NICE National Institute for Health and Care Excellence

NICE guidance

Darolutamide with androgen deprivation therapy for treating hormone-relapsed non-metastatic prostate cancer

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations 4

2 Information about darolutamide 5

Marketing authorisation indication 5

Dosage in the marketing authorisation 5

Price 5

3 Committee discussion 6

Treatment pathway 6

Clinical effectiveness 8

Cost effectiveness 12

Conclusion 20

4 Implementation 21

5 Appraisal committee members and NICE project team 22

Appraisal committee members 22

NICE project team 22

1 Recommendations

1.1 Darolutamide with androgen deprivation therapy (ADT) is recommended, within its marketing authorisation, as an option for treating hormone-relapsed prostate cancer in adults at high risk of developing metastatic disease. It is recommended only if the company provides darolutamide according to the commercial arrangement.

Why the committee made these recommendations

When prostate cancer no longer responds to hormone treatment (ADT), but has not spread beyond the prostate, the only current option is to continue ADT. Darolutamide added to ADT would be another option at this stage.

Clinical trial evidence shows that people taking darolutamide with ADT have more time before their prostate cancer spreads compared with ADT alone. Although the trial results suggest that darolutamide with ADT increases the length of time people live, it is unclear by how much in the long term.

Despite this, the cost-effectiveness estimates are within what NICE normally considers a cost-effective use of NHS resources. So darolutamide with ADT is recommended as an option.

2 Information about darolutamide

Marketing authorisation indication

2.1 Darolutamide (Nubeqa, Bayer) is indicated 'for the treatment of adult men with non-metastatic castration resistant prostate cancer who are at high risk of developing metastatic disease'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics.

Price

2.3 The list price of darolutamide 300 mg is £4,040 per 112 tablets (excluding VAT; BNF online, accessed September 2020). The company has a commercial arrangement. This makes darolutamide available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by Bayer, a review of this submission by the evidence review group (ERG), NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence.

Treatment pathway

Few people have hormone-relapsed non-metastatic cancer and treatment aims to delay metastasis

3.1 Hormone-relapsed cancer no longer responds to androgen deprivation therapy (ADT). Darolutamide is indicated for treating hormone-relapsed prostate cancer that is at high risk of metastasising. This is the same indication appraised in NICE's technology appraisal guidance on enzalutamide, but enzalutamide is not recommended for this population. ARAMIS, the trial that informed darolutamide's marketing authorisation (see section 3.4) defined high risk as a prostate specific antigen (PSA) level of 2 nanograms per millilitre or more that has doubled in 10 months. The company estimated that around 2% to 3% of people with prostate cancer in the UK have hormone-relapsed non-metastatic prostate cancer. The aim of treatment is to delay metastatic disease, which is associated with reduced quality of life and survival. The committee concluded that a small proportion of people with prostate cancer have hormone-relapsed non-metastatic prostate cancer and treatment aims to delay metastasis.

There is an unmet need for a treatment for hormone-relapsed non-metastatic prostate cancer, and this causes anxiety for patients

3.2 Current treatment for hormone-relapsed non-metastatic prostate cancer is to continue ADT, even though the cancer may not be responding to it. The patient experts explained that people have to wait for their cancer to metastasise before they can get the next effective treatment. This can

cause great anxiety for them. They see their PSA levels rising and know they are at high risk of developing metastases, but are not taking an effective treatment. The patient experts commented that detecting metastases as early as possible means people can have the next clinically effective treatment. Metastases are usually detected by an MRI or CT scan. The clinical experts stated that clinicians sometimes offer more frequent scans and more sensitive, but less routinely used, scanning techniques to 'hunt' for metastases. If found, they can prescribe the next clinically effective treatment for patients. They also stated that these scans would reduce if another treatment was available. The patient experts said that having an effective treatment would reduce their anxiety. Also, delaying metastases and the associated symptoms of metastatic disease, which greatly affect quality of life, is really important to them. The committee concluded that there is an unmet need for a clinically effective treatment for hormone-relapsed non-metastatic prostate cancer. This disease causes anxiety for patients and may increase the frequency of MRI and CT scans.

Darolutamide, enzalutamide or abiraterone are used only once in the prostate cancer treatment pathway

3.3 NICE recommends the androgen receptor inhibitors enzalutamide and abiraterone in its technology appraisal guidance on:

- enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated
- enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen
- abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated

- abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen.

  These drugs can be used only once in the prostate cancer treatment pathway according to NHS England's commissioning policy. The clinical experts confirmed that this is because of the similar way the 3 drugs work. This means that if a person's prostate cancer metastasised on darolutamide, it would be expected to be resistant to enzalutamide or abiraterone when used as treatments for metastatic disease. The Cancer Drugs Fund clinical lead confirmed that NHS England would not commission enzalutamide or abiraterone after darolutamide. The committee concluded that darolutamide, enzalutamide or abiraterone would be used only once in the treatment pathway for prostate cancer.

Clinical effectiveness

The ARAMIS results comparing darolutamide plus ADT with placebo plus ADT are in line with planned analyses

3.4 ARAMIS was a double-blind international randomised controlled trial comparing darolutamide plus ADT (n=955) with placebo plus ADT (n=554). Its primary endpoint was metastasis-free survival, that is, the time from randomisation to confirmed evidence of metastasis or death from any cause. Secondary outcomes included, among others, overall survival and time to starting cytotoxic chemotherapy. Exploratory outcomes included quality of life, measured using the EQ-5D questionnaire, and time to starting antineoplastic therapy (other than chemotherapy). The trial also recorded how long people continued to take darolutamide and their reason for stopping it. People entering the study had an MRI and a CT scan and were excluded if they had metastases. The trial pre-specified final analyses for metastasis-free survival and overall survival based on the number of events needed to show a difference between the trial arms for these outcomes. The differences in metastasis-free survival and overall survival between the groups were considered statistically significant at p values of less than or equal to 0.05 and 0.018. The final analysis for metastasis-free survival and interim analyses for overall survival were done in September 2018. At

this time, the trial was unblinded and people who had placebo could cross over to have darolutamide if their cancer had not metastasised. The final analysis of overall survival was done in November 2019. The committee concluded that the 2 data cuts reflected the trial's statistical analysis plan.

Some people in ARAMIS had metastases at baseline, and the trial is generalisable to the population in the NHS

3.5 The company did an independent central radiological review of the MRI and CT scans to check eligibility for ARAMIS. This showed that a small proportion of people had metastases at the start of the trial. The company commented that this proportion was higher in the placebo plus ADT arm (7%) than in the darolutamide plus ADT arm (5%). It did analyses adjusting for this (see section 3.9). The committee noted that there may be people in NHS clinical practice diagnosed with non-metastatic prostate cancer who have undetectable metastases on MRI or CT scan. So, the trial population would reflect the population in NHS clinical practice. The committee also appreciated that the central review may have produced false positive results. It concluded that the population in ARAMIS was generalisable to the population seen in NHS clinical practice.

Darolutamide plus ADT extends metastasis-free survival

3.6 In ARAMIS, the median survival on darolutamide plus ADT was 40.4 months and on placebo plus ADT it was 18.4 months. The hazard ratio was 0.41 (95% confidence interval 0.34 to 0.50). The committee concluded that darolutamide plus ADT extended metastasis-free survival and was clinically effective.

Darolutamide extends overall survival during the trial, but treatments offered for metastatic disease make the longer-term benefit unclear

3.7 In the final analysis of overall survival people had been followed for up to 5 years. Only a small proportion of people in both the darolutamide plus

ADT arm and the placebo plus ADT arm had died (the proportions are academic in confidence and cannot be reported here). Fewer people died in the darolutamide plus ADT arm than in the placebo plus ADT arm. The hazard ratio for overall survival for darolutamide plus ADT compared with placebo plus ADT and the 95% upper limit of the confidence intervals were less than 1. So, overall survival was better with darolutamide plus ADT (the data are academic in confidence and cannot be reported here). The committee noted that overall survival depends on the treatments for non-metastatic disease and on the follow-on treatments taken after the cancer has metastasised. It discussed the choice of treatments, and the proportion of people taking these treatments in ARAMIS, in relation to NHS practice. It noted that the trial was blinded until September 2018, so investigators would not know a person's first treatment, which could determine the next treatment. The committee also noted that some people in ARAMIS who had enzalutamide or abiraterone for metastatic disease (after first having darolutamide), would not be offered these in NHS practice (see section 3.3). The company suggested that this meant survival after stopping darolutamide may have been underestimated in ARAMIS because abiraterone and enzalutamide are expected to be ineffective after darolutamide. The ERG noted that a smaller proportion of people had abiraterone or enzalutamide after ADT alone than would be expected in the NHS. The clinical experts suggested that survival on enzalutamide, abiraterone or docetaxel after ADT alone was similar. The committee also noted that a smaller proportion of people in each arm of the trial had gone on to have a follow-on treatment than would be expected in the NHS. It concluded that the data suggested that darolutamide extended overall survival over the duration of the trial. But how long this lasted after the trial was unclear, partly because of the follow-on treatments taken after the cancer had metastasised.

Adjusting the ARAMIS estimates of overall survival is unclear and the results may be biased against darolutamide

3.8 In ARAMIS, at the time of the final analysis of the primary endpoint, people randomised to placebo plus ADT whose disease had not metastasised could switch to darolutamide. When ARAMIS was unblinded in September 2018, 170 people in the placebo plus ADT arm

switched to darolutamide. The committee noted it could not assess the company's 2 methods (Iterative Parameter Estimation and the Rank Preserving Structural Failure Time method) to adjust for the effect of treatment switching on overall survival because the company did not present details of these analyses. The company stated that adjusting for switching did not greatly affect the estimates of the treatment effect on overall survival and introduced uncertainty. The committee was aware that the key assumption in the methods is that the treatment effect is the same in people who switch to darolutamide and in people who were initially randomised to have darolutamide. The committee did not have evidence for this assumption. The company chose to use unadjusted survival estimates in its model. The committee appreciated that estimates of overall survival benefit with darolutamide plus ADT compared with ADT alone could be conservative. That is, they may underestimate the benefit of darolutamide plus ADT over ADT alone. The committee noted that people who had no metastases in September 2018 and switched from placebo to darolutamide would have been followed only until the final overall survival analysis in November 2019. Given the low death rates over trial follow up, switching may not have had a large effect on the overall survival estimates. The committee concluded that it could not determine whether the assumptions behind the adjustment methods were met. Also, using unadjusted results may bias the overall survival estimates in ARAMIS against darolutamide.

Adjusting outcomes for people with metastases at baseline by censoring may favour ADT alone

3.9 The ARAMIS statistical analysis was done in an intention-to-treat population. However, in the company's economic model the data had an additional adjustment. This involved censoring people who had been found by central independent radiological review to have metastases at baseline. The company used these censored results to make Kaplan–Meier plots of the trial data for metastasis-free survival and overall survival. It extrapolated these data over the period beyond the end of the trial. The committee noted that Kaplan–Meier plots of survival data take into account the number of events and the number of people at risk of having an event over time. Censoring people at baseline may mean that the risk of having an event was slightly underestimated. The

committee was concerned about 'informative censoring', that is, the risk of outcomes differing because of censoring. However, the committee noted that because more people in the placebo plus ADT arm had metastases at baseline than in the darolutamide plus ADT arm, the company's approach may have made the extrapolated estimates for ADT alone appear better than if they had been extrapolated without censoring. The committee concluded that censoring people with baseline metastases in ARAMIS may disadvantage darolutamide plus ADT and favour ADT alone.

Some people choose to stop darolutamide before their cancer metastasises

3.10 The clinical experts explained that darolutamide was well tolerated in ARAMIS. The marketing authorisation states that darolutamide plus ADT can be taken until cancer metastases; in ARAMIS around 9% of people stopped treatment because of adverse events. The committee discussed that, in general, people stayed on darolutamide longer based on the analysis of September 2018 than based on the later analysis of November 2019. A clinical expert explained that people may stop treatment even when their PSA levels were stable if they have fatigue, an adverse event that may not normally lead someone to stop treatment. The clinical experts considered this would be more likely to occur later in the study than earlier. The committee questioned whether people would stop treatment if they thought it was stopping their cancer from progressing. It noted the difference in the results from the 2 data cuts and considered that unblinding the study in September 2018 may have affected people's choice to stop darolutamide, but it concluded that the reason for the different results in the 2 data cuts was unclear. Overall, the committee concluded that darolutamide was well tolerated in the trial, but some people chose to stop it before their cancer metastasised.

Cost effectiveness

The model structure is appropriate for decision making

3.11 To estimate the cost effectiveness of darolutamide plus ADT compared

with ADT alone, the company used a partitioned survival model. The company used data on metastasis-free survival and overall survival to model 3 health states: non-metastatic hormone-relapsed prostate cancer, metastatic hormone-relapsed prostate cancer and death. In the non-metastatic health state people could be on or off treatment. In the metastatic health state, the company modelled the costs and utility associated with 3 lines of treatment followed by best supportive care (see section 3.14). Using this type of model meant that time in the metastatic health state was determined by the overall survival estimates and the metastasis-free survival estimates from ARAMIS. The committee considered this to be an appropriate approach. It concluded that the model structure was appropriate for decision making.

Extrapolating the most mature data and considering a more pessimistic approach are appropriate

3.12 The data in the model came from different data cuts:

- September 2018 for metastasis-free survival

- November 2019 for time to stopping darolutamide and overall survival.

The committee understood that no further data were collected on metastasis-free survival, the primary endpoint, after September 2018. It shared the ERG's concerns that the time to stopping darolutamide based on 2019 data was shorter than when based on 2018 data (see section 3.10). The committee noted the ERG's concerns about the possibility that if the time to stopping darolutamide decreased with more mature data, the estimates of metastasis-free survival may also have decreased if this outcome had been measured until 2019. The committee noted that the company extrapolated the 2018 data on metastasis-free survival data with a Weibull model, which gave the best fit. The ERG provided a more pessimistic Gompertz extrapolation of these data to account for the possibility that metastasis-free survival would also decrease had it been measured until 2019. The clinical experts at the meeting stated that the ERG's Gompertz model was overly pessimistic. They expected some people taking darolutamide to still have non-metastatic disease at 7 years, contrary to the ERG's modelling of all people having metastatic disease by this point. The committee concluded that extrapolating from the most mature data was appropriate and using different data cuts introduced uncertainty. It further concluded that considering a more pessimistic extrapolation in addition to the company's extrapolation was reasonable to assess the impact on the cost-effectiveness results (see section 3.19).

The long-term modelled survival estimates are highly uncertain and it is appropriate to consider other approaches

3.13 The company used a Weibull model to extrapolate overall survival beyond the end of ARAMIS. This predicted that 28% of people would be alive in the darolutamide plus ADT arm after 10 years compared with 9% in the ADT alone arm. At 20 years, it predicted that around 2% of people in the darolutamide plus ADT arm and 0% in the ADT alone arm would be alive. The ERG explained that its clinical expert advised that the predictions of long-term survival were reasonable in people who take ADT alone, but the company may have overestimated the proportion of people taking darolutamide plus ADT who would still be alive at 20 years, in part because the modelled cohort had an average age of 74 years. The ERG suggested an alternative extrapolation of the darolutamide plus ADT arm using a generalised gamma extrapolation. This predicted that 7% of

people would be alive at 10 years and nobody would be alive at 20 years. The ERG stated that its clinical expert advised that long-term survival on darolutamide would likely be between the values extrapolated by the Weibull and the generalised gamma models. Acknowledging that they lacked long-term experience with darolutamide the clinical experts at the committee meeting stated that they expected around 30% of people in this population to be alive at 10 years and it was plausible that some people would be alive at 20 years. The committee noted that the company's modelled survival for ADT alone seemed lower than what the clinical experts considered plausible. It also noted that there were no longer-term data to validate the modelled long-term survival estimates with either treatment. Because the trial data were immature the committee concluded that the estimates of long-term extrapolated survival were highly uncertain. The committee further concluded it was appropriate to consider these approaches in its decision making:

- the company's approach
- the ERG's approach using the average of the generalised gamma and Weibull to extrapolate survival on darolutamide beyond the period covered by ARAMIS
- other ERG scenarios, which reduced the overall survival estimate for darolutamide (see section 3.16).

The company models fewer active treatments after darolutamide plus ADT than after ADT alone, which reflects expected NHS practice

3.14 In the company model, once people had progressed to metastatic disease, they had 3 lines of treatment and then best supportive care. The company presented the different treatment options with the expected proportion of people who would have them. The committee noted:

- The company suggested that around 2.5% to 5% of people would have abiraterone after darolutamide in the darolutamide plus ADT arm. The committee noted that the NHS would not offer abiraterone after darolutamide in clinical practice; this may overestimate the costs in the ADT alone arm and bias the cost-effectiveness estimates to favour darolutamide.
- A higher proportion of people had best supportive care rather than a clinically effective treatment as their first, second or third treatment after darolutamide plus ADT compared with ADT alone. The committee agreed that this reflected expected NHS practice, that is, people would have fewer active treatment options after darolutamide plus ADT than after ADT alone.

The ERG's estimates of time on treatments for metastatic disease are more plausible than the company's

3.15 The company estimated how long people took treatments for metastatic disease (see section 3.14). It used the median treatment duration for first, second and third treatments for hormone-relapsed metastatic prostate cancer from NICE's technology appraisal guidance on enzalutamide for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated and abiraterone for treating metastatic hormone-relapsed prostate cancer before chemotherapy is indicated. The company then estimated the mean time on each treatment from the median times, by assuming an exponential distribution. The committee considered that 2 changes proposed by the ERG to the company's approach were reasonable:

- Modelling abiraterone or enzalutamide as second or third treatments for metastatic prostate cancer using observed values for progression-free survival and duration of treatment at this position in the treatment pathway rather than as first treatments, as modelled by the company. The company had used data from trials of abiraterone and enzalutamide for hormone-relapsed metastatic prostate cancer before docetaxel, the COU-AA-302 and PREVAIL trials respectively. The ERG used data from the COU-AA-301 trial for abiraterone and the AFFIRM trial for enzalutamide, which assessed abiraterone and enzalutamide for hormone-relapsed metastatic prostate cancer after docetaxel.

- Basing duration of best supportive care on the observed duration of ADT alone taken before chemotherapy in PREVAIL. ADT in PREVAIL was considered to be best supportive care. This was different to the company's approach, which used the average progression-free survival on the active treatments in the company's model (that is, abiraterone, enzalutamide, cabazitaxel, radium-223 and docetaxel) to estimate the duration of best supportive care.

  The committee concluded that the company's approach to modelling follow-on treatments was broadly appropriate but agreed that the ERG's assumptions were more plausible than the company's.

It is plausible that survival with metastatic disease after darolutamide plus ADT would be 3 to 4 months shorter than after ADT alone

3.16 The company's model predicted that people would live 2 more months with metastatic disease after darolutamide plus ADT than after ADT alone. The committee agreed with the ERG that this was implausible, because people would have access to more active treatments after ADT alone than after darolutamide plus ADT. The ERG did a scenario analysis in which it equalised the hazards of dying in the modelled darolutamide plus ADT arm and in the modelled ADT alone arm at 5 years. This reduced the overall survival estimates for darolutamide. Also, the model predicted that people would live an extra 8 months with metastatic disease after ADT compared with after darolutamide plus ADT. The clinical experts explained that although it was plausible that survival with metastatic disease after ADT alone would be longer than after darolutamide plus ADT, the ERG's scenario overestimated the difference. The clinical experts stated that recent trials of new drugs for hormone-relapsed metastatic prostate cancer had shown a 3 to 4-month survival advantage compared with a non-active comparator. They said that therefore they would expect survival with metastatic disease after darolutamide plus ADT to be at most 3 to 4 months shorter than after ADT alone. The committee concluded that it was plausible that survival with metastatic disease after darolutamide plus ADT would be 3 to 4 months shorter than after ADT alone.

The frequency and costs of monitoring and hospital appointments are between the company's and ERG's estimates

3.17 The company and ERG had different assumptions on the frequencies of monitoring and costs of hospital appointments. The company based its assumptions on a retrospective cohort study from an NHS trust, which collected data from 44 people with hormone-relapsed non-metastatic prostate cancer since 2011. The committee noted that monitoring practices can change over time. The ERG based its preferences on NICE's technology appraisal guidance on enzalutamide for hormone-relapsed non-metastatic prostate cancer. A patient expert, clinical experts and patient groups explained that people have fewer scans and community nurse visits than suggested by the ERG, but more visits to specialist nurses than suggested by the company. The committee concluded that the frequency and costs of monitoring and hospital appointments would lie between the company's and ERG's estimates.

The company's modelled utility values are appropriate

3.18 The company used EQ-5D data from ARAMIS to estimate that the utility value in the non-metastatic health state was 0.813 in both the darolutamide plus ADT and ADT alone modelled treatment arms. The mean utility value in the metastatic health state took into account the proportions of people having each follow-on treatment and the duration of each treatment. This was 0.731 in the darolutamide plus ADT modelled arm and 0.777 in the ADT alone modelled arm. The company used utility values associated with the various follow-on treatments, and disutility values for symptomatic skeletal events, from NICE's technology appraisal guidance on enzalutamide for non-metastatic hormone relapsed prostate cancer and enzalutamide for metastatic hormone-relapsed prostate cancer before chemotherapy is indicated. The committee concluded that the company's modelled utility values were appropriate.

The preferred modelling assumptions give an ICER in the range reflecting a cost-effective use of NHS resources

3.19 Because darolutamide and the follow-on treatments in the model (abiraterone, enzalutamide, cabazitaxel and radium-223) have

confidential patient access schemes, the exact incremental cost-effectiveness ratios (ICERs) cannot be presented here. The committee noted that:

- Using a Gompertz model rather than a Weibull model to extrapolate data on metastasis-free survival from ARAMIS increased the ICER from the company's base case.
- If survival after metastatic disease was modelled to be longer after ADT alone than after darolutamide plus ADT, this increased the ICER from the company's base case.
- Using the ERG's assumptions on monitoring frequency and costs increased the ICER.

The committee considered that the most relevant scenarios for decision making were:

- The ERG's base case, but with the overall survival hazards in the darolutamide plus ADT arm equalised to ADT alone at 7 years. This scenario estimated that people having darolutamide plus ADT would live 3 months less with metastatic prostate cancer than people having ADT alone. The ICER for this scenario was between £20,000 and £30,000 per quality-adjusted life year (QALY) gained.
- The ERG's base case, but with the company's Weibull extrapolation of the ARAMIS data on metastasis-free survival, and the overall survival hazards equalised to ADT alone at and beyond 11 years. This scenario estimated that people having darolutamide plus ADT would live 4 months less with metastatic prostate cancer than people having ADT alone. The ICER for this scenario was under £20,000 per QALY gained.

The committee noted that both these scenarios resulted in an ICER for darolutamide plus ADT compared with ADT alone in the range that NICE usually considers a cost-effective use of NHS resources.

Darolutamide is innovative

3.20 The committee agreed that there is an unmet need for clinically effective treatments for hormone-relapsed non-metastatic prostate cancer.

Having a treatment that delays metastases by a median of 22 months compared with the only treatment available to patients, ADT alone, is a step change for this population. The committee noted that having an effective treatment for non-metastatic prostate cancer may reduce the number of 'extra' or more sensitive scans being used to detect metastases so that people can then have the next available clinically effective treatment (see section 3.2). This potential benefit had not been included in the company's modelling. The committee concluded that darolutamide plus ADT is innovative.

Conclusion

Darolutamide plus ADT is recommended

3.21 The committee concluded that its preferred modelling scenarios resulted in an ICER that reflects good value for scarce NHS resources. It noted that darolutamide is clinically effective and innovative, and there is an unmet need for treatment for hormone-relapsed non-metastatic prostate cancer. The committee agreed that darolutamide plus ADT was a cost-effective use of NHS resources for treating hormone-relapsed prostate cancer at high risk of metastasising.

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or fast track appraisal), at which point funding will switch to routine commissioning budgets. The NHS England and NHS Improvement Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a person has hormone-relapsed non-metastatic prostate cancer and the doctor responsible for their care thinks that darolutamide with androgen deprivation therapy is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

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