PUBLIC SUMMARY DOCUMENT
Product: Cabazitaxel, injection set containing 1 single use vial concentrate for I.V. infusion, 60 mg (anhydrous) in 1.5 mL with diluent, Jevtana®
Sponsor: Sanofi-Aventis Pty Ltd
Date of PBAC Consideration: November 2011

1. Purpose of Application
The submission sought an Authority Required listing for treatment of hormone refractory metastatic carcinoma of the prostate (mHRPC) in patients previously treated with a docetaxel containing regimen.

2. Background
At the July 2011 meeting, the PBAC rejected a submission for cabazitaxel for an Authority Required listing for the treatment of hormone refractory metastatic carcinoma of the prostate in a patient previously treated with a docetaxel containing regimen on the basis of a high and uncertain cost-effectiveness ratio.

For full details refer to the July 2011 Public Summary Document.

3. Registration Status
On 8 December 2011, cabazitaxel was TGA registered for the following indication:

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

4. Listing Requested and PBAC's View
Authority Required
Treatment of hormone refractory metastatic carcinoma of the prostate in a patient previously treated with a docetaxel-containing regimen.

The requested listing was unchanged, refer to July 2011 Public Summary Document.

5. Clinical Place for the Proposed Therapy
Refer to July 2011 Public Summary Document.

6. Comparator
The comparator was unchanged, refer to July 2011 Public Summary Document.

7. Clinical Trials
The clinical trials were unchanged, refer to July 2011 Public Summary Document.

8. Results of Trials
To address the PBAC's concerns from July 2011, the submission further analysed the clinical trial data.

The submission stated that no changes were made to the extrapolations for survival due to the relatively high proportion of benefit captured within trial and the good fit of the Weibull curve to the observed data.

The submission stated that most of the survival benefit attributed to cabazitaxel in the economic evaluation was observed during the clinical trial period ("within-trial"). With approximately 75% of the survival benefit captured within the trial (3.18 months/4.26 months ≈ 0.75) and therefore 25% of the survival benefit for cabazitaxel was derived from beyond the trial period (1.08 months/4.26 months).

The submission agreed with the PBAC (from July 2011) that most of the gain with cabazitaxel is spent on the progressive disease state in the terminal or end of life phase of the disease with increased toxicity.

Of the 4.26 months overall survival advantage:
- 74% (3.14 months) is spent in the end of life phase (progressive disease)
- 17% (0.74 months) is spent free of progression but with toxicities and
- the remaining 9% (0.38 months) is spent free of progression and free of toxicity.

For PBAC's view, see Recommendation and Reasons.

9. Clinical Claim

The clinical claim was unchanged, refer to July 2011 Public Summary Document.

10. Economic Analysis

The submission offered an updated price proposal and provided an updated economic evaluation which tested the impact of wider use of G-CSF based on the TROPIC trial.

The revised base case incremental cost per extra quality adjusted life year (QALY) gained was estimated to be in the range of $45,000 and $75,000.

The submission stated that the utility values used in the July 2011 submission, particularly for the progressive disease health state, are lower – and therefore more conservative – than has been reported elsewhere. The submission stated that the utility values have not been updated for this re-submission, although a sensitivity analysis using the NICE utility values was included. When the utility values, as derived using the EQ-5D from the Early Access Program (EAP) were used, the ICER was reduced to the range of $15,000 and $45,000 per extra QALY.

For PBAC's view, see Recommendation and Reasons.

11. Estimated PBS Usage and Financial Implications

The submission presented no updated information.

12. Recommendation and Reasons

The PBAC noted that the updated price proposal for cabazitaxel gave an estimated base case ICER between $45,000 – $75,000, which the PBAC still considered was unacceptably high. The PBAC agreed that use of the costs of G-CSF from the TROPIC trial was appropriate, however, the ICER, if used in all cycles and in all patients was estimated to between $75,000 – $105,000, which is unacceptably high.

In July 2011, the PBAC considered that most of the survival gain with cabazitaxel was beyond the trial period and was based on time spent in the terminal or end of life phase of the

disease with increased toxicity. The PBAC noted that no changes had been made to the extrapolation of survival in the resubmission and that 25% of the survival benefit for cabazitaxel was captured from beyond the trial period (1.08 m/4.26 m), which was a mean and not median value. However, the PBAC considered that the survival benefit was still a source of uncertainty, especially in light of the high ICER and that most of the mean overall survival gain of 4.26 months is spent in the progressive disease state (3.14 months). The PBAC recalled that when considering docetaxel for PBS listing for hormonal refractory metastatic prostate cancer, the greatest proportion of the 3.73 months gain in extrapolated mean overall survival was spent in the TWIST state (no toxicity and no progression) and that this was an important consideration in the recommendation to list docetaxel.

The PBAC agreed that the utility values used in the submission were conservative and acceptable.

The PBAC considered that a new price proposal would be necessary for the ICER to be acceptable.

The PBAC therefore rejected the submission on the basis of a high and uncertain cost-effectiveness ratio

The PBAC also acknowledged and noted the consumer comments on this item.

Recommendation:
Reject

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

Sanofi is disappointed by this decision but is committed to continuing to work with the PBAC to ensure that Jevtana is made available on the PBS for Australian men who have prostate cancer.