Innovation

Treatment options for patients with mCRPC are non-curative, and life expectancy is only about 3 years.<sup>3</sup> Despite recent advances, nearly all mCRPC patients experience disease progression and cancer-specific mortality. Persistent or reactivated androgen receptor signalling and/or activation of pathways in cross-talk with androgen receptor signalling are key drivers of mCRPC progression. Evidence suggests that androgen receptor signalling promotes translation of D-type cyclins resulting in CDK4 and 6 activation and cell cycle progression. Abemaciclib is a selective inhibitor of CDK4 and 6. Preclinical studies with prostate cancer cell lines and xenograft models showed that abemaciclib induces cell cycle arrest and tumour growth inhibition. The addition of abemaciclib to androgen receptor targeted therapy such as abiraterone acetate and prednisone (AAP) may provide an effective treatment for mCRPC patients.<sup>4</sup> If licensed, abemaciclib in combination with AAP will offer an additional treatment option for patients with mCRPC.

### Regulatory & Development Status

Abemaciclib in combination with AAP does not currently have Marketing Authorisation in the EU/UK for any indication.

Abemaciclib is currently licenced in the UK for the treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2)- negative locally advanced or metastatic breast cancer in combinations with an aromatase inhibitor, or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy.<sup>2</sup>

Abemaciclib is in phase II and phase III development, as a monotherapy or in combination therapy for the following indications:<sup>5</sup>

- Biliary Tract Carcinoma
- Prostate Cancer
- Breast Cancer
- Head and Neck Cancer
- Non Small Cell Lung Cancer

## Patient Group

### Disease Area and Clinical Need

Prostate cancer is the most common cancer in older men in the UK.<sup>6</sup> It affects the prostate, a small gland in the pelvis found only in men, which is located between the penis and the bladder and surrounds the

urethra. The main function of the prostate is to help in the production of semen.<sup>7</sup> In advanced prostate cancer, the cancer has spread from the prostate to other parts of the body (metastatic). It most commonly spreads to lymph nodes in other parts of the body or to the bones.<sup>8</sup> Prostate cancer cells usually need testosterone to grow.<sup>9</sup> Prostate cancer that has spread to other parts of the body and which keeps growing even when the amount of testosterone in the body is reduced to very low levels (via androgen deprivation therapy) is identified as mCRPC.<sup>10</sup> Prostate cancer is more common in black Caribbean and black African men than in white men and is less common in Asian men.<sup>6</sup> Prostate cancer does not usually cause any symptoms until the cancer has grown large enough to put pressure on the tube that carries urine from the bladder out of the penis (urethra).<sup>7</sup> Prostate cancer is a significant cause of morbidity and mortality in men, especially in those over the age of 75 years and impacts on their daily lives, particularly physical and emotional health, relationships and social life.<sup>11</sup>

Prostate cancer accounts for 27% of all new cancer cases in males in the UK (2017 data).<sup>12</sup> Around 55–65% of people with prostate cancer develop metastatic disease. Over 90% of people with metastatic prostate cancer initially respond to hormonal therapy but eventually become resistant to it.<sup>13</sup> In England, in 2017 there were 41,201 registrations of newly diagnosed cases of malignant neoplasm of prostate (ICD10 code C61). Of these, 8,490 cases were diagnosed at stage 4 (metastatic).<sup>14</sup> According to Hospital Episode Statistics (HES) data, in 2021-22 there were 73,256 admissions with a primary diagnosis of neoplasm of the prostate (ICD-10 code C61), resulting in 77,547 finished consultant episodes (FCE), 71,095 bed days and 54,896 day cases.<sup>15</sup> In England and Wales in 2020, there were 10,971 deaths where malignant neoplasm of prostate (ICD-10 code C61) was recorded as the underlying cause.<sup>16</sup> Latest published survival statistics (patients diagnosed in 2013-2017) report a 1-year net survival rate of 88.3% and a 5-year net survival rate of 49% for men diagnosed with stage 4 prostate cancer.<sup>17</sup>

### Recommended Treatment Options

As an option for treating metastatic hormone-relapsed prostate cancer after androgen deprivation therapy has failed, and before chemotherapy is indicated, NICE recommends:<sup>18</sup>

- docetaxel, within its licensed indications, as a treatment option for people with hormone refractory prostate cancer only if their Karnofsky Performance-Status score is 60% or more.<sup>19</sup>
- Abiraterone in combination with prednisone or prednisolone
- Corticosteroid such as dexamethasone
- Enzalutamide

### Clinical Trial Information

<p><b>Trial</b></p>	<p><a href="#">NCT03706365</a>; <a href="#">EudraCT2016-004276-21</a>; <b>CYCLONE 2</b>; A Phase 2/3, Randomized, Double-Blind, Placebo-Controlled Study of Abiraterone Acetate Plus Prednisone With or Without Abemaciclib in Patients With Metastatic Castration-Resistant Prostate Cancer <b>Phase II/III- Recruiting</b> <b>Location(s):</b> 6EU countries, UK, US, and other countries <b>Primary completion date:</b> December 2023</p>
<p><b>Trial Design</b></p>	<p>Randomised, double blind, parallel assignment</p>
<p><b>Population</b></p>	<p>N=350 (estimated); Subjects aged 18 and over with histologically confirmed adenocarcinoma of the prostate.</p>

Intervention(s)	Abiraterone plus prednisone administered orally and abemaciclib administered orally
Comparator(s)	Matched placebo
Outcome(s)	Radiographic Progression Free Survival (rPFS) [Time Frame: Baseline to Radiographic Disease Progression or Death from Any Cause (Estimated up to 21 Months)]  See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

### Estimated Cost

Abemaciclib is already in marketed in the UK. The NHS indicative price for abemaciclib tablets are as follows:<sup>20</sup>

- Abemaciclib 50mg, 100mg and 150mg tablets; 28 tablets (prescription only medicine) cost £1475.00 (Hospital only)
- Abemaciclib 50mg, 100mg and 150mg tablets; 56 tablets (prescription only medicine) cost £2950.00 (Hospital only)

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal guidance in development. Nivolumab in combination for treating hormone relapsed metastatic prostate cancer before chemotherapy (GID-TA10490). Expected date of issue to be confirmed.
- NICE technology appraisal guidance in development. Pembrolizumab with docetaxel for treating hormone-relapsed metastatic prostate cancer untreated with chemotherapy (GID-TA10668). Expected date of issue to be confirmed.
- NICE technology appraisal guidance. Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases (TA412). September 2016.
- NICE technology appraisal guidance. Abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA387). July 2016.
- NICE technology appraisal guidance. Enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated (TA377). January 2016.
- NICE clinical guideline. Prostate cancer: diagnosis and management (NG131). May 2019.
- NICE quality standard. Prostate cancer (QS91). December 2021.

#### NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Specialised Kidney, Bladder and Prostate Cancer Services (Adult). B14/S/a.
- NHS England. Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) in the treatment of Prostate Cancer. 16031/P. July 2016.

- NHS England. Clinical Commissioning Policy: Proton Beam Therapy for Cancer of the Prostate. 16020/P. July 2016.

#### Other Guidance

- Cassinello J, Arranz JÁ, Piulats JM, Sánchez A, Pérez-Valderrama B, Mellado B, et al. SEOM clinical guidelines for the treatment of metastatic prostate cancer. 2017.<sup>21</sup>
- Public Health England. Prostate Cancer Risk Management Programme. March 2016.<sup>22</sup>
- ESMO Guidelines Committee. Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2015.<sup>23</sup>

### Additional Information

### References

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