National Cancer Medicines Advisory Group (NCMAG) Programme
NCMAG110 Abiraterone acetate | Advice Document v1.0 | July 2023

Abiraterone acetate plus prednisolone in combination with androgen deprivation therapy for the treatment for newly diagnosed low-risk metastatic hormone-sensitive prostate cancer patients who are not suitable for currently accessible on-label alternatives.

NCMAG Decision| off-label use is **supported**

This advice applies only in the context of the NHSScotland national framework contract, delivering the cost-effectiveness results upon which the decision was based, or a national framework contract or list price that is equivalent or lower.

The generic product available at the lowest acquisition cost should be prescribed.

[A] NCMAG considers proposals submitted by clinicians for use of cancer medicines outwith SMC remit. For more detail on NCMAG remit please see our website.

Decision rationale

After consideration of all the available evidence regarding the benefits and risks, the council were satisfied with the clinical and cost-effectiveness of abiraterone acetate plus prednisolone in combination with androgen deprivation therapy for the proposed patient population.

Governance Arrangements

Each NHS board must ensure all internal governance arrangements are completed before medicines are prescribed. The benefits and risks of the use of a medicine should be clearly stated and discussed with the patient to allow informed consent.

Proposal Details	
Proposers	The Cross-Scotland uro-oncology consultant group with support from specialist cancer pharmacists.
Medicine Name	Abiraterone
Cancer type	Prostate Cancer

Proposed off-label use[B,C]	Treatment for newly diagnosed low-risk metastatic hormone-sensitive prostate cancer patients who are not suitable for currently accessible on-label alternatives.
Medicine Details	Form: Tablet Dose: 1,000mg once daily Treatment may be continued until progression or unacceptable toxicity

Proposed advice eligibility criteria	Unsuitable for on-label options due to:
	• frailty
	• pharmacological contraindications
	• or the following comorbidities:
	  • risk of seizure - for example due to prior brain injury, prior seizure, concomitant seizure-threshold lowering medication
	  • risk of significant cognitive impairment, such as in patients with pre-existing cognitive impairment

[B] Abiraterone has a marketing authorisation for the following indications:

- the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer (mHSPC) in adult men in combination with androgen deprivation therapy (ADT)
- the treatment of metastatic castration resistant prostate cancer (mCRPC) in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated
- the treatment of mCRPC in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen.

[c] NCMAG has issued advice for abiraterone use in adults with high-risk hormone-sensitive non-metastatic prostate cancer

1. Current Management Context

Prostate cancer incidence, prognosis and symptoms

Prostate cancer is uncommon in men under 50 years and is most commonly diagnosed in males aged 70-74 years of age.[1] A total of 4,265 patients were diagnosed with prostate cancer in Scotland in 2021, with approximately 27% having metastatic disease.[2] Metastatic disease is thought to be incurable although approximately 50% of patients will survive five years.[3]

The split between low and high-risk newly diagnosed metastatic hormone sensitive prostate cancer (mHSPC) classifications have been reported to be relatively even.[4] Hormone sensitive prostate cancer is androgen driven and responds to treatments that reduce androgen levels. Eventually cancer resistance to low levels of androgen develops, disease progresses and is known as castration resistant.[5] Symptoms commonly experienced by prostate cancer patients include urinary problems, fatigue, weight loss and bone pain.[6]

Treatment context of proposed off-label use

Currently accessible licensed (also known as on-label) treatment options for the management of mHSPC, regardless of risk-category, include ADT alone or ADT in combination with docetaxel, apalutamide or enzalutamide. Abiraterone with prednisone or prednisolone in combination with ADT is an accessible on-label option for patients with newly diagnosed high-risk mHSPC. High-risk disease is defined as having at least two of the following three risk factors: Gleason score of ≥8, presence of 3 or more lesions on bone scan or presence of measurable visceral (excluding lymph node disease) metastasis. The abiraterone regimen has not received marketing authorisation for the treatment of patients with 'low-risk' mHSPC i.e. patients without high-risk disease. Currently, patients who are low-risk and unsuitable for licensed alternatives (e.g. due to frailty, pharmacological contraindications, previous seizures or cognitive impairment) are treated with ADT alone.

Guidelines from National Comprehensive Cancer Network (NCCN), the European Association of Urology (EAU) and the European Society of Medical Oncology (ESMO) supports the use of the abiraterone regimen in patients with newly diagnosed mHSPC regardless of risk group.[5, 7, 8]

Abiraterone pharmacology

Abiraterone inhibits CYP17 intracellular production of testosterone within the adrenal glands and prostate cancer cells. This creates a more complete block of androgen's effects compared to ADT alone, causing cancer cell death. It is necessary to administer a glucocorticoid (usually prednisolone) to reduce mineralocorticoid excess.[9]

2. Evidence Review Approach

A literature search to identify clinical and economic evidence was conducted on key electronic databases including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, major international health technology agencies, as well as a focused internet search. The search strategy

comprised both Medical Subject Headings and keywords. The main search concepts were abiraterone, metastatic, low-risk and prostate cancer. Titles and abstracts were screened by one reviewer with a second opinion sought by another reviewer when required. The included key research study was critically appraised using the Cochrane risk of bias version 2.0 tool.

3. Clinical Evidence Review Summary

Clinical Efficacy Evidence

Evidence overview

The key evidence source considered relevant to this proposal is the 'abiraterone comparison' study within the 'Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy multi-arm, multi-stage (STAMPEDE) platform.[10] The five-year follow-up data (data base lock April 2020) for the metastatic patient group of this study have recently been reported.[10] Results were presented by disease risk group unlike the first analysis (data base lock February 2017; 'James first analysis').[10, 11] A previously conducted post-hoc sub-study which explored outcomes by risk group based on the James first analysis (data base lock August 2018) will also be presented.[4]

Study population in context of the proposed population

Evidence for the use of abiraterone in the proposed off-label group of low-risk mHSPC patients who are considered unsuitable for on-label options (docetaxel, enzalutamide and apalutamide) was not identified. Therefore, the low-risk mHSPC group within the 'abiraterone comparison' study was considered to be the most relevant evidence to support the proposed use. Results reported in this section relate to this wider population.

Evidence comparing androgen deprivation therapy versus abiraterone combination

The 'abiraterone comparison' study randomly assigned patients (1:1) to receive either androgen deprivation therapy only (ADT) or in combination with oral abiraterone acetate and oral prednisolone (referred hereon as the AAP combination group). Patients were followed-up 6-weekly until 6 months after randomisation, 12-weekly to 2 years, 6-monthly to 5 years and then annually.[11] To allow results to be reported by disease risk group, the metastatic group of patients were retrospectively classified (n=1,003; ADT only group n=502; AAP combination group n=501) according to the definition used in the LATITUDE study.[12] The LATITUDE study is the key study supporting the marketing authorisation for abiraterone in the high-risk metastatic population.[12] High-risk disease was defined as at least two of the following: ≥3 bone metastases; visceral metastases; Gleason score ≥8.

The primary outcome was overall survival, and the key secondary outcomes were failure-free survival (FFS; the intermediate primary outcome) and safety (see Table 1 for definitions).

Results from the STAMPEDE 'abiraterone comparison' study

The median duration of follow-up was 73 months. Median age at randomisation was 67 years (IQR 62 to 71 years) with 941 (94%) patients having newly diagnosed disease and 62 (6%) having

relapsing disease. The number of patients retrospectively classified as low-risk, high-risk or unclassified were 436 (43%), 473 (47%) and 94 (9%), respectively.[10] Based on the limited baseline data available for the metastatic group, patient characteristics appear balanced between the treatment groups.[10] Baseline characteristics by risk group were not reported.

In the metastatic (any disease risk) group, overall survival and FFS significantly improved in the AAP combination group compared to the ADT alone group (Table 1). The relative effect estimates for the low-risk group appear consistent with the estimates for the metastatic (any risk) group. Similarly, the secondary outcomes also favoured the AAP combination over ADT alone with the estimates of treatment effect for the low-risk group being consistent with the metastatic (any risk) group.

Results from the post hoc sub-study

A previously conducted sub-study of the metastatic group of patients using the results from the James first analysis aimed to explore whether the treatment effect of the AAP combination was consistent across low-and high-risk disease.[4, 11] The metastatic group of patients were retrospectively classified using baseline imaging into disease risk groups according to the LATITUDE definition. Baseline characteristics by risk group were balanced between treatment groups. The relative effect estimates for each of the risk groups show consistency with the estimates at the five-year follow-up (Table 1). An interaction test for heterogeneity across the low and high-risk subgroups did not indicate a significant difference in relative treatment effects.[4]

Table 1 Results for metastatic study population and by risk classification for overall survival and FFS[4, 10]

Outcome		**ADT only** (n=502)[A,B]	**ADT plus AAP** (n=501)
Subgroup			
Overall survival			
Overall (any risk group)	**Events (%)**	**329 (66)**	**244 (49)**
	% alive at 5 years (95%CI)	41% (37-45)	60% (55-64)
	HR, 95%CI	**0.60 (0.50-0.71)**	
Overall (first analysis)		*0.61 (0.49-0.79)*	
Low risk (final analysis)	Events (%)	118 (54)	75 (36)
	% alive at 5 years (95%CI)	55% (48-61)	72% (65-77)
	HR, 95%CI	0.54 (0.40-0.74)	
Low risk (first analysis)		*0.66 (0.44-0.98)*	
High risk (final analysis)	Events (%)	178 (77)	145 (60)
	% alive at 5 years (95%CI)	28% (22-34)	49% (43-55)
	HR, 95%CI	0.54 (0.43-0.69)	
High risk (first analysis)		*0.54 (0.41-0.70)*	

Failure-free survival			
Overall (any risk group)	**Events (%)**	**437 (87)**	**282 (56)**
	% event-free at 5 years (95%CI)	13% (11-17)	45% (41-50)
	HR, 95%CI	**0.34 (0.29-0.40)**	
Overall (first analysis)		*0.32 (0.26-0.37)*	
Low risk (final analysis)	Events (%)	178 (81)	92 (44)
	% event-free at 5 years (95%CI)	21% (16-26)	61% (54-67)
	HR, 95%CI	0.32 (0.25-0.42)	
Low risk (first analysis)		*0.24 (0.17-0.33)*	
High risk (final analysis)	Events (%)	215 (93)	165 (68)
	% event-free at 5 years (95%CI)	6% (3-9)	31% (25-37)
	HR, 95%CI	0.28 (0.22-0.36)	
High risk (first analysis)		*0.31 (0.25-0.39)*	

Note: results in italics are as reported in post hoc sub-study (based on the James first analysis). These results vary slightly from those reported in the first results paper analysis due to the removal of unclassified patients in the sub-group analysis.

Definitions: Overall survival: defined as the time from randomisation to death from any cause. Failure-free survival: time to the first of the following forms of treatment failure: biochemical (prostate-specific antigen) failure; progression of local, lymph-node, or distant metastases; or death from prostate cancer.

[A] 14 patients recruited at sites in Switzerland were removed from analysis by risk group. The further 88 patients in the unclassified group were included in the analysis by risk group but are not included in this table.

[B] Number of patients in each subgroup varies: low risk; n=220 in the androgen deprivation therapy (ADT) only group, n=208 in abiraterone acetate and prednisolone plus ADT (AAP combination) group; high risk; n=232 in ADT only group and n=241 in AAP combination group.

Network meta-analysis of treatments in metastatic hormone sensitive prostate cancer

Six systematic reviews and network meta-analyses (NMAs) were identified which assessed systemic therapies in mHSPC and included the relevant comparison (ADT alone versus AAP combination).[13-18] The NMAs used data from the LATITUDE study and the STAMPEDE 'abiraterone comparison' study to inform this comparison. Subgroup analyses based on disease volume (low/high-volume using the CHAARTED classification) indicated benefit in both the high- and low-volume mHSPC patient groups.[13-18] The two systems used to classify risk and volume (LATITUDE low/high-risk and CHAARTED low/high-volume) have been previously shown to largely agree.[11] Consistency between the results for the NMA subgroup analyses (indirect evidence) and the 'abiraterone comparison' study reported by risk group (direct evidence) is supportive of the evidence for benefit in low-risk mHSPC patients.

Patient-reported outcomes

Quality of life (QoL) was included as a secondary outcome, however, results have not been reported separately. The QoL data were used to inform the cost-effectiveness analysis described in section 7.[19]

Safety evidence

Safety data on the use of the AAP combination for the low-risk mHSPC group alone are not available. The James first analysis for the full population (includes non-metastatic and metastatic patients), reported that 47% of patients in the AAP combination group versus 33% in the ADT group had grade 3 or worse adverse events (AEs). The most common type of AE grade 3 or higher for the AAP combination group versus the ADT group were: endocrine disorders including hot flushes and impotence (14% versus 14%); cardiovascular disorders (10% versus 4%), musculoskeletal disorders (7% versus 5%) and hepatic disorders including increased alanine aminotransferase (7% versus 1%).[11] The 'abiraterone comparison' study offers summary safety data for the metastatic group (any disease risk) reported at two years after randomisation and at four years after randomisation by treatment group. There were no significant differences between grade of adverse events between the treatment groups at two years and at four years. The worst grade toxicity reported at four years for patients receiving AAP combination and ADT alone, respectively, is as follows – grade 0: 12% versus 10%; grade 1: 38% versus 50%; grade 2: 34% versus 24%; grade 3: 15% versus 16%; grade 4: 0.1% versus 0%.

Quality assessment of clinical evidence

A few concerns in relation to risk of bias were identified on appraisal of the STAMPEDE 'abiraterone comparison' study. The 'abiraterone comparison' study was open-label and all outcomes may be susceptible to performance bias. The blinded status of the individuals who assessed progression and other subjective outcomes is unclear, which may pose a risk of detection bias. The study was not designed to detect differences between subgroups of patients, therefore, comparisons across groups should be interpreted with caution. The statistical robustness of the post hoc (unplanned) analyses (reporting on the low-and high-risk subgroups) is uncertain due to the lack of control for multiplicity and the lack of formal power calculations.

Classifying patients into risk groups retrospectively has limitations. For example, initial study data fields may not have included all items specific to this research question which has likely led to missing data (9% of patients were unclassified). Both studies did use independent review which offers some reassurance. The post hoc subgroup included a second, independent review of the initial subgroup risk classification. Agreement between the primary and independent review was reported to be high (>90%) in the post hoc subgroup study.[4]

Clinical effectiveness considerations

The addition of AAP combination to ADT significantly improved overall survival as well as secondary outcomes

The James final analysis of the abiraterone comparison study had a median follow-up time of 73 months. There was a clinically meaningful improvement in overall survival with the use of AAP combination over ADT alone in the overall study population and in the low-risk cohort of patients. In the low-risk subgroup there were 118 deaths in the ADT alone arm (n = 220) and 75 deaths in the ADT plus AAP arm (n = 208). The percentage of patients alive at 5 years was 55% and 72%,

respectively. The final analysis also had narrow confidence intervals for overall survival for both high-risk and low-risk disease. This gives reassurance in the relative overall survival effect across risk categories. The improvement in overall survival was maintained at follow-up, despite 30% of ADT alone patients receiving abiraterone as a post-progression treatment. Similarly, the secondary outcomes also favoured the AAP combination over ADT alone with the estimates of treatment effect for the low-risk group and high-risk group appearing consistent.

Unplanned, post-hoc subgroup analyses are less robust and should be interpreted with caution. However, the consistent direction of treatment effect in the unplanned analyses, when compared to the primary analysis, along with the inclusion of more than 200 patients in each arm gives reassurance that the results of the James final analysis are sufficiently robust.

There are a lack of efficacy data of AAP combination in the specific proposed population

The proposed use covers the use of abiraterone in patients for whom licensed alternatives are unsuitable. Currently accessible licensed alternatives in this setting are docetaxel, apalutamide and enzalutamide. Reasons for unsuitability can include concerns about fatigue, cognitive impact or pharmacological interactions and contraindications. While there are no specific data examining a population with these clinical profiles, the treatment efficacy of AAP combination remains remarkably consistent across various trial populations, when compared to ADT alone.[4, 10-12, 20] This consistency is observed across different stages of hormone-sensitive metastatic disease, such as high-risk and low-risk disease; high volume and low volume as well as low-volume and low-risk disease. A similar and consistent treatment effect has also been demonstrated in the non-metastatic hormone-sensitive setting.[21] While the magnitude of the effect may be lower in some patients, the consistent direction of relative treatment effects across multiple treatment populations provides some reassurance.

There are some uncertainties regarding the generalisability of the results

The STAMPEDE platform had inclusive eligibility criteria, and all patients used in the James final analysis were recruited from the UK. The median age of men randomised to the 'abiraterone comparison' of STAMPEDE was 67 years which is lower than the median age of patients diagnosed with prostate cancer in Scotland (70 to 74 years). Patients with clinically significant cardiovascular disease were excluded from the study, which aligns with the licensed use of abiraterone, and may limit generalisability of study results to this patient group. Due to the lack of an analysis of the low-risk subgroup based on performance status it is uncertain what effect this may have on clinical outcomes. Furthermore, there were low numbers of patients with performance status one or two which may limit the applicability of the efficacy and safety results in patients with poor performance status.

The profile of subsequent lines of treatment received following disease progression in STAMPEDE are considered to be reflective of subsequent treatments used in NHSScotland. However, detail on subsequent treatments based on risk-status was not provided. There is, however, uncertainty if patients who are unsuitable for currently available licensed alternatives would receive any treatment post progression with AAP combination.

AAP combination has an acceptable toxicity profile but there are limited specific safety data in the low-risk group

The LATITUDE final analysis, which examined high-risk patients only, reported Grade 3-4 adverse events in 68% of abiraterone patients and 50% of placebo patients. Hypertension and hypokalaemia were the most common treatment related side effects. Treatment was discontinued due to adverse effects in 16% of abiraterone patients and 10% of placebo patients, respectively.

The James first analysis, which included both metastatic and non-metastatic patients, reported that the main Grade 3 or higher adverse events associated with AAP combination were cardiovascular disorders, hypertension, hypokalaemia (low potassium) and musculoskeletal disorders. The James final analysis did not provide a breakdown of adverse events between high-risk and low-risk groups, or toxicity types. While safety data specific to the low-risk group is not available, there is no clear clinical reason to expect meaningful differences in the relative adverse effect profile due to risk status. The adverse event profile from the James first analysis is similar to the on-label side effect profile, with which clinicians have extensive experience in managing.

4. Patient group summary

Two patient group partner statements from Prostate Scotland and Prostate Cancer UK were received and used to inform Council review and decision-making. The key points are summarised below –

- There are high levels of anxiety and uncertainty experienced by those living with prostate cancer about when the cancer may stop responding to hormone therapy. This highlights the importance of having treatments which can help delay the progression of cancer before it becomes hormone resistant.
- The patient group partners believe that there is an unmet treatment need for low-risk metastatic hormone sensitive prostate cancer who are not able to have docetaxel, enzalutamide or apalutamide.
- Findings of engagement activities by those living with prostate cancer revealed strong support in favour of abiraterone being available for this group of patients.

In summary, both patient group partners believe that the availability of abiraterone for low-risk hormone sensitive metastatic prostate cancer could improve the quality of patients' lives and delay the progression of the cancer.

5. Benefit-risk balance

The AAP combination improved 5-year overall survival from 55% to 72% in newly diagnosed low-risk metastatic prostate cancer patients. The AAP combination is well tolerated with no identified unexpected side effects in this off-label population compared to its licensed indications.

6. Council Review |Clinical benefit-risk balance evaluation

After consideration of all the available evidence regarding the clinical benefits and risks, the Council were satisfied that the case had been made for the clinical effectiveness of abiraterone acetate plus prednisolone in combination with androgen deprivation therapy for the treatment of newly diagnosed low-risk metastatic hormone-sensitive prostate cancer patients who are not suitable for currently accessible on-label alternatives.

7. Economic Evidence Review Summary

Economic Overview

Five economic evaluations were identified in the literature search, providing pairwise comparisons of the AAP combination versus ADT alone in adult patients with metastatic (any risk) hormone sensitive prostate cancer. Four of these were from a non-UK perspective.[22-25] One study was from a UK perspective and was the preferred study due to its increased generalisability to the proposal.[19]

Type of economic evaluation

The economic evaluation was a cost-utility analysis, using outcome data from the STAMPEDE platform study James first analysis (data base lock February 2017).[11] The model used was an individual patient simulation with a lifetime time horizon. The model health states captured disease progression from hormone sensitive to castration resistant prostate cancer, with death states included. The study perspective was indicated to be from an English NHS perspective.

Population, intervention, comparator and outcomes

The population used in the study was men with high-risk localised, locally advanced, recurrent or metastatic prostate cancer starting first-line ADT. Subgroup results based on non-metastatic and metastatic disease were provided.

The intervention was AAP (abiraterone acetate 1000mg/day plus prednisolone 5mg/day) plus standard of care (SOC) treatment with ADT. Patients with metastatic disease at baseline received AAP treatment until progression. SOC was hormone therapy for at least 2 years with radiotherapy in pre-selected patients. The comparator was SOC alone. Clinical outcomes used in the model were overall survival, failure free survival and severe adverse events. The outcome of the economic model was quality adjusted life years (QALYs).

Costs

Costs included were intervention and comparator medicines, monitoring, subsequent medicines (docetaxel, enzalutamide, cabazitaxel and radium-223), general disease management, severe adverse events, and end of life care. A 3.5% annual discount rate for both costs and QALYs was applied.

Key results

Abiraterone acetate has been available as a generic product in the UK since autumn 2022. The study used the originator branded abiraterone acetate 500mg BNF list price of £2,735 for 56 tablets to derive the base case ICER of £47,503 per QALY gained for AAP+SOC. The incremental mean per patient cost was £70,246, primarily the result of abiraterone acquisition costs. The incremental mean per patient QALYs were 1.48. This was primarily from the increased time spent in the hormone sensitive health states. When using the cheapest generic abiraterone acetate 500mg BNF list price (as of May 2023) of £190 for 56 tablets, the ICER decreased to £3,572. The ICERs do not take into account the confidential national framework prices available for other medicines, however results using national framework prices for abiraterone were considered in confidence.

Cost-effectiveness considerations

Generalisability of results

This STAMPEDE trial based economic evaluation allowed for a comparison between the relevant intervention (AAP combination) and the relevant comparator (ADT alone). Results were reported for the metastatic subgroup, which partially aligns with the proposed population. The model structure used appropriate health states to capture disease progression, and utilised individual patient level data from the trial to generate survival functions to simulate transitions between the health states. Utility values were derived from the EQ-5D-3L data collected during the STAMPEDE 'abiraterone comparison' study.[11] As the key data in the economic evaluation were from a highly relevant clinical study, the results generated are likely to have increased generalisability.

NHSScotland national framework prices for abiraterone were considered in confidence to increase generalisability of the ICER results.

Limitations

There were limitations of the economic study that increased uncertainty in the derived ICER results. Firstly, since the publication of the economic study, updated outcome data have become available in the James final analysis.[10] Although the updated hazard ratios for overall survival and failure-free survival in the metastatic patient group were similar, the use of updated data would have likely facilitated increased accuracy of long-term survival predictions and confidence in the results.[10, 11 4] However, as these hazard ratios were similar the impact on the ICER is likely to be minimal. Secondly, some health state transitions in the economic model had small event numbers, which required joint survival models for groups of transitions, rather than preferred individual survival models. However, the largest number of recorded transitions were in the metastatic patient population, potentially limiting this issue. Thirdly, EQ-5D-3L data were not routinely collected post-progression, potentially leading to inaccurate health state utility values in the post progression health states. Finally, alternate parametric survival models, a key driver of most oncology economic models, were not included as part of sensitivity analysis. As there is no further planned analysis in the economic study, the effect of alternate survival curves remains unknown.

However, given the low ICER when using the generic abiraterone medicine cost, alternate survival models would be unlikely to change the ICER substantially.

There were limitations affecting the generalisability of results to NHSScotland. Firstly, the economic evaluation did not report separate results for low and high-risk metastatic patients. Although there is clinical data to support similar hazard ratios for overall survival and failure-free survival in the updated data cut of these two risk groups, this was not a consideration in the economic evaluation and the results remain unknown with no option to explore this uncertainty.[10] Secondly, docetaxel and enzalutamide were included as subsequent treatments. However, the proposed population is unsuitable for these. The incremental cost for these was small, suggesting a limited cost impact, although the effect on clinically modelled outcomes is uncertain. The generalisability of results is therefore potentially limited.

Summary

The suitably robust results of the economic evaluation provided indicative evidence that the AAP combination would likely be cost-effective at conventional thresholds.

These results showed relevance to the proposal, with a comparison between the AAP regimen and ADT alone, with results for the metastatic (any risk) subgroup. Where generalisability was most limited was the lack of reporting of results for the low-risk metastatic subgroup of interest. Further limitations of the study and generalisability should be noted when considering the ICER results.

8. Council review | Cost-effectiveness evaluation

After considering all the available evidence, the Council were satisfied that the case for cost effectiveness had been made for the generic product based on NHSScotland national framework contract pricing.

9. Service Impact

It is estimated that the eligible population for AAP combination would be between 80 to 100 patients. Patients will require monthly clinic visits initially with fortnightly liver enzyme tests for the first three months. Once patients are established and tolerating treatment, they may be transitioned to eight weekly or 12 weekly dispensing of abiraterone. Some patients may experience increased blood pressure while on treatment with abiraterone, management of which could pose additional burden on services.

10.Budget Impact

NCMAG is unable to publish the 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 national framework contract pricing.

11.Acknowledgements

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This advice represents the view of the NCMAG Council 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.

Minor document amendments

Date	Previous version	Amendment	Updated version	Approved by