ADDENDUM- AUGUST 2013

PUBLIC SUMMARY DOCUMENT
Product: SUNITINIB, capsule, 12.5 mg, 25 mg, 50 mg (as malate), Sutent®
Sponsor: Pfizer Australia Pty Ltd
Date of PBAC Consideration: August 2013

1. Purpose of Application

The re-submission sought an extension to the current Authority Required benefit to include initial and continuing treatment of metastatic, unresectable, well-differentiated malignant pancreatic neuroendocrine tumour (or carcinoma) (pNET) in patients who are symptomatic (despite somatostatin analogues) or who have documented disease progression.

2. Background of previous considerations by the PBAC

This was the fourth submission requesting an Authority Required listing for the use of sunitinib in the treatment of pancreatic NET (pNET).

The PBAC rejected previous submissions on the basis of an unacceptably high and uncertain incremental cost-effectiveness ratio (ICER) compared to best supportive care (placebo). In March 2012 the re-submission was deferred due to price negotiations with the sponsor.

At each of the previous meetings, the PBAC acknowledged there was a high clinical need for treatment for this rare type of tumour.

A copy of the Public Summary Document (PSD) from the July 2012 meeting is available at http://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2012-07/sunitinib

3. Listing Requested and PBAC's View

The requested listing was the same as for the July 2012 submission.

4. Summary of re-submission

As in previous submissions, listing was requested on a cost effectiveness basis. The re-submission claimed superior clinical effectiveness over best supportive care/placebo in the treatment of unresectable pNET. The re-submission also claimed similarities between the cost-effectiveness analyses for the pNET and renal cell carcinoma (RCC) indications.

The present re-submission proposed that when considering the cost-effectiveness of pNET, the ICER which was accepted for sunitinib renal cell carcinoma (RCC) indication was a more appropriate reference frame than that of gastrointestinal stromal tumour (GIST).

The re-submission also regarded the RCC indication to be similar to pNET, in relation to clinical need, that is, it is in an area of high clinical need where no effective alternative treatments are available. The rarity of pNET and the potential number of patients expected to receive treatment with sunitinib was noted.

The re-submission noted parallels with the clinical options available for RCC at the time of the PBAC's recommendation, where only supportive care would have been available in the absence of a PBS-listed treatment, unlike with GIST where imatinib was available as first line treatment before moving to sunitinib.

The re-submission proposed a risk share arrangement.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Trials

The re-submission presented clinical data to support survival claims for sunitinib across the three sunitinib indications

A comparison of clinical trial and adjusted survival outcomes for sunitinib

	Observed median PFS Sunitinib vs. BSC	**Observed median OS Suntinib vs. BSC**	**Adjusted median OS Sunitnib vs. BSC**
pNET (36 months follow-up)	11.4 vs. 5.5 months HR=0.418, p=0.000118	30.5 vs. 24.4 months HR=0.737, p=0.1926	30.5 vs. 17.5 months[1] HR=0.499, p=0.0035
RCC (final analysis, 21 months follow-up)	11 vs. 5.1 months HR 0.538, p<0.000001	26.4 vs. 21.9 months HR=0.821 p=0.051	26.4 vs. 15.7 months[2] HR and p-value not available as adjustment via landmark analysis
GIST (final analysis, 52 months follow-up)	5.3 vs. 1.4 months HR 0.347, p<0.001	16.8 vs. 15 months HR = 0.876 p=0.306	16.8 vs. 9 months[3] HR 0.505

- [1]Adjusted for cross over using a rank preserving structural failure time (RPSFT) model
- [2]BSC/Placebo observed, Gleave 1998.
- [3] Adjusted for cross over using a RPSFT model

6. Revised Estimated PBS Usage and Financial Implications

The utilisation estimates were the same as for the previous submissions. The re-submission estimated that extending the listing of sunitinib to include pNET patients would result in less than 10,000 patients per year in Year 5. The estimated net cost to the PBS was less than $10 million in the fifth year of listing.

For PBAC's view, see Recommendation and Reasons.

7. Clinical Claim

The re-submission claimed sunitinib was superior in terms of comparative effectiveness and inferior in terms of comparative safety, compared to best supportive care/placebo. The PBAC recalled that these claims were previously accepted as reasonable.

8. Economic Analysis

The re-submission presented a comparison of incremental life year gain (LYG) and incremental quality adjusted life years (QALYs) for the three indications, RCC, GIST and pNET.

The ICERs for the three indications were between $45,000-$75,000/QALY.

The cost-effectiveness claims for pNET were based on the similarity of the cost-effectiveness analysis of RCC and pNET, in terms of:

- the clinical trial outcomes observed;
- the overall survival gain predicted and the statistical analyses presented to predict the overall survival gain;

- the duration of a 10 year lifetime horizon, and the extent of extrapolation of clinical trial data out to a lifetime horizon;
- the estimated life-years gained and the estimated Quality Adjusted Life Year (QALY) gain.

9. Recommendation and Reasons

The PBAC noted no new clinical or economic data were provided but instead the re-submission highlighted parallels with the clinical options available for RCC at the time of PBAC recommendation (where only supportive care would have been available in the absence of a PBS-listed treatment), compared to GIST (for which imatinib was available in first line before moving to sunitinib).

The PBAC noted the value of the ICER for pNET was between the accepted ICERs for the RCC and GIST indications and considered that the proposed ICER for pNET was closer to that of RCC than for GIST.

The PBAC noted the actual utilisation of sunitinib was lower than expected for the RCC and GIST indications. The sponsor's offer to renegotiate the current risk share arrangement to include sunitinib for pNET was also noted.

The PBAC noted that since the last submission in July 2012, no new or alternative treatments have become available for patients with pNET. The committee recalled it had accepted that sunitinib provided a survival benefit for patients with pNET in its past considerations of the submissions, and again recognised the significant unmet clinical need in patients with pNET. The committee was concerned about the equity of access to sunitinib in the absence of a PBS listing for pNET, noting that current access to treatment was dependent upon the funding arrangements in the various States and Territories.

Taking into account the high and unmet clinical need, the lack of alternative treatments, the rarity of this condition, the small number of patients predicted to use this drug, and the relatively modest overall financial impact on the PBS, the PBAC considered sunitinib was acceptably cost effective for pNET.

The PBAC noted the sponsor's advice that the 37.5mg strength of sunitinib is not currently commercially produced. This would require a patient on a daily dose of 37.5mg to use separate prescriptions for 25mg and 12.5mg, with the associated extra co-payment. The PBAC considered that should the 37.5mg strength become available, this would be more convenient for patients and prescribers.

The PBAC recommended that the Drug Utilisation Subcommittee (DUSC) analyse patterns and duration of sunitinib use following listing.

Recommendation:
Recommended.

Name Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
SUNITINIB 12.5 mg capsule, 28	1	2	Sutent	PF
SUNITINIB 25 mg capsule, 28	1	2	Sutent	PF
SUNITINIB 50 mg capsule, 28	1	2	Sutent	PF

Condition:	Metastatic or unresectable, well-differentiated malignant pancreatic neuroendocrine tumour (pNET)
Treatment phase:	Initial treatment
Restriction:	Authority required
Clinical criteria:	Patient must be symptomatic (despite somatostatin analogues) OR Patient must have documented disease progression
Prescriber Instructions	Disease progression must be documented Treatment is for monotherapy only
Administrative Advice	No applications for increased maximum quantities and/or repeats will be authorised

Name Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
SUNITINIB 12.5 mg capsule, 28	1	5	Sutent	PF
SUNITINIB 25 mg capsule, 28	1	5	Sutent	PF
SUNITINIB 50 mg capsule, 28	1	5	Sutent	PF

Condition:	Metastatic or unresectable, well-differentiated malignant pancreatic neuroendocrine tumour (pNET)
Treatment phase:	Continuing treatment
Restriction:	Authority required
Clinical criteria:	Patient must have metastatic or unresectable, well-differentiated malignant pancreatic neuroendocrine tumour (pancreatic NET) AND Patient must have previously been issued with an authority prescription for sunitinib

Prescriber Instructions	Patient must not have progressive disease Treatment is for monotherapy only

10. 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.

11. Sponsor's Comment

The sponsor has no comment.