Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
www.scottishmedicines.org.uk
Delta House 50 West Nile Street Glasgow G1 2NP Tel 0141 225 6999 Chairman: Professor Jonathan G Fox

2nd Re-Submission

cabazitaxel 60mg concentrate and solvent for solution for infusion (Jevtana®)
SMC No. (735/11)

Sanofi

04 November 2016

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 Scotland. The advice is summarised as follows:

ADVICE: following a second resubmission assessed under the end of life process

cabazitaxel (Jevtana®) is accepted for restricted use within NHS Scotland.

Indication review: cabazitaxel in combination with prednisone or prednisolone is indicated for the treatment of adult patients with hormone refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen.

SMC restriction: for use in patients who have received at least 225mg/m^2 (three cycles) of docetaxel and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

In an open-label, multicentre, randomised-controlled, phase III study in patients with metastatic hormone refractory prostate cancer, treatment with cabazitaxel plus prednisone/prednisolone was associated with an extended median overall survival of 2.4 months compared with an alternative chemotherapy regimen.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of cabazitaxel. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

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

Overleaf is the detailed advice on this product.

Chairman,
Scottish Medicines Consortium

Indication

Cabazitaxel in combination with prednisone or prednisolone is indicated for the treatment of adult patients with hormone refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen.

Dosing Information

The use of cabazitaxel should be confined to units specialised in the administration of cytotoxics and it should only be administered under the supervision of a physician experienced in the use of anticancer chemotherapy. Facilities and equipment for the treatment of serious hypersensitivity reactions like hypotension and bronchospasm must be available.

Premedication should be administered at least 30 minutes before administration of cabazitaxel. In addition antiemetic prophylaxis is recommended and the patients should be adequately hydrated. See summary of product characteristics for further detail.

Cabazitaxel 25mg/m^2 administered as a one-hour intravenous infusion every three weeks in combination with oral prednisone or prednisolone 10mg administered daily throughout treatment.

Product availability date

20 May 2011.
Cabazitaxel meets SMC end of life criteria in this treatment setting.

Summary of evidence on comparative efficacy

Cabazitaxel is a taxane anti-neoplastic agent with activity against tumours sensitive and insensitive to docetaxel. Cabazitaxel disrupts the microtubular network in cells which results in the inhibition of mitotic and interphase cellular functions. It is indicated in patients with metastatic hormone refractory prostate cancer (mHRPC) who have received treatment with docetaxel.[1] Treatment of mHRPC is evolving and since the pivotal study was conducted other treatments including abiraterone and enzalutamide have been licensed. Currently, the optimal sequencing of treatments or combination of therapies is uncertain.[2] The submitting company has requested that SMC considers cabazitaxel when positioned for use in patients who have received at least 225mg/m^2 (three cycles) of docetaxel and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

TROPIC, an open-label, randomised, phase III study, was conducted in men with pathologically proven prostate cancer refractory to hormone therapy, with documented disease progression during or after completion of docetaxel treatment and an ECOG performance status of 0 to 2.[3-5] Patients with measurable disease were required to have documented disease progression by Response Evaluation Criteria in Solid Tumours (RECIST) with at least one visceral or soft-tissue metastatic lesion. Patients with non-measurable disease were required to have rising serum prostate-specific antigen (PSA) concentrations or the appearance of at least one new demonstrable radiographic lesion.

Patients were randomised equally, stratified by disease measurability (measurable versus non-measurable) and ECOG performance status (0 to 1 versus 2), to cabazitaxel 25mg/m^2 intravenously (IV) (n=378) or mitoxantrone 12mg/m^2 IV (n=377) on day one of a three week cycle for up to 10 cycles or until disease progression. In addition, all patients received oral prednisone/prednisolone 10mg daily. Patients treated with cabazitaxel received premedication as recommended in the Summary of Product Characteristics. Antiemetic prophylaxis was given at the physicians' discretion. Prophylactic

granulocyte colony-stimulating factor (G-CSF) was permitted from cycle two onwards, at the physicians' discretion, following first occurrence of either neutropenia (≥7 days) or neutropenia complicated by fever or infection.[3]

The primary outcome was overall survival, calculated from the date of randomisation to death. At the date of the final analysis (cut-off, 25 September 2009, median follow-up 12.8 months) 234 deaths had occurred in the cabazitaxel group and 279 in the mitoxantrone group. Median overall survival was 15.1 months for cabazitaxel versus 12.7 months for mitoxantrone; HR 0.70, 95% confidence interval (CI): 0.59 to 0.83, p<0.0001.[3] In an updated analysis (median follow-up 25.5 months and event accrual rate of 75% of study population [585/755]), the proportion of patients who survived at least two years was 16% (60/378) in the cabazitaxel group and 8.2% (31/377) in the mitoxantrone group; HR 0.72, 95% CI: 0.61 to 0.84, p<0.0001.[4]

Secondary outcomes included progression free survival (PFS), defined as the time from randomisation to the first date of progression measured by PSA progression, tumour progression, pain progression, or death. Median PFS was 2.8 months in the cabazitaxel group and 1.4 months in the mitoxantrone group; HR 0.74, 95% CI: 0.64 to 0.86, p<0.0001.[3] Other secondary endpoints are reported in table 1, below.

Table 1: Other secondary endpoints from the TROPIC study [3,5]

	Cabazitaxel	Mitoxantrone	Hazard ratio (95% CI) p-value
PSA response, % (n/N)	39% (129/329)	18% (58/325)	p=0.0002
Tumour response rate, % (n/N)	14% (29/201)	4.4% (9/204)	p=0.0005
Pain response, % (n/N)	9.2% (16/174)	7.7% (13/168)	p=0.63
Median time to tumour progression, months	8.8	5.4	0.61 (95% CI: 0.49 to 0.76) p<0.0001
Median time to PSA progression, months	6.4	3.1	0.75 (95% CI: 0.63 to 0.90) p=0.001
Median time to pain progression, months	11.1	Not reached	0.91 (95% CI: 0.69 to 1.19) p=0.52

CI=confidence interval; PSA=prostate-specific antigen; N=total number of patients; n=number of responders. PSA response was defined as a reduction in serum PSA concentration of ≥50% in patients with a baseline value of ≥20 microgram/L; tumour response rate was measured in patients with measurable disease (RECIST) and included complete plus partial responses; Pain response was assessed using the McGill-Melzack present pain intensity scale combined with an analgesic score.

Summary of evidence on comparative safety

In TROPIC, the proportion of patients with treatment-emergent adverse events of at least grade 3 was 57% for cabazitaxel versus 39% for mitoxantrone. Discontinuations due to treatment emergent adverse events were higher in the cabazitaxel group (18%) than in the mitoxantrone group (8.4%).[3]

Haematological adverse events were common, with neutropenia (all grades) occurring in 94% versus 88% of patients in the cabazitaxel and mitoxantrone groups respectively, and neutropenia of at least grade 3 in 82% versus 58% of patients. Treatment with cabazitaxel was also associated with higher rates (≥grade 3) of leukopenia (68% versus 42%), anaemia (11% versus 4.9%) and thrombocytopenia (4.0% versus 1.6%). Febrile neutropenia occurred in 28 (7.5%) cabazitaxel-treated patients and five (1.3%) mitoxantrone-treated patients.[3]

Non-haematological adverse events (≥grade 3 and occurring in ≥3% of patients in either group) included diarrhoea (6.2% versus <1%), fatigue (4.9% versus 3.0%), asthenia (4.6% versus 2.4%) and back pain (3.8% versus 3.0%). Peripheral neuropathy of any grade was reported in 14% of patients in the cabazitaxel group versus 3.2% of patients in the mitoxantrone group. Three patients in each group had grade 3 peripheral neuropathy. Peripheral oedema of any grade occurred in 9.2% of patients in both groups.[3]

There were 18 (4.8%) versus nine (2.4%) deaths ≤30 days after the last dose of study drug in the cabazitaxel and mitoxantrone groups respectively. In the cabazitaxel group, all deaths were reported as adverse events: neutropenia and clinical consequences/sepsis (n=7), cardiac (n=5), renal failure (n=3), dehydration/electrolyte imbalance, cerebral haemorrhage and unknown cause (n=1 each).[3]

Summary of clinical effectiveness issues

Treatment of mHRPC is evolving and since the pivotal study was conducted a number of treatments including abiraterone and enzalutamide have been licensed. These have altered treatment pathways for patients with mHRPC.[2] The submitting company notes that the terms mHRPC and metastatic castration-resistant prostate cancer (mCRPC) are often used interchangeably. As a result of abiraterone and enzalutamide being accepted for use in the pre-chemotherapy setting, it is expected that this will become the predominant treatment pathway. The submitting company considers that patients with mCRPC will receive abiraterone or enzalutamide in the pre-chemotherapy setting and then, following docetaxel, the only options are cabazitaxel or best supportive care. Clinical experts consulted by SMC have confirmed that this is the most likely treatment pathway. They also note some patients may still receive abiraterone or enzalutamide post-docetaxel, and those patients with symptomatic bone metastases and no known visceral metastases may receive treatment with radium-223 dichloride pre- or post-docetaxel. The submitting company acknowledged these alternative treatment pathways but did not present any direct or indirect comparative evidence for cabazitaxel versus abiraterone, enzalutamide or radium-223 dichloride.

Cabazitaxel meets SMC end of life criteria. In the control arm of the pivotal study, where mitoxantrone is a proxy for best supportive care, median overall survival was 12.7 months.[3]

Clinical experts consulted by SMC considered that there is unmet need for patients who have received abiraterone or enzalutamide and have progressed on docetaxel, where there are currently no treatment options. Clinical experts noted that these patients generally have good performance status.

In the TROPIC study, cabazitaxel resulted in a statistically significant extension in median overall survival of 2.4 months compared with mitoxantrone. There were also statistically significant differences for most secondary endpoints, including PFS, in favour of cabazitaxel. Although cross-over was not permitted, 12% of patients in the mitoxantrone group went on to receive tubulin-binding drugs at progression.[3] The study population did not include patients who had received abiraterone or enzalutamide prior to docetaxel, as described in the predominant treatment pathway. The submitting company provided observational data from a number of studies that indicate the efficacy of cabazitaxel is unaffected by prior use of such treatments. Further evidence was provided from the PROSELICA study which included a subgroup of patients who received treatment with abiraterone or enzalutamide prior to the use of docetaxel, in line with the predominant treatment pathway. PROSELICA was a multi-centre, open-label, randomised, phase III, non-inferiority, post-marketing requirement study.[6,7] It was designed to test non-inferiority (in terms of overall survival) of cabazitaxel 20mg/m² (n=598) versus cabazitaxel 25mg/m² (n=602) in adult men with mCRPC with progressive disease previously treated with a docetaxel-containing regimen. Post-hoc analyses of PROSELICA enabled subgroup comparison of patients who received prior treatment with abiraterone or

enzalutamide (n=308) versus those who had not (n=892) – the results of these analyses have been deemed to be confidential by the submitting company but suggest that the results of the TROPIC study remain relevant to the proposed predominant treatment pathway, and clinical experts consulted by SMC agree with this assumption.

The submitting company has requested that SMC considers cabazitaxel when positioned for use in patients who have received at least 225mg/m^2 (three cycles) of docetaxel and have an ECOG performance status of 0 or 1. In TROPIC there was no significant difference in overall survival observed in some subgroups including patients who had received a total docetaxel dose less than 225mg/m^2 and in those with an ECOG performance status of 2.[3] The submitting company presented data for overall survival and PFS from an unpublished subgroup analysis of 632 patients (84% of ITT population) who received at least 225mg/m^2 of docetaxel and had an ECOG performance status of 0 or 1. These patients were considered most relevant in terms of eligibility for cabazitaxel in clinical practice. These data were used in the base case economic analysis.

While fewer patients in the cabazitaxel than mitoxantrone group discontinued from the TROPIC study due to disease progression (49% versus 72%), more discontinued due to adverse events (18% versus 8.4%). Haematological adverse events were common with the most frequent (at least grade 3 in severity) being neutropenia, leukopenia, and anaemia.[3]

While TROPIC did not measure health-related quality of life (HRQoL), some HRQoL data are available from the UK early access programme (EAP).[8] This was a non-comparative, open-label study that included 112 patients treated with cabazitaxel plus prednisolone for a maximum of 10 cycles, although the protocol was amended to allow treatment beyond 10 cycles if additional clinical benefit was anticipated. The mean EQ-5D-3L index and visual analogue scale scores remained stable and there were some slight improvements with subsequent cycles of chemotherapy.[8,9]

Clinical experts consulted by SMC considered that cabazitaxel is a therapeutic advancement due to the additional overall survival seen in the pivotal study and the availability of another line of treatment. They considered that the introduction of cabazitaxel will have service implications for secondary care in terms of delivery of chemotherapy.

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

Summary of patient and clinician engagement

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of cabazitaxel, as an end-of-life medicine, in the context of treatments currently available in NHS Scotland.

The key points expressed by the group were:

- mHRPC which has progressed after docetaxel is a debilitating clinical condition. Most patients are symptomatic, predominantly from skeletal related events including metastatic spinal cord compression, which significantly impacts on quality of life.

- Limited options remain at the late stage in the prostate cancer treatment pathway.

- There is a small group of patients who are still fit enough to receive cytotoxic treatment after disease progression. These are typically patients with good performance status with resistance to docetaxel or with visceral metastases who are unsuitable for radium 223.

- The increased survival shown in the TROPIC study may be conservative given the active comparator of mitoxantrone, which was likely to be more effective than best supportive care. Patients and patient groups stressed that any additional time was very precious and the knowledge that a further line of treatment was available would bring hope for the future.

- Attention was also drawn to more recent data showing stable quality of life with a trend towards improvement and reduction in the incidence of pain[6].

- Use of cabazitaxel may prevent hospital admissions for symptom control and also reduce the need for palliative radiotherapy and morphine analgesia. Treatment appears to be well tolerated in practice (less toxic than docetaxel). Patient groups highlighted that patients value the opportunity of making an informed decision on the risks and benefits of treatment themselves.

- The PACE group was of the view that this medicine should be made available in NHS Scotland, in line with the licensed indication in patients with good performance status fit enough to receive a further line of chemotherapy.

Additional Patient and Carer Involvement

We received patient group submissions from Prostate Scotland, Edinburgh & Lothian Prostate Cancer Support Group, Prostate Cancer UK, and Tackle Prostate Cancer which are all registered charities. Prostate Scotland and the Edinburgh & Lothian Prostate Cancer Support Group have not received any pharmaceutical company funding in the last two years. Prostate Cancer UK has received 0.06% pharmaceutical company funding, but none from the submitting company. Tackle Prostate Cancer has received 22% pharmaceutical company funding, but none from the submitting company. Representatives from Edinburgh & Lothian Prostate Cancer Support Group and Prostate Cancer UK also participated in the PACE meeting. The key points of their submission are included in the full PACE statement. Prostate Scotland and Tackle Prostate Cancer did not participate in the PACE meeting, although highlighted many of the points captured through PACE

Summary of comparative health economic evidence

The submitting company presented a cost-utility analysis comparing cabazitaxel to best supportive care (BSC) in men with mHRPC who had previously received docetaxel. BSC consisted of 80% BSC and 20% chemotherapy, which reflected a BSC and chemotherapy mix from a UK observational study. The economic model was a standard three-state area under the curve model with stable, progressive disease and death states, and a 10 year time horizon. The base case analysis used data from the sub-group of the TROPIC study population relating only to patients with an ECOG performance status of 0 or 1 and who had received docetaxel as a first-line treatment. Based on SMC clinical expert feedback, the comparator of BSC can be considered appropriate given the predominant treatment pathway is expected to be the use of abiraterone or enzalutamide pre-docetaxel, hence leaving cabazitaxel or BSC/palliative chemotherapy as the main options post-docetaxel.

For the base case comparison with BSC, the company performed a trial-based analysis of cabazitaxel versus mitoxantrone, with the efficacy of the latter assumed to represent the outcomes associated with BSC. Data for overall survival (OS) and PFS from the TROPIC sub-group were used and extrapolated to the lifetime of the patient using the Weibull and log-normal parametric functions respectively. Utility values based on the EQ-5D were derived from the cabazitaxel UK EAP, with an increasing utility over time estimated for the PFS state (0.68 at baseline to 0.82 at treatment cycle 10), and a utility of 0.63

for the progressive disease state based on patients who had progressed in the EAP. Adverse event disutilities were estimated based on published studies.

Medicine acquisition costs were included, and the doses and treatment duration as in the TROPIC and a UK observational study were used, accounting for relative dose intensity and discontinuation rates for reasons other than progression, and a BSA of $1.9m^2$ estimated by UK expert clinical opinion. It is also worth noting that the analysis assumed 1.0006 vials of cabazitaxel were used per administration cycle to take into account wastage and the proportion of patients who may require a second vial. In addition, the analysis assumed that patients would receive cabazitaxel for a maximum of 10 cycles. Resource-use data included the costs of medicines, pre-medications, concomitant medications, administration and treatment of adverse events. Costs of routine management associated with the stable disease and progressive disease state, and end of life hospitalisation estimates, were based on a UK retrospective study on resource use in second line mHRCP conducted in 5 UK cancer centres (between 2007-11). Where necessary, these were supplemented by UK expert clinical opinion. In the base case, post-progression palliative chemotherapy for the cabazitaxel and BSC arms (eg docetaxel, mitoxantrone, cyclophosphamide), and use of BSC in 80% of patients (assumed to consist of analgesics, radiotherapy, bisphosphonates) was derived from the UK observational study.

A Patient Access Scheme (PAS) was proposed by the submitting company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHS Scotland. Under the PAS, a simple discount is offered on the price of the medicine.

The base case incremental cost per quality adjusted life year (QALY) gained for cabazitaxel versus BSC was estimated to be £45,459 with PAS, based on an incremental cost of £10,553 and incremental QALYs of 0.232 (discounted life years gained of 0.338 or 4.1 months).

Use of different parametric functions for OS extrapolation resulted in an incremental cost-effectiveness ratio (ICER) range of £34.8k-£47.8k /QALY with PAS. Varying utility in the progressive disease state by ±10% had some impact on the ICER, producing a range of £43k - £48.2/QALY. Scenario analysis which used 100% BSC costs for the BSC comparator and removed G-CSF prophylaxis, discontinuations, AE costs and disutilities associated with mitoxantrone generated an ICER of £48.7k. The company also provided a scenario analysis applying a mix of 0% BSC and 100% chemotherapy in the progressed disease state which generated an ICER of £50.6k. The results were also not highly sensitive to a range of other sensitivity analyses performed including using a shorter time horizon of 5 years, excluding discontinuations, use of the whole ITT population, excluding adverse event disutilities and varying stable disease utilities.

As well as the cost per QALY being relatively high, the key weaknesses and uncertainties with the economic analysis were as follows:

- The base case analysis in this second resubmission compared cabazitaxel with BSC, where BSC consisted of 80% BSC and 20% chemotherapy, and therefore did not use the medicine cost of mitoxantrone. However, it is worth noting that G-CSF prophylaxis, discontinuations, and AE costs and disutilities for BSC were still based on mitoxantrone data. However, the company also presented an analysis which assumed a 100% BSC mix and removed G-CSF prophylaxis, discontinuations, AE costs and disutilities associated with mitroxantrone. This analysis generated an ICER of £48.7k.
- An indirect comparison and an economic analysis versus abiraterone and enzalutamide were presented as part of the first resubmission; however, this second resubmission focused on a comparison versus BSC. The company has reported that abiraterone and enzalutamide would be used before cabazitaxel which leaves BSC as the appropriate comparator. The company also did not consider radium-223 as a relevant comparator due to differences in licenses, modes of action, outcome definitions and therapeutic benefits between the medicines.

After considering all the available evidence and the output from the PACE process, the Committee accepted cabazitaxel for restricted use in NHS Scotland.

Additional information: guidelines and protocols

The European Society of Medical Oncology 2015 guideline for the diagnosis, treatment and follow-up of cancer of the prostate recommends treatment with docetaxel for mCRPC. Radium-233 is also recommended in symptomatic, bone-predominant non-visceral metastatic disease. The guideline advises that chemotherapy naive asymptomatic/mildly symptomatic men should receive abiraterone or enzalutamide, with sipuleucal-T as an additional option in this patient group. The publication notes that optimal sequencing or combination of therapies is unknown. In the post-docetaxel setting, recommended options are: abiraterone, cabazitaxel, enzalutamide and radium-223 (in those with no visceral disease).[2]

The European Association of Urology produced guidelines on prostate cancer in 2015. Salvage hormonal treatment with abiraterone or enzalutamide is recommended as a treatment option in mCRPC. Docetaxel at a dose of 75mg/m^2 every three weeks is recommended in patients eligible for salvage cytotoxic therapy. Abiraterone, enzalutamide and cabazitaxel are advised as second line treatment options following recurrence after docetaxel salvage therapy. In patients with symptomatic bone metastasis and who are ineligible for or have progressed after treatment with docetaxel, radium-233 is recommended as a treatment option. The guideline notes that no clear recommendation can made in regards to the most effective second line treatment as no clear predictive factors exist.[10]

The National Institute of Health and Care Excellence (NICE) published a guideline on the diagnosis and management of prostate cancer, in 2014. In metastatic hormone relapsed disease, docetaxel is recommended as a treatment option when the Karnofsky performance status score is >60%. NICE advises that docetaxel treatment should cease after disease progression, severe adverse events or completion of up to 10 cycles. Repeat cycles of docetaxel are not recommended if there is disease recurrence after a planned course of chemotherapy. Corticosteroids (eg dexamethasone 0.5mg daily) may be offered as a third line therapy after anti-androgen and androgen deprivation therapy in this patient group. The guideline does not make any recommendations for CRPC following cytotoxic therapy, and refers to the NICE technology appraisal guidance on abiraterone.[11]

Additional information: comparators

Best supportive care (eg, mitoxantrone), abiraterone, enzalutamide, radium-223 dichloride.

Cost of relevant comparators

Drug	Dose Regimen	Cost per cycle (£)	Cost for six* cycles (£)	Cost for eight** months (£)
Cabazitaxel plus prednisolone	**Cabazitaxel 25mg/m^2 IV every three weeks plus prednisolone 10mg orally daily**	**3,697**	**22,182**	**N/A**
Radium-223 dichloride	55kBq per kg body weight intravenously, given at 4 week intervals for 6 injections	4,040	24,240	N/A
Abiraterone plus prednisolone	Abiraterone 1g orally once daily plus prednisolone 10mg orally once daily	N/A	N/A	23,716
Enzalutamide	160mg orally once daily	N/A	N/A	23,700
Mitoxantrone plus prednisolone	Mitoxantrone 12mg/m^2 IV every three weeks plus prednisolone 10mg orally once daily	154	924	N/A

Doses are for general comparison and do not imply therapeutic equivalence. Costs do not take any patient access schemes into consideration. Costs are from eVadis and British National Formulary Online on 26 August 2016 and, for chemotherapy, are based on body surface area of 1.8m^2; cost for radium based on adult body weight of 70kg and taken from the Scottish Medicines Consortium advice on radium-223 dichloride (Xofigo®), SMC Drug ID 1077/15, published 12 October 2015.

*Cost for six cycles has been provided (median for cabazitaxel from TROPIC study), however cabazitaxel may be given for up to 10 cycles (cost for 10 cycles = £36,970); median number of cycles of mitoxantrone in the TROPIC study was four.

**Costs for abiraterone and enzalutamide for eight months have been provided (median treatment duration from pivotal studies).

IV=intravenous; N/A=not applicable.

Additional information: budget impact

The submitting company estimated the population eligible for treatment to be 291 patients in year 1, rising to 294 patients in year 5, and an estimated uptake of 5% (15 patients) in year 1 and 20% (59 patients) in year 5. As the uptake estimates appear low relative to SMC clinical expert views, the medicines budget impact may be underestimated.

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 commercially confidential.**

References

The undernoted references were supplied with the submission.

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6. NCT01308580. Cabazitaxel at 20 mg/m² compared to 25 mg/m² with prednisone for the treatment of metastatic castration resistant prostate cancer (PROSELICA). www.clinicaltrials.gov.

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8. Bahl A, Masson S, Malik Z, Birtle AJ, Sundar S, Jones RJ, et al. Final quality of life and safety data for patients with metastatic castration-resistant prostate cancer treated with cabazitaxel in the UK Early Access Programme (EAP) (NCT01254279). BJU International. 2015;116(6):880-7.

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10. Mottet N, Bellmunt J, Briers E, et al. Guidelines on prostate cancer. European Association of Urology 2015; www.uroweb.org.

11. National Institute for Health and Care Excellence. Prostate cancer: diagnosis and management, clinical guideline 175. 2014; www.nice.org.uk.

This assessment is based on data submitted by the applicant company up to and including 12 October 2016.

**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_statements/Policy_Statements*

Drug 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 drug 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 NHS Scotland 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 NHS Scotland 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.