AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Abiraterone acetate (ZYTIGA®), enzalutamide (Xtandi®) and apalutamide (Erleada®) for the treatment of hormone-sensitive prostate cancer during the COVID-19 pandemic

December 2020

ONE WALES INTERIM COMMISSIONING DECISION DURING THE COVID-19 PANDEMIC

Abiraterone acetate (ZYTIGA®), enzalutamide (Xtandi®) and apalutamide (Erleada®) for the treatment of hormone-sensitive prostate cancer during the COVID-19 pandemic

Date of advice: December 2020

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

Using the agreed starting and stopping criteria, enzalutamide (Xtandi®) can be made available within NHS Wales for the treatment of high-risk locally advanced, and metastatic hormone-sensitive prostate cancer during the COVID-19 pandemic. Abiraterone acetate (ZYTIGA®) can be made available for patients who are intolerant of enzalutamide or where enzalutamide is deemed to be unsuitable. These recommendations apply only in circumstances where the approved commercial arrangement prices are applied.

Abiraterone acetate (ZYTIGA®) is licensed for the treatment of newly diagnosed high-risk metastatic hormone-sensitive prostate cancer in adult men in combination with androgen deprivation therapy. For the licensed indications, this One Wales Interim Commissioning decision is interim to subsequent Health Technology Assessment advice from AWMSG or NICE becoming available.

Enzalutamide (Xtandi®) is not licensed to treat these indications and abiraterone acetate (ZYTIGA®) is not licensed to treat low-risk metastatic disease or high-risk locally advanced disease. Each provider organisation must ensure all internal governance arrangements are completed before these medicines are prescribed. The risks and benefits of the off-label use of these medicines for these indications should be clearly stated and discussed with the patient to allow informed consent. Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

It is the view of the Interim Pathways Commissioning Group (IPCG) that apalutamide (Erleada®) should not be supported within NHS Wales for the treatment of these

indications. Patients who are currently receiving apalutamide (Erleada®) should have the option to continue therapy until they and their consultant consider it appropriate to stop.

This advice will be reviewed after 6 months or earlier if new evidence or information becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Interim Commissioning decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Interim Commissioning decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice promotes consistency of access across NHS Wales.

Start and stop criteria for enzalutaimde (Xtandi®) and abiraterone acetate (ZYTIGA®) for the treatment of hormone-sensitive prostate cancer during the COVID-19 pandemic

Start criteria:
Enzalutamide treatment may be given to newly diagnosed patients eligible to start treatment with docetaxel, or patients who have received less than five cycles of docetaxel before stopping due to the COVID-19 pandemic, in line with the following criteria:

1. Patients with high-risk, locally advanced prostate cancer. High-risk is defined as T3/T4 staging or Gleason score 8 to 10 or PSA > 40 ng/ml.
2. Metastatic prostate cancer.

Where enzalutamide is deemed to be unsuitable due to the risk of significant drug interactions with concomitant medicines or the presence of significant co-morbidities or other relevant patient factors, or intolerance to enzalutamide due to adverse effects, abiraterone acetate may be given (in line with the criteria above).

Stop criteria:
For patients with high-risk, locally advanced prostate cancer or node positive disease but no distant metastases and receiving radical radiotherapy stop treatment after:

1. Completion of two years of treatment with enzalutamide or abiraterone acetate, or
2. Poor tolerance or refusal to continue, or
3. Evidence of disease progression (defined below).

For patients with metastatic, high-risk locally advanced disease and not receiving radiotherapy stop treatment after:

1. Poor tolerance or refusal to continue
2. Evidence of disease progression (defined below).

Disease progression is defined as:

- Radiological progression
- Clinical progression
- PSA progression:
    - If the PSA nadir is > 50% of the last pre-treatment PSA
    - For patients whose PSA falls by > 50% of the last pre-treatment PSA but remains above 4 ng/ml, PSA progression when PSA is confirmed as increasing by 50% above the nadir level
    - For patients whose PSA falls below 4 ng/ml, PSA relapse is defined as either 50% increase from their nadir or the PSA increasing above 4 ng/ml, whichever is greater.

This advice will be reviewed after 6 months or earlier if new information becomes available.

One Wales Interim Commissioning Process
Interim Pathways Commissioning Group (IPCG) summary of decision rationale

Medicines: **abiraterone aceate (ZYTIGA®), enzalutamide (Xtandi®), apalutamide (Erleada®)**
Indication: **treatment of high-risk, locally advanced and metastatic hormone-sensitive prostate cancer (HSPC) during the COVID-19 pandemic**
Meeting date: **26 October 2020**

Criteria	IPCG opinion
Clinical effectiveness	IPCG notes that the clinical effectiveness evidence is from two randomised controlled trials (RCTs) and a post hoc subgroup analysis for abiraterone acetate, two RCTs for enzalutamide and one for apalutamide. IPCG notes that the agents are comparable in efficacy to docetaxel based on an indirect treatment analysis. IPCG is aware of limited effectiveness data in the high risk, locally advanced population for abiraterone acetate and the lack of available data for this group for apalutamide and enzalutamide. IPCG considers that the evidence provided demonstrated clinical effectiveness.
Cost-effectiveness	IPCG notes that the cost-effectiveness evidence is from NICE and SMC's appraisals of abiraterone acetate for the treatment of newly diagnosed high-risk metastatic hormone sensitive prostate cancer. The company provided AWTTC with the model submitted to SMC. IPCG acknowledges that the cost-effectiveness estimates are subject to significant uncertainties. IPCG notes that the results from the SMC model for abiraterone acetate for high-risk metastatic hormone sensitive prostate cancer compared with ADT alone, [confidential data removed]. IPCG notes that no cost-effectiveness studies have been undertaken for enzalutamide or apalutamide for the indications under consideration, or for abiraterone for the treatment of low-risk metastatic and high-risk locally advanced hormone-sensitive prostate cancer.
Budget impact	IPCG considers that the estimate of patient numbers reported is reasonably accurate. IPCG is aware of the regional differences in uptake of these three medicines in Wales during the first four months of the One Wales decision which was issued in April 2020. This will continue to be monitored and reported back at the 6 month review. IPCG acknowledges that budget impact estimates are subject to uncertainty. IPCG notes the differences in acquisition costs between the three agents.
Other factors	IPCG notes that enzalutamide and, for patients intolerant of enzalutamide, abiraterone acetate are recommended options in England for patients with newly diagnosed metastatic HSPC instead of docetaxel during the COVID-19 pandemic, in line with the NICE guideline: COVID-19 rapid guideline: delivery of systemic anticancer treatments. Abiraterone acetate is recommended in Scotland for the treatment of newly diagnosed low-risk metastatic HSPC during the pandemic. Abiraterone acetate is available in Scotland for high-risk metastatic HSPC following a recommendation by SMC. Docetaxel was previously available via One Wales interim commissioning for use in patients with high risk locally advanced, and metastatic HSPC. This advice was retired from One Wales as it became

	standard of care following the publication of NICE guidance for the treatment of prostate cancer. These oral treatments are being considered as alternatives to docetaxel during COVID-19 as they are less likely to cause neutropenia and require fewer hospital visits. IPCG is aware of the differences in monitoring profiles between these medicines and potential for drug interactions which may have implications on treatment choice.
Final recommendation	IPCG recommends that enzalutamide (Xtandi®) continues to be made available for the treatment of high-risk locally advanced, and metastatic, hormone-sensitive prostate cancer during the COVID-19 pandemic, and that abiraterone acetate (ZYTIGA®) continues to be made available for patients who are intolerant of enzalutamide. It is the view of the IPCG that apalutamide (Erleada®) should not be supported within NHS Wales for the treatment of these indications. Patients who are currently receiving apalutamide (Erleada®) should have the option to continue therapy until they and their consultant consider it appropriate to stop. The advice will be reviewed after 6 months or earlier if new evidence of information becomes available.
Summary of rationale	IPCG considers abiraterone acetate and enzalutamide are clinically effective treatment options and are reasonable value for money for the indications under consideration as an alternative to docetaxel during the COVID-19 pandemic.