Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	National Lung Cancer Forum for Nurses
Location	Wales
Conflict	No
Notes	I have in the past received an honourarium for some work I did with other professionals about the management of Tarceva
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The accessibility of an effective, well tolerated oral maintenance therapy for NSCLC patients within the homecare setting should be given due consideration. Pemetrexed has recently received regulatory and NICE approval as a maintenance agent after first-line chemotherapy, but only in patients with non-squamous histology who have not previously received pemetrexed. Erlotinib is the only maintenance agent with a license which includes patients with squamous histology and for patients who have already received pemetrexed as part of first-line chemotherapy. After first line chemotherapy, most patients currently experience a break in their active treatment until their disease returns. Â This is when second line treatment is considered. For many patients this is a less than ideal approach, as only a minority of UK patients (around one-third) actually receive second-line treatment at relapse. Â This is usually because disease progression is identified too late, performance status has already declined and further treatment would not be appropriate. Â Therefore the ability to administer erlotinib in the first line maintenance setting should be seen as an opportunity to prolong survival for advanced NSCLC patients by ensuring that patients who can benefit from therapy receive it.
Section 2 (The technology)	Erlotinib is also well suited to the maintenance setting as it has been shown to delay disease and therefore symptom progression, is orally administered (does not require hospital resources for I.V administration) and is generally well tolerated. Because of its toxicity profile – it is devoid of the myelosuppresion and other non-specific toxicities of conventional cytotoxic drugs and its main side-effects are mild-moderate rash and diarrhoea. Â These can usually be managed by simple symptomatic interventions or by dose modification. As an oral agent erlotinib offers benefits to patients who do not wish to attend the hospital regularly for the intravenous (IV) administration required with pemetrexed and to hospital departments already struggling to deliver the volumes of IV chemotherapy treatments.
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	Unless erlotinib receives NICE guidance for maintenance therapy, Â patients who received pemetrexed as part of their first line treatment (rapidly becoming the majority of non squamous patients) or who have squamous histology will not have the opportunity for life extending maintenance therapy.
Section 5 (Implementation)	
Section 6 (Related NICE guidance)	
Section 7 (Proposed date of review of guidance)	

Date	15/12/2010

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	No
Notes	Honoraria for advisory boards,speaker fees
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The preliminary recommendation is incorrect given the data and the discrepency between the JMEN pemetrexed and SATURN erlotinib assessments. The confusion and difference of opinion between the Â local ERG Â and the Licensing Authority re the robustness of the SATURN data and subsequent statistical analysis needs resolution. The ERG and other comments reveal confusion and unsupported opinions which have produced a negative effect.Some will be detailed. There seems to be an inherent prejudice in this ACD against erlotinib
Section 2 (The technology)	The erlotinib side effect profile detailed above is remarkably slight given the toxicity of cytotoxic drugs. An oral convenient drug without cytotoxic side effects is a very welcome option after 1st line chemotherapy. It should be noted that in the maintenance ,2nd and 3rd line settings there is no evidence that the Overall Survival is depenedent on EGFR mutation status (which captures the sensitivity of SE Asian and never/light smoker population) commnented in section 3 and 4.Therefore in this setting the UK population will be similar to the global study population.
Section 3 (The manufacturer's submission)	It is intriguing as to why the methodology and estimations of the local ERG is always chosen in Â preliminary ACDs over that of other submissions e.g manufacturers ,EMEA,etc. Where is the evidence to support this systematic choice? The ERG view that the results are not generalised within the UK is nonsense.SATURN is not a 1st line trial but a maintenance trial and by definition the patients will be fitter.Furthermore there is no evidence that other than EGFR mutation status which captures smoking history/SE asian ethnicity etc that global patients are any different from the UK patients in terms of treatment survival in advanced NSCLC.Paclitaxel/vinorelbine has never been compared against pemetrexed. The comment on post progression treatment(PPT) as not having marketing authorisation is common,even in JMEN pemetrexed trial which NICE approved.From randomised trials there is no evidence that one cytotoxic is superior overall for survial nor was pememetrexed vs. erlotinib,therefore the OS gain is not due to PPT.The stable disease subgroup,was determined as robust by the licensing authority ,perhaps the ERG should reconsider its view.
Section 4 (Consideration of the evidence)	Currently patients wait for progression and then some receive 2nd line. Maintenance assists a group of patients who would drop out and never receive any 2nd line.Thus fewer patients will benefit form 2nd line cf.to maintenance The S124 pemetrexed trial result may show benefit after first line pemetrexed. Re relatively small numbers in subgroups these are LESS in the gefitinib 1st line trial wrt EGFR mutation status.The proportion of patients from South East Asia and the never smokers are LESS than the number of other recent trials, particularly the JMEN trial.Thus SATURN has fewer favourable patients.The 30% of stable disease patients with PS0 is a very realistic value in a maintenance(not 1st) trial.Erlotinib overall survival is not dependant on mutation status either in the maintenance setting or 2nd 3rd line.Mutation testing in UK is not comprehensive ,it is inconceivable that all mutation positive patients would be given ist line gefitinib, these remaining patients could well benefit form erlotinib.
Section 5	

(Implementation)	
Section 6 (Related NICE guidance)	
Section 7 (Proposed date of review of guidance)	
Date	16/12/2010