

**4.1 CRIZOTINIB  
200 mg capsule, 60 and 250 mg capsule, 60;  
Xalkori®; Pfizer Australia Pty Ltd.**

**1 Purpose of Application**

1.1 The minor resubmission sought PBS listing of crizotinib at a proposed dispensed price; the price proposed at the March 2014 PBAC consideration.

**2 Requested listing**

Name, Restriction, Manner of administration and form	Max. Qty	No.of Rpts	Proprietary Name and Manufacturer	
CRIZOTINIB			Xalkori	Pfizer
crizotinib 200 mg capsule	60	1		
crizotinib 250 mg capsule	60	1		
<b>Category / Program</b>	GENERAL – General Schedule (Code GE)			
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives			
<b>Episodicity:</b>				
<b>Severity:</b>	Locally advanced or metastatic			
<b>Condition:</b>	non-small cell lung cancer			
<b>PBS Indication:</b>				
<b>Treatment phase:</b>				
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input checked="" type="checkbox"/> Authority Required - Emergency <input checked="" type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined			
<b>Clinical criteria:</b>	Patient must have a WHO performance status of 2 or less.  AND  Patient must have disease progression following treatment with a least 1 platinum-based chemotherapy agent.  AND  Patient must have evidence of an anaplastic lymphoma kinase (ALK) gene rearrangement in tumour material.  AND  The treatment must be as monotherapy.			

- 2.1 The requested basis for listing is cost-effectiveness compared with pemetrexed.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

### **3 Background**

- 3.1 Crizotinib was TGA-registered on 27 September 2013 for the treatment of patients with anaplastic lymphoma kinase (*ALK*)-positive advanced non-small cell lung cancer (NSCLC). The PBAC has considered crizotinib twice previously.
- 3.2 The first submission of crizotinib was presented to the November 2013 PBAC meeting for consideration. The PBAC deferred its consideration of crizotinib, seeking input on a respecified economic evaluation and MSAC advice on a number of aspects of the co-dependent testing of *ALK* gene rearrangements.
- 3.3 A minor resubmission was presented for consideration at the March 2014 PBAC meeting offering a price reduction of crizotinib by [REDACTED]% from \$[REDACTED] to an effective price of \$[REDACTED]. The economic evaluation in the resubmission, which was not independently evaluated or considered by the Economics Sub-Committee (ESC): (a) retained the incremental median OS per treated patient as 12.0 months; (b) did not include broader mutation testing costs; (c) included a nominal annual cost of \$50 for ophthalmological testing costs included; and (d) reduced the crizotinib price to estimate a revised ICER as \$45,000/QALY - \$75,000/QALY (reduced from the previous ICER of \$45,000/QALY - \$75,000/QALY).
- 3.4 At the March 2014 meeting, the PBAC reaffirmed that: (a) the quality and oversight of *ALK* testing are fundamental prerequisites for the use of crizotinib; (b) the claim of incremental overall survival gain of 12.0 months for crizotinib over pemetrexed was implausible; (c) crizotinib is likely to be used after disease progression and a stopping rule would not be practical; and (d) at least a 30% price reduction would be needed to achieve an acceptable ICER and a greater price reduction should be required because the less confidently estimated overall survival of pemetrexed should be increased consistent with the evidence of an improved treatment effect in patients with *ALK*-positive NSCLC. The PBAC requested that any further submission for crizotinib should be a major submission incorporating the advice from MSAC, subject to independent evaluation and consideration by ESC.
- 3.5 The March 2014 PBAC meeting deferred its consideration of crizotinib to ascertain the applicant's input on the Committee's proposed approach to achieve acceptable cost-effectiveness and until such time as MSAC decides to support the corresponding MBS listing of *ALK in situ* hybridisation (ISH) testing (and any other associated molecular testing advised by MSAC) for patients with NSCLC.
- 3.6 The PBAC noted that the 3 October 2014 extraordinary MSAC meeting had considered the co-dependent application for a new MBS item for anaplastic lymphoma kinase (*ALK*) gene rearrangement testing to help select eligible patients with NSCLC for crizotinib treatment. MSAC again deferred the application for the requested MBS item until such time as the PBAC makes a decision regarding the corresponding PBS listing of crizotinib. MSAC advised that, if the PBAC subsequently decides to recommend to the Minister that crizotinib be listed on the

PBS for the treatment of advanced NSCLC, then MSAC would support an expedited process of reconsideration. This process would be undertaken to ensure MSAC support for public funding of ALK testing is aligned with the circumstances recommended by PBAC. MSAC indicated its intended support for the corresponding MBS listing by foreshadowing its expected advice, and by providing advice on matters that PBAC had referred to it.

#### **4 Clinical place for the proposed therapy**

- 4.1 Crizotinib was proposed for PBS listing as second-line therapy (following disease progression after treatment with a least one platinum-based chemotherapy agent) in ALK-positive patients with locally advanced or metastatic NSCLC.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

#### **5 Comparator**

- 5.1 The resubmission accepted the November 2013 PBAC preference for pemetrexed as the sole comparator.

#### **6 Consideration of the evidence**

##### **Sponsor hearing**

- 6.1 There was no hearing for this item as it was a minor submission.

##### **Consumer comments**

- 6.2 The PBAC noted and welcomed the input from individuals (261), via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with crizotinib including the ability to return to work, fewer side effects as an alternative to IV chemotherapy.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

##### **Clinical trials**

- 6.3 The randomised clinical trial forming the basis of the comparison between crizotinib and pemetrexed was unchanged from the previous submission. No new data were presented in the resubmission.

##### **Comparative effectiveness**

- 6.4 The PBAC noted that no new data for comparative effectiveness were presented in the resubmission. As previously, the PBAC considered that crizotinib is more effective than pemetrexed with an accepted difference in median progression-free survival gain of 3.5 months. The PBAC reaffirmed its view that, although an

incremental overall survival gain was likely, the claim of an incremental overall survival gain of 12.0 months for crizotinib over pemetrexed was overestimated.

- 6.5 The PBAC noted that the resubmission reiterated the applicant's arguments for why overall survival estimates for pemetrexed from other sources should be compared against the overall survival results for crizotinib extracted from its randomised trial. Studies were also summarised to dispute PBAC's concern that being *ALK*-positive may predict an improved treatment effect following pemetrexed. These were further refined in the pre-PBAC response. After considering this information, the PBAC concluded that no compelling conclusions could be drawn about the extent of incremental overall survival gain for crizotinib over pemetrexed in *ALK*-positive NSCLC. The reiterated arguments and studies were not considered sufficient to change this situation.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

### **Comparative harms**

- 6.6 The PBAC noted that no new data for comparative harms were presented in the resubmission.

### **Clinical claim**

- 6.7 As previously, the PBAC accepted the claims for crizotinib having superior effectiveness and non-inferior safety compared to pemetrexed, but considered that the approach taken in the original submission and repeated in the resubmissions overestimated the incremental overall survival gain.

### **Economic analysis**

- 6.8 The PBAC noted the resubmission argued that the economic analysis presented in the March 2014 submission was reasonable and rejected the PBAC's suggestion in March 2014 that the price of crizotinib should fall by 30%. The PBAC noted there were no new data presented in the resubmission to support the price proposed by the sponsor.
- 6.9 As previously, The PBAC considered the incremental overall survival gain of 12.0 months for crizotinib over pemetrexed, which was modelled in the economic analysis was implausible.
- 6.10 Attempts to verify the respecified ICERs presented in the March 2014 submission are shown below.

**Attempt to verify the respecified base case ICER to March 2014 PBAC meeting, stepped**

Step	Prob. of death per cycle mult. factor (pem arm)	Prob. of death per cycle mult. factor (criz arm)	Crizotinib price reduction	Modelled			ICER
				Crizotinib median OS (months)	Pem median OS (months)	Incremental OS benefit	
November 2013 base case	1	1	0%				
Nominal \$50 cost for AEs	1	1	0%				
Reduced price of criz (\$ )	1	1					
Pem costs only	1	1					
Decrease criz median OS to 20.3*	1	1.11					

\* To generate the ICER estimated for the March 2014 meeting required a larger estimate for the crizotinib median OS and thus for the incremental OS benefit.

Abbreviations: criz=crizotinib; mult=multiplication; OS=overall survival; pem=pemetrexed; prob=probability

**Attempts to verify the ICER sensitivity analyses after reducing the estimated incremental overall survival benefit**

Analysis	Prob. of death per cycle mult. factor (pem arm)	Prob. of death per cycle mult. factor (criz arm)	Crizotinib price reduction	Modelled			ICER
				Criz median OS (months) (un-adjusted)	Pem median OS (months) (un-adjusted)	Incremental OS benefit (unadjusted)	
March 2014 base case	1	1.11					
reduce criz OS (3.1 month diff)	1	1.764					
reduce criz OS (3.5 month diff)	1	1.734					
increase pem OS (3.1 month diff)	0.331	1.11					
increase pem OS (3.5 month diff)	0.341	1.11					
<b>Estimates corrected for mis-specification of the incremental OS benefit</b>							
reduce criz OS (3.1 month diff)	1	2.37					
reduce criz OS (3.5 month diff)	1	2.27					
increase pem OS (3.1 month diff)	0.348	1.11					
increase pem OS (3.5 month diff)	0.359	1.11					

Abbreviations: criz=crizotinib; mult=multiplication; OS=overall survival; pem=pemetrexed; prob=probability

- 6.11 As shown in the table above, the ICER is between \$105,000/QALY - \$200,000/QALY based on PBAC's previously accepted incremental OS gain of 3.1 – 3.5 months.
- 6.12 The PBAC agreed that the MSAC advice did not have important consequences for the estimated ICER (see table below). The main source of uncertainty was the extent of incremental OS gain. The PBAC expected that reducing the sensitivity of ALK testing to 69% would have a larger effect on the ICER, but did not consider that this additional consideration should change the overall outcome of its consideration because, although the true performance of ALK testing in Australia is not yet known, it is likely to fall somewhere between the estimate of 69% and the performance of ALK testing in the randomised trial.

**Assessment of consequences of four aspects of MSAC advice on base case ICER to March 2014 PBAC meeting, stepped**

Base case to March 2014 meeting		
1. Prevalence (3%)		
2. PEI fee on IHC test		
3. Sample referral fee on FISH		

4. Re-testing rate of FISH (8.5%)

6.13 Noting the applicant's refusal to consider a 30% price reduction as suggested in March 2014, the PBAC considered that a Managed Entry Scheme (MES), modified from that proposed in the resubmission to the March 2014 meeting, would be the next best alternative. An MES provided a mechanism to address the uncertainty related to the magnitude of clinical benefit while providing early access to those patients for whom there is a high clinical need. The PBAC considered that any such MES for crizotinib should be guided by the following conditions.

- The initial entry price for the MES would be as requested, relying on the base case ICER presented to the March 2014 meeting (with its ICER of \$45,000/QALY - \$75,000/QALY, noting the unresolved concerns that this ICER favours crizotinib). The MES framework would include a mechanism for payment of a rebate with interest to the Commonwealth should crizotinib fail to deliver on its claimed benefits. On submission of new information as outlined below, there would be no option for an increase in price of crizotinib, as the higher price would already have been paid since entry onto the PBS.
- The possible outcomes following consideration of the new information in the MES would be that either:
  - the price of crizotinib would reduce; or
  - the price of crizotinib would be maintained.
- The Commonwealth would bear the upfront risk associated with the uncertain clinical benefit. Accordingly, should this modelled extent of benefit not be realised with reference to the information outlined below, then the sponsor would rebate the Commonwealth to the effect of:
  - the ensuing price reduction required to meet the same ICER with reduced clinical benefits, multiplied by;
  - the number of PBS-dispensed prescriptions of crizotinib between the date of listing and the date of implementation of the price reduction, and after applying;
  - an interest rate deemed appropriate by the Commonwealth.
- The new information requested is the proportion of the first 50 consecutive patients to start therapy with crizotinib after any PBS listing begins (i.e. excluding patients who are continuing therapy with crizotinib already started before any PBS listing begins) who are alive 365 days after starting therapy with crizotinib. For comparison, the estimate of this proportion modelled from the randomised trial is ██████% (see figure and table below, based on the model used to verify the base case ICER to the March 2014 meeting). This is intended to address the lesser uncertainty that overall survival following crizotinib is overestimated by the trial, for example, because patients with brain metastases were excluded.
- This result would be provided as soon as possible after the 50<sup>th</sup> consecutive patient has been followed for 365 days. This sample size was proposed on the expectation that, with the estimated number of incident patients, it would take approximately two years to generate the data.
- To address the greater uncertainty of the overall survival following pemetrexed being underestimated by the model, there would be a 1% increase in the modelled proportion of pemetrexed patients who are alive at day 365 for every 1% that the observed PBS result is below the estimate of 68.9%. This uncertainty is primarily due to the cross-over to crizotinib in the pemetrexed arm of the trial following a progression event. The intended effect of this adjustment on the

model would be to shift the modelled overall survival arm for crizotinib towards the x-axis, complemented by the same proportional shift in the modelled overall survival arm for pemetrexed away from the x-axis and towards the modelled overall survival arm for crizotinib. This approach would be required on the grounds that it has already been established that it is no longer possible to observe the overall survival following pemetrexed in crizotinib-eligible patients. The survival curve from Hanna et al, 2004 relied upon for pemetrexed was generated more than ten years ago (between 2001 and 2003) and better survival is expected today because of improved pathological and molecular classification of non-small cell lung cancer.

- However, as the PBAC has accepted from the data already available that there is likely to be a greater overall survival with crizotinib than with pemetrexed, this approach of adjusting up the modelled proportion of pemetrexed patients alive at day 365 to match any observed reduction in the observed proportion of crizotinib patients alive at day 365 would apply until these estimates are equal (at 48% alive at day 365 in each arm).
- Given the small sample sizes contributing to the model, there would be no adjustment through the use of a confidence interval around any estimate.
- Given the importance of obtaining reliable data from the first 50 consecutive PBS-subsidised patients previously untreated with crizotinib, PBS listing would not proceed until the sponsor can show to the satisfaction of the Department that it can collect the requested data.
- If the sponsor cannot deliver the data within the estimated 2-year timeframe, the penalty should be a price reduction for crizotinib (with associated rebate and interest) on assumption of an incremental overall survival of 3.1 months.
- These arrangements would apply irrespective of whether the sponsor subsequently seeks first-line listing for crizotinib. However any submission for crizotinib with reference to treatment of other non-*ALK*-positive patient groups (e.g. those with *ROS* mutations) should proceed on its own merits.
- The nature of these arrangements (without details of the consequences for pricing) would be made public, particularly to inform sponsors of second-generation *ALK* inhibitors. If the PBAC recommends listing of a second generation *ALK* inhibitor before the requested data become available, then there would be a price reduction for crizotinib (with associated rebate and interest) on assumption of an incremental overall survival of 3.1 months. If these sponsors can subsequently demonstrate clinical superiority over crizotinib, these arrangements for crizotinib would not hinder access to the relevant pricing information to fully inform the consequential ICER for the second-generation *ALK* inhibitor.
- The table below, which was modified from Table 7 in the resubmission to the March 2014 PBAC meeting, demonstrates the price reduction consequences back-calculated from the model for each additional 1% that the observed proportion of crizotinib patients is below the ██████% estimated for the model from the trial.



Observed and modelled overall survival related to the base case ICER submitted to the March 2014 PBAC meeting

**[FIGURE REDACTED]**

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

- 6.14 The PBAC noted that these modifications to the proposal in the resubmission to the March 2014 meeting also represent modifications to the MES framework which was prepared in the context of the 2010-2014 Memorandum of Understanding between the Commonwealth and Medicines Australia.
- Although the PBAC is expected under this existing framework to recommend coverage at a price justified by the existing evidence, and the PBAC view is that the existing evidence would require a reduced price, this expectation is essentially fulfilled with these modifications by putting in place a rebate plus interest.
  - Although submission of more conclusive evidence of cost-effectiveness is expected under this existing framework to support listing of the medicine at a higher price, there should be no option for a higher price with these modifications because a higher entry price is being offered for initial listing.
  - Consistent with this existing framework, the MES arrangements for crizotinib would need to be formalised in any Deed of Agreement established for the purposes of PBS listing.
  - Consistent with this existing framework, any other unexpected but relevant developments emerging before the new information is provided, such as unexpected safety signals, will be considered according to usual PBAC processes.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

### **Estimated PBS usage & financial implications**

- 6.15 The PBAC noted the resubmission did not present new estimated PBS usage and financial implications. At March 2014 meeting, the PBAC considered the financial estimates were less than \$10 million per year.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

## **7 PBAC Outcome**

- 7.1 The PBAC recommended an Authority required listing of crizotinib for the treatment of patients with *ALK*-positive advanced non-small cell lung cancer
- 7.2 The PBAC recalled that, in March 2014, it had deferred its consideration of crizotinib to ascertain the applicant's input on the Committee's proposed approach to achieve acceptable cost-effectiveness and until such time as MSAC supports the corresponding MBS listing of *ALK* ISH testing for patients with NSCLC. The PBAC noted that MSAC now supports *ALK* ISH testing, but the applicant has not agreed with the proposed approach to achieve acceptable cost-effectiveness.

- 7.3 Given the small number of patients expected to be eligible for crizotinib and the clinical need for a more effective alternative than pemetrexed, and noting the difficult consequences for patients following the sponsor's decision to stop its compassionate access program, the recommendation is intended to enable early access whilst obtaining more data.
- 7.4 In making its recommendation, the PBAC noted that, as previously, it accepted that an incremental overall survival gain was likely, however the extent of incremental overall survival gain of 12.0 months for crizotinib over pemetrexed is overestimated. The PBAC considered the more likely incremental overall survival gain is between 3.1 – 3.5 months.
- 7.5 The PBAC noted that the resubmission reiterated the applicant's arguments and summary of studies to dispute PBAC's March 2014 conclusions regarding this overall incremental survival gain. After considering the resubmission, the PBAC concluded that, given both the limitations of the randomised trial (small sample size, immature follow-up and post-progression cross-over to crizotinib in the pemetrexed arm) and also the usual concerns with attempting comparative treatment effect inferences by comparing across results for different groups of patients, no completely compelling conclusions could be drawn about the extent of incremental overall survival gain for crizotinib over pemetrexed in *ALK*-positive NSCLC. The reiterated arguments and studies were not considered sufficient to change this situation.
- 7.6 The PBAC considered that the structure of the model was reasonable, and the version as verified above was accepted, noting that further variations reflecting MSAC-advised revised inputs would not be reopened in any reconsideration of crizotinib given that the bias is in favour of crizotinib.
- 7.7 The PBAC noted that there is likely to be a reluctance to use first-line platinum-based chemotherapy in some patients before starting crizotinib and that omitting the platinum requirement has little consequence for the financial implications to the PBS. On this basis, the PBAC recommended that the reference to platinum-based chemotherapy in the requested restriction should be omitted. The PBAC also noted that this part of its recommendations was supported by the input from consumers, and the recently presented results of PROFILE 1014 at the 2014 ASCO annual meeting (reference 129938-144; randomised trial of first-line crizotinib and pemetrexed-platinum chemotherapy prolonging median progression-free survival by 3.9 months; HR: 0.454; 95% CI 0.346 to 0.596) being similar to those of the key second-line trial.
- 7.8 The PBAC considered a Grandfather restriction would be appropriate, and may also help to distinguish between PBS-subsidised patients who have or have not previously been treated with crizotinib.
- 7.9 A Written Authority is required for eligible crizotinib patients.
- 7.10 Crizotinib should not be treated as interchangeable with any other drug.
- 7.11 The PBAC advised that crizotinib is not suitable for prescribing by nurse practitioners.
- 7.12 The PBAC recommended that the Safety Net 20 Day Rule should not apply.

7.13 The PBAC noted that this resubmission is not eligible for an Independent Review.

**Outcome:**

Recommended

**8 Recommended listing**

8.1 Add new item for initial treatment:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
CRIZOTINIB			Xalkori	Pfizer
crizotinib 200 mg capsule	60	1		
crizotinib 250 mg capsule	60	1		

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	
<b>Severity:</b>	Stage IIIB (locally advanced) or Stage IV (metastatic)
<b>Condition:</b>	non-small cell lung cancer (NSCLC)
<b>PBS Indication:</b>	
<b>Treatment phase:</b>	Initial treatment
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	The treatment must be as monotherapy,  AND  The condition must be non-squamous type non-small cell lung cancer (NSCLC) or not otherwise specified type NSCLC,  AND  Patient must have a WHO performance status of 2 or less.
<b>Population criteria</b>	Patient must have evidence of an anaplastic lymphoma kinase (ALK) gene rearrangement in tumour material, defined as $\geq 15\%$ positive cells by fluorescence in situ hybridisation (FISH) testing.

8.2 Add new item for continuing treatment:

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Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
CRIZOTINIB			Xalkori	Pfizer
crizotinib 200 mg capsule	60	1		
crizotinib 250 mg capsule	60	1		

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	
<b>Severity:</b>	Stage IIIB (locally advanced) or Stage IV (metastatic)
<b>Condition:</b>	non-small cell lung cancer (NSCLC)
<b>PBS Indication:</b>	
<b>Treatment phase:</b>	Continuing treatment
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	The treatment must be as monotherapy,  AND  Patient must have previously been issued with an authority prescription for this drug,  AND  Patient must not have progressive disease.

8.3 Add new item for grandfathered patients:

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
CRIZOTINIB			Xalkori	Pfizer
crizotinib 200 mg capsule	60	1		
crizotinib 250 mg capsule	60	1		

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Episodicity:</b>	

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<b>Severity:</b>	Stage IIIB (locally advanced) or Stage IV (metastatic)
<b>Condition:</b>	non-small cell lung cancer (NSCLC)
<b>PBS Indication:</b>	
<b>Treatment phase:</b>	Grandfather
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required - Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	<p>Patient must have received this drug before the date of listing (to be determined),</p> <p>AND</p> <p>The treatment must be as monotherapy,</p> <p>AND</p> <p>The condition must be non-squamous type non-small cell lung cancer (NSCLC) or not otherwise specified type NSCLC,</p> <p>AND</p> <p>Patient must have a WHO performance status of 2 or less,</p> <p>AND</p> <p>Patient must not have progressive disease.</p>
<b>Population criteria:</b>	Patient must have evidence of an anaplastic lymphoma kinase (ALK) gene rearrangement in tumour material.

## 9 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.

## 10 Sponsor's Comment

Pfizer welcomes the decision made by the Pharmaceutical Benefits Advisory Committee (PBAC) to recommend the listing of XALKORI® (crizotinib) on the Pharmaceutical Benefits Scheme (PBS) for patients with anaplastic lymphoma kinase positive (ALK positive) advanced non-small cell lung cancer. This is a rare type of lung cancer that typically affects younger people who are non-smokers.

Pfizer would like to provide the following updates to the information provided in this Public Summary Document to reflect agreements reached in meetings with the Department of Health that occurred after the PBAC recommendation:

- A timeframe for the delivery of the results of the managed entry scheme is agreed to be 14-months after the 50th study eligible patient is initiated on crizotinib.
- A new deed of agreement will be negotiated in the event that a second generation ALK inhibitor is listed on the PBS, before the results of the managed entry scheme are delivered to the Department of Health.

Pfizer is working to reach an agreement with the PBAC and the Department of Health to ensure XALKORI is available on the PBS as soon as possible.