Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2215

abiraterone acetate 500mg film-coated tablets (Zytiga®)

Janssen-Cilag Ltd

6 December 2019

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the orphan medicine process

abiraterone acetate (Zytiga®) is accepted for use within NHSScotland.

Indication under review: abiraterone acetate with prednisone or prednisolone for the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer in adult men in combination with androgen deprivation therapy.

Abiraterone acetate in combination with prednisone and androgen deprivation therapy demonstrated superiority over androgen deprivation therapy alone for improving progression-free survival and overall survival.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of views from a Patient and Clinician Engagement (PACE) meeting.

Chairman
Scottish Medicines Consortium

Indication

Abiraterone acetate with prednisone or prednisolone for the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer (mHSPC) in adult men in combination with androgen deprivation therapy (ADT).[1]

Dosing Information

The recommended dose is 1,000mg (two 500mg tablets) as a single daily dose that must not be taken with food. The tablets should be taken at least one hour before or at least two hours after eating. For men with high risk mHSPC, abiraterone is to be taken with 5mg prednisone or prednisolone orally once daily. Medical castration with luteinising hormone releasing hormone (LHRH) analogue should be continued during treatment in patients not surgically castrated.

Abiraterone should be prescribed by an appropriate healthcare professional.[1]

Product availability date

12 October 2017

Abiraterone acetate meets SMC orphan equivalent criteria for this indication.

Summary of evidence on comparative efficacy

Abiraterone acetate, the pro-drug of abiraterone, inhibits androgen biosynthesis. This reduces testosterone production which negatively impacts on tumour growth. Androgen deprivation with LHRH analogues or orchiectomy, decreases androgen production in the testes but does not affect production in the tumour or by the adrenal glands.[1, 2] Abiraterone acetate (henceforth referred to as abiraterone), in combination with prednisolone or prednisone, is the first of its class to be licensed for the treatment of newly diagnosed high risk mHSPC in adult men in combination with ADT.

The key evidence for this submission comes from LATITUDE, a multicentre, randomised, double-blind, phase III, superiority study in patients with newly diagnosed high risk mHSPC. The study compared abiraterone plus prednisone plus ADT with ADT plus matching placebos. The study included adult men with metastases, confirmed within three months prior to randomisation and an Eastern Co-operative Oncology Group (ECOG) performance status of no greater than 2. Patients were considered high risk if they had at least two of the following prognostic factors: a Gleason score ≥8 (scale ranges from 2 to 10 with higher scores indicating more aggressive disease), the presence of ≥3 lesions on a bone scan, and the presence of measurable visceral (excluding lymph node disease) metastasis on computerised tomography (CT) or magnetic resonance imaging (MRI) scan (according to Response Evaluation Criteria in Solid Tumours [RECIST] version 1.1 criteria).[2-4]

Patients were randomised equally to receive abiraterone 1,000mg orally once daily plus prednisone 5mg orally once daily plus ADT (n=597, abiraterone group) or ADT plus matching placebo (n=602,

placebo group) in continuous 28-day treatment cycles.[3] Randomisation was stratified by presence of measurable visceral disease (yes or no) and ECOG performance status (0-1 or 2). Patients who had not undergone surgical castration were treated with ongoing ADT to reach or maintain a serum testosterone level <50ng per decilitre (1.7nmol/L).[2-4] Choice of medical ADT (such as LHRH agonist) was at the investigator's discretion; dosing was required to be consistent with the respective marketing authorisation.[4] Treatment continued until disease progression, withdrawal of consent, dosing non-compliance, unacceptable toxicity or death.[3, 4]

The co-primary outcomes were overall survival, defined as time from randomisation to death from any cause, and investigator-assessed radiographic progression free survival (PFS), defined as time from randomisation to occurrence of radiographic progression according to RECIST 1.1.[3] Both outcomes were assessed in the intention-to-treat population (ITT), which comprised all randomised patients.[3, 4] Treatment with abiraterone plus prednisone plus ADT, compared with ADT plus placebo, was associated with significantly longer median overall survival and radiographic PFS.[2-4] Detailed results are presented in Table 1.

Table 1. Analyses of overall survival and radiographic PFS, co-primary outcomes of the LATITUDE study (ITT population).[2-5]

		Abiraterone plus prednisone plus ADT (n=597)	**Placebo plus ADT (n=602)**
Median overall survival			
First interim overall survival analysis (data cut-off 31/10/16). Median follow-up 30.4 months.	Events, n	169	237
	Median, months	Not reached	34.7
	Hazard ratio (95% CI)	0.62 (0.51 to 0.76), p<0.001	
	24-month event-free rate	77%	69%
	36-month event-free rate	66%	49%
Final overall survival analysis (data cut-off 15/08/18). Median follow-up 51.8 months.	Events, n	275	343
	Median, months	53.3	36.5
	Hazard ratio (95% CI)	0.66 (0.56 to 0.78), p<0.001	
Radiographic progression-free survival			
Final radiographic PFS analysis (data cut-off 31/10/16). Median follow-up 30.4 months.	Events, n	239	354
	Median, months	33.0	14.8
	Hazard ratio (95% CI)	0.47 (0.39 to 0.55), p<0.001	
	24-month event-free rate	61%	35%
	36-month event-free rate	47%	21%

PFS= progression-free survival, defined as time from randomisation to occurrence of radiographic progression according to RECIST 1.1, 95% CI = 95% confidence intervals.

Considering the clinical benefit demonstrated at the time of the primary radiographic PFS analysis (data cut-off 31 October 2016), an independent data and safety monitoring committee recommended unblinding patients and investigators. Patients in the placebo group who had not experienced disease progression were allowed to cross over to receive abiraterone plus prednisone plus ADT (n=60).[3] Sensitivity analyses of overall survival were conducted to evaluate the impact of treatments received subsequent to study treatment as a higher proportion of patients in the placebo group received life-extending subsequent therapy (41% versus 21% for the abiraterone group). Subsequent therapies included docetaxel, cabazitaxel, abiraterone acetate plus prednisone, enzalutamide, and radium-223.[2, 4] Analyses adjusting for subsequent treatments (hazard ratio [HR] 0.48) and using censoring at the time of initiation of life-extending subsequent anticancer therapy (HR 0.58) were both consistent with the first interim and final overall survival analysis.[4]

The following secondary outcomes were all supportive of the findings for the co-primary outcomes: time to subsequent therapy for prostate cancer, time to initiation of chemotherapy, time to prostate specific antigen (PSA) progression and time to skeletal-related event.[2, 4]

For the patient reported secondary outcome, time to pain progression (the time from randomisation to when a patient experienced ≥30% increase from baseline according to the Brief Pain Inventory short form, observed as two consecutive evaluations), the median time was not reached in the abiraterone group compared to 16.6 months in the placebo group (HR 0.69, 95% confidence interval [CI]: 0.58 to 0.83).[4]

STAMPEDE is an ongoing open-label, multi-arm, multi-stage phase II/III study that aims to assess varied therapeutic regimens in the management of high risk locally advanced or metastatic hormone-naïve prostate cancer. The primary outcome was overall survival and PFS was assessed as a secondary outcome. It included comparisons of the abiraterone regimen (abiraterone plus prednisone/prednisolone plus ADT) with ADT alone and the abiraterone regimen with docetaxel plus prednisolone plus ADT (docetaxel regimen) over different time periods. One post hoc analysis of a subgroup of patients with high risk metastatic disease (n=473) included patients randomised to receive the abiraterone regimen (n=241) or ADT alone (n=232). The analysis was conducted after a median follow-up of 41.5 months, and 230 deaths (49% of the subgroup). Median overall survival was not presented, HR=0.54 (95%CI: 0.41 to 0.70). The Kaplan Meier survival estimates at 36 months were 65% and 45% in the abiraterone and ADT groups respectively.[6, 7] A total of 283 patients (60%) had experienced disease progression, HR= 0.46 (95%CI: 0.36 to 0.59).[6]

An opportunistic comparison of patients with high risk locally advanced or metastatic hormone-naïve prostate cancer who had been randomised to receive the abiraterone regimen (n=377) or the docetaxel regimen (n=189) was conducted. The results of this analysis should be interpreted with caution. For the overall study population there was no evidence of a difference between treatment regimens for overall survival, HR 1.16 (95% CI: 0.82 to 1.65), and results suggest an advantage for patients treated with the abiraterone regimen in terms of PFS, HR 0.65 (95% CI: 0.48 to 0.88). Of the

overall study population 60% (342/566) had metastatic disease, overall survival for this subgroup was consistent with the overall study population: HR 1.13 (95% CI: 0.77 to 1.66).[8]

The submitting company presented Bayesian network meta-analyses (NMAs) based on four studies (LATITUDE,[2, 3] CHAARTED,[9, 10] GETUG-AFU-15[9, 11] and STAMPEDE[6-8]). The NMAs were conducted in patients with metastatic hormone sensitive prostate cancer and provided relative estimates for efficacy outcomes including overall survival and PFS, safety outcomes (any-grade adverse events [AEs] and grade ≥3 AEs), and health-related quality of life outcomes (change from baseline in Functional Assessment of Cancer Therapy – Prostate and Brief Pain Inventory – Short Form scores). Reported results suggest progression-free survival is likely to be longer for patients treated with the abiraterone regimen compared with the docetaxel regimen. The abiraterone regimen was associated with a favourable effect on health-related quality of life outcomes compared with the docetaxel regimen.[12]

A published NMA, based on the same 4 studies (3 in the base-case with STAMPEDE data included in an exploratory analysis), comparing these treatments in newly diagnosed patients with high risk and/or high-volume mHSPC concluded the abiraterone regimen was likely to be at least as effective as the docetaxel regimen in reducing the risk of death and was likely to be better at preventing disease progression and improving quality of life.[12]

*Other data were also assessed but remain confidential.**

Summary of evidence on comparative safety

The safety profile of abiraterone plus prednisone plus ADT is consistent with the known profile described in the population diagnosed with metastatic castration-resistant prostate cancer (mCRPC). Overall the safety profile is considered manageable and treatment is considered to be well tolerated. Safety analyses were performed in all randomised patients who received at least one dose of the study medicine (n=1,199). Patients in the abiraterone group received treatment for almost twice as long as patients in the placebo group (24 and 14 months respectively).[4]

In the LATITUDE study, the following were reported in the abiraterone (597) and placebo groups (602) respectively: treatment-emergent adverse events 95% and 93%, grade 3 or 4 adverse events 63% and 48%, adverse events leading to dose reduction or interruption 35% and 18%, serious adverse events 32% and 25%, adverse events leading to treatment discontinuation 16% and 10%.[3 4]
In the abiraterone and placebo groups, respectively, the most common grade 3 or 4 adverse events were hypertension (21% and 10%), hypokalaemia (12% and 2%), alanine aminotransferase increase (5.7% and 1.3%) and hyperglycaemia (5.2% and 3.7%).[3] Three treatment-related deaths were reported in each of the abiraterone (gastric ulcer perforation, sudden death, and cerebrovascular accident) and placebo groups (sudden death, cerebrovascular accident, and pneumonia).[4]

Summary of clinical effectiveness issues

Hormone sensitive prostate cancer is androgen dependent and responds to treatment that decreases androgen levels.[4] Prognostic factors for high risk disease include a PSA greater than 20ng/mL; having a tumour affecting both sides of the prostate gland and having a Gleason score of 8 to 10. Due to the nature of the disease, the majority of patients diagnosed with high risk mHSPC present with bone metastases, which increase the burden of disease and are a major cause of morbidity and mortality.[4] Treatment options include ADT with or without docetaxel (off-label). Androgen deprivation therapy can effectively control disease in patients with low-risk disease and few metastases, however most patients will develop high risk castration-resistant disease. ADT alone has been associated with poor survival due to patients progressing to hormone-resistant disease. The combination of ADT plus off-label docetaxel has been shown to provide significant benefit on overall survival, however, docetaxel is associated with clinically significant toxicities such as myelosuppression, including febrile neutropenia, fatigue, alopecia, diarrhoea, neuropathy and peripheral oedema.[4] Many men are considered to be not fit enough for treatment with, or refuse the offer of, docetaxel. Approximately 40% of patients with newly diagnosed metastatic prostate cancer were reported to receive treatment with docetaxel.[13] The proportion is likely to be higher in patients with high risk disease and may have increased since publication of this study. Abiraterone meets SMC orphan equivalent criteria for this indication. Clinical experts consulted by SMC considered that abiraterone fills an unmet need in this therapeutic area, particularly for patients who have contraindications to or are unsuitable for treatment with docetaxel.

In the LATITUDE study, abiraterone plus prednisone plus ADT demonstrated a statistically and clinically significant increase in median radiographic progression-free survival (33 months versus 15 months, hazard ratio: 0.47). Both the initial and final overall survival analyses reported statistically significant differences favouring treatment with abiraterone. Additionally, quality of life outcomes and secondary outcomes were supportive of the co-primary outcomes.[2-4]

Overall survival data were immature at the time of the primary analysis (34% overall event rate) and subsequent therapies and treatment cross-over are likely to confound the final analysis. At the time of final analysis of LATITUDE, there was an imbalance in the number of patients who received life-extending subsequent therapies (30% versus 57% in the abiraterone and placebo groups respectively),[3] this included 12% of patients in the placebo group who had crossed over to receive the abiraterone regimen. The subsequent treatments received by patients in LATITUDE may not accurately reflect the number of treatments expected for metastatic castration resistant prostate cancer in Scottish clinical practice. Sensitivity analyses considering the impact of subsequent therapies were consistent with the final analysis.

Several patient reported outcome measures were collected at different time points and multiplicity could be an issue, although repeated-measures analyses were used to adjust for this over time[14] Prolonging the time patients are progression-free and delaying the time to toxic chemotherapy is likely to improve patients' quality of life.

The STAMPEDE study provides direct evidence comparing the abiraterone regimen with the docetaxel regimen, however the data comes from an opportunistic post hoc, subgroup analysis. Consequently, the studies were not appropriately powered for these subgroups and the risk of a false positive result was uncontrolled. Results of these analyses therefore, need to be interpreted with some caution.

Limitations of the indirect evidence include: clinical and methodological heterogeneity across the studies included in the NMA, combining different definitions of PFS, the inclusion of a study considered to be at high risk of bias, inconsistency across the base-case and sensitivity analyses for PFS, and uncertainty with the interpretation of the clinical meaningfulness of the selected safety and health-related quality of life outcomes. The company did not present indirect comparison safety results for grade ≥3 adverse events as initially stated and did not include hypokalaemia or hypertension as reported adverse events. An inference of a PFS advantage for the abiraterone regimen appears acceptable. However, for overall survival this is uncertain.

Daily oral abiraterone may provide patients with an alternative to intravenous docetaxel which is administered once per cycle for 6 cycles. The abiraterone regimen may help reduce pressure on parenteral chemotherapy administration services.

Clinical experts consulted by SMC considered that the place in therapy of abiraterone is as an alternative to docetaxel based treatment for patients with high risk mHSPC. They considered the introduction of abiraterone at this stage in the treatment pathway may impact on the patient and/or service delivery as monitoring of serum transaminases is required prior to starting treatment, every two weeks for the first three months of treatment and monthly thereafter. Monthly monitoring of blood pressure, serum potassium and fluid retention is also recommended.

Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of abiraterone, as an orphan-equivalent medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Metastatic prostate cancer is an incurable life limiting disease and symptoms associated with disease progression such as fatigue, urinary problems, pain and bone fractures can be highly debilitating.
- There is a need for more treatments in this disease area to support patient choice. This need is particularly great for patients considered unsuitable for chemotherapy as the alternative is hormone deprivation therapy alone. Abiraterone extends survival compared to hormone deprivation therapy alone.

- Current available data suggest abiraterone and docetaxel have comparable overall survival benefit in this setting, however docetaxel may be less preferable for some patients as adverse effects may be more severe.
- Treatment with abiraterone could support patients to live independently as it is an oral medicine compared with docetaxel which is administered intravenously in a clinical setting.
- Abiraterone may maintain patients' quality of life and extend survival allowing them to fully participate in financial and social aspects of family life for longer. This would have important psychological benefits for families and carers.

Additional Patient and Carer Involvement

We received patient group submissions from Prostate Cancer UK, Prostate Scotland and Tackle Prostate Cancer. All three organisations are registered charities. Prostate Cancer UK has received <0.15% pharmaceutical company funding in the past two years, including from the submitting company. Tackle Prostate Cancer has received 60% pharmaceutical company funding in the past two years, including from the submitting company. Prostate Scotland has not received any pharmaceutical company funding in the past two years. Representatives from all three organisations participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

Summary of comparative health economic evidence

The submitting company presented a cost- utility analysis of abiraterone plus prednisolone for the treatment of adult men with newly diagnosed high risk mHSPC in combination with ADT. Pairwise comparisons were provided against ADT alone, and against the off-label combination of ADT plus docetaxel.

The cost-utility analysis used a 'semi-Markov' approach across six health states (mHSPC [progression-free]; mHSPC [progressive disease]; mCRPC 1st line (on/off treatment); mCRPC 2nd line; mCRPC 3rd line). This involved use of a partitioned survival model to define transition from the 'mHSPC (progression free)' health state to 'mHSPC (progressive disease)' (based on radiographic progression-free survival), as well as transition from any state to death. Survival data were obtained from the LATITUDE clinical study for comparison of the abiraterone regimen with ADT alone, and from a network meta-analysis described above for comparison with the docetaxel regimen. Other transitions were modelled using mean health state transitions estimated within a previous SMC submission (873/13). A 33 year time horizon was used.

Utility estimates were derived from EQ-5D-5L data collected in the LATITUDE study, and subsequently 'cross-walked' to EQ-5D-3L index scores, as appropriate. A regression model was used to adjust for covariates such as age, baseline utility and adverse events. A relative ratio was derived from a previous SMC submission (873/13) to estimate later line utilities. These resulted in a variety of

estimates specific to the individual treatments, with a greater range in utility estimates than observed in previous submissions.

The submission considered a comprehensive range of costs including medicines acquisition costs, adverse event management, costs of subsequent treatment, and both scheduled and unscheduled medical resource use. Treatment duration for abiraterone was calculated by applying a risk ratio to radiographic PFS data, however alternative approaches involving the extrapolation of time to treatment-discontinuation data were preferred for consistency with the estimation of radiographic PFS and overall survival across the time horizon. Sources for assigning costs were generally appropriate and relevant to NHSScotland.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. A PAS discount is in place for enzalutamide (often used as a later line treatment for patients receiving ADT alone or ADT plus docetaxel) and this was included in the results used for decision-making by using estimates of the comparator PAS price.

SMC is unable to present the results provided by the company which used an estimate of the PAS price for enzalutamide or the PAS for abiraterone due to commercial confidentiality and competition law issues. The results at list price (Table 2) are shown below.

Table 2: Base case results (list price)

Technology	Incremental QALYs	ICER (£/QALY)
ADT alone	0.987	£90,483
AAP + ADT		
Docetaxel + ADT	0.401	£201,527
AAP + ADT		

Key: AAP, abiraterone acetate + prednisolone; ADT, androgen deprivation therapy; ICER, incremental cost-effectiveness ratio; incr., incremental; LYG, life years gained; mHSPC, metastatic hormone sensitive prostate cancer; PAS, patient access scheme; QALY, quality-adjusted life year.

A number of scenario analyses were included in the submission and obtained through correspondence with the company. These indicated that the cost-effectiveness results against both comparator treatments were upwardly sensitive to the modelling of treatment discontinuation and the assumed frequency of consultant visits during abiraterone treatment. In the case of the comparison with docetaxel plus ADT, the results were also sensitive to the methods of extrapolation of PFS and to the assumption of no OS benefit for abiraterone. The results at list prices are shown in table 3.

Table 3: Key scenario analyses (list price)

Model assumption	Number	Scenario	ICER vs ADT alone	ICER vs docetaxel + ADT
Base case			£90,483	£201,527
NMA	1.	NMA excluding STAMPEDE	N/A	£214,683
Treatment discontinuation	2.	TTD curve (Weibull)	£101,335	£228,256
Survival extrapolation for rPFS	3.	Log-logistic (stratified)	£97,395	£212,780
	4.	Log-normal (stratified)	£97,517	£220,945
	5.	Gamma (stratified)	£99,177	£207,858
	6.	Gompertz (stratified)	£89,075	£200,789
	7.	Exponential (stratified)	£97,922	£206,369
	8.	Weibull (unstratified)	£89,956	£200,202
Survival extrapolation for OS	9.	Log-logistic (stratified)	£76,402	£170,390
	10.	Log-normal (stratified)	£64,853	£159,450
	11.	Gamma (stratified)	£104,706	£198,479
	12.	Gompertz (stratified)	£104,146	£222,774
	13.	Exponential (stratified)	£78,371	£173,232
	14.	Weibull (unstratified)	£94,354	£205,006
Relative effect versus docetaxel	15.	Equivalent OS benefit for docetaxel (including STAMPEDE data)	N/A	£295,167
	16.	Equivalent OS benefit for docetaxel (excluding STAMPEDE data)	N/A	£322,810
Frequency of oncologist appointments	17.	Increased frequency of oncology appointments during abiraterone treatment (1 monthly)	£93,234	£208,303

Key: AA, abiraterone acetate; ADT, androgen deprivation therapy; AE, adverse events; HR, hazard ratio; HRQL, health related quality of life; ICER, incremental cost-effectiveness ratio; NMA, indirect treatment comparison; mCRPC, metastatic castration resistant prostate cancer; mHSPC, metastatic hormone sensitive prostate cancer; N/A, not applicable; OS, overall survival; PAS, patient access scheme; rPFS, radiographic progression-free survival; SRE, skeletal-related events; TTD, time to discontinuation.

There are a number of important weaknesses to the analysis:

- Results from the NMA suggest that abiraterone is likely to result in PFS advantages over docetaxel, however it is uncertain whether these would translate to improvements in overall survival. Application of equivalent survival benefits for abiraterone and docetaxel is likely to result in an upwards influence on the ICER.
- Alternative approaches to modelling radiographic PFS and/or time-to-treatment discontinuation also lead to higher ICER estimates than assumed in the base case analysis.

- The survival estimates provided for the comparators are likely to underestimate survival outcomes anticipated in Scottish clinical practice due to higher anticipated use of post-progression therapies such as abiraterone than those observed within the key clinical trials. However, the use of more conservative assumptions highlight that this only has a moderate influence on the ICER.

The Committee also considered the benefits of abiraterone in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that the criterion for a substantial improvement in life expectancy was satisfied. In addition, as abiraterone is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence, the output from the PACE process, and application of the appropriate SMC modifiers, the Committee accepted abiraterone for use in NHSScotland.

*Other data were also assessed but remain confidential.**

Additional information: guidelines and protocols

The National Institute for Health and Care Excellence (NICE), published 'Prostate cancer: diagnosis and management' guideline number 131 in 2019. This guideline stratifies the risk of disease according to PSA levels, Gleason score and clinical stage, with patients being considered high risk when their PSA is greater than 20ng/mL or have a Gleason score of 8 to 10 or a clinical stage equal or greater than T2c. For patients with newly diagnosed metastatic prostate cancer who do not have any significant comorbidities, these guidelines recommend treatment with docetaxel chemotherapy, with or without daily prednisolone. It is also recommended that androgen deprivation therapy (ADT) should be offered within 12 weeks before starting treatment with docetaxel. Additionally, these guidelines recommend that all men diagnosed with metastatic prostate cancer should be offered bilateral orchidectomy as an alternative to continuous luteinising hormone-releasing hormone (LHRH) agonist therapy. Combined androgen blockade is not recommended as a first line treatment. Anti-androgen monotherapy with bicalutamide is recommended for patients willing to accept its adverse events with the aim of preserving their sexual function. If these patients do not experience a satisfactory sexual function, bicalutamide treatment should cease and ADT should be offered.[15]

The European Society for Medical Oncology (ESMO) published in 2015 its clinical practice guidelines 'Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up'. For men newly diagnosed with hormone sensitive disease continuous ADT is recommended in the first-line setting. For men fit enough for chemotherapy, ADT with docetaxel chemotherapy is recommended as first-line treatment.[16] An e-update to this guideline in 2017 indicates that ADT plus abiraterone with prednisone may be considered as a first-line treatment.[17]

The European Association of Urology (EAU) in liaison with the European Society for Radiotherapy and Oncology (ESTRO) and the International Society for Geriatric Oncology (SIOG) published 'EAU-ESTRO-SIOG Guidelines on Prostate Cancer, Part II: Treatment of Relapsing Metastatic and Castration-

Resistant Prostate Cancer' in 2016 and update in 2017. These guidelines are consistent with the ESMO e-update from 2017.[18, 19]

Additional information: comparators

Androgen deprivation therapy alone, docetaxel (off-label) plus androgen deprivation therapy.

Cost of relevant comparators

Medicine	Dose Regimen	Cost per year (£)
abiraterone acetate plus prednisolone plus triptorelin	• **1g oral once daily** • **5mg oral once daily** • **11.25mg intramuscular injection every 3 months**	**36,393**
docetaxel (off-label) plus prednisolone plus triptorelin	• 75mg/m^2 intravenous injection, day 1 repeat every 21 days for 6 cycles • 5mg twice daily oral during the 6 cycles of treatment • 11.25mg intramuscular injection every 3 months	Year 1: 4,443 Subsequent years: 828
triptorelin	11.25mg intramuscular injection every 3 months.	828

Doses are for general comparison and do not imply therapeutic equivalence. Costs from BNF online on 03 September 2019. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take any patient access schemes into consideration. Docetaxel dose based on body surface area of 1.8m^2 for an adult.

Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 460 patients to which confidential estimates of treatment uptake were applied**.**

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

*Other data were also assessed but remain confidential.**

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This assessment is based on data submitted by the applicant company up to and including 11 October 2019.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local

use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.