csas
Commissioning Support
Appraisals Service

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21st February 2012

National Institute for Health and Clinical Excellence

Dear Kate,

RE: Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer

On behalf of Commissioning Support, Appraisals Service (CSAS), Solutions for Public Health, I would like to submit our comments on the appraisal consultation document for erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer. We are in agreement with the recommendations in the ACD not to recommend erlotinib for this indication as on the basis of the evidence considered it is unlikely that this treatment can be considered clinically and cost effective in real life clinical practice.

- **Doublet chemotherapy was not considered as an alternative first-line treatment.** Clinical trials have compared erlotinib with platinum doublet chemotherapy. The manufacturer submitted no evidence for the cost effectiveness of erlotinib compared to doublet chemotherapy. The Appraisal Committee, based on the input of clinical specialists, has agreed that platinum doublet chemotherapy is rarely used as first-line treatment for patients with EGFR-TK mutation positive NSCLC, and considered gefitinib only to be the appropriate comparator.
- **No studies directly compare erlotinib with gefitinib.** Gefitinib is current standard first-line treatment for this patient group and no direct comparison between these treatments is available. Based on the input of clinical specialists that these are similar treatments with similar efficacy, the Appraisal Committee concluded that erlotinib and gefitinib should be assumed to have equal efficacy in terms of median progression free survival, about 9.7 months for erlotinib compared to 5.2 months for platinum doublet chemotherapy.
- **There is insufficient evidence to assess the cost-effectiveness of erlotinib compared to gefitinib.** The Appraisal Committee did not have sufficient information to assess the most plausible ICER for erlotinib compared to gefitinib. They disagree with key assumptions made in the manufacturer's model, and have requested an additional analysis that assumes equal progression free survival and utility of the progression free state for the main comparison (erlotinib versus gefitinib).
- **Adverse events associated with erlotinib treatment were moderate.** The severity of adverse events was similar between erlotinib and gefitinib, however, each had a different profile of adverse events. Clinical specialists have indicated that there may be an advantage to having a choice between treatments to improve the management of patients experiencing more serious side effects.

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- **The manufacturer may have underestimated the eligible population.** The manufacturer's estimate of 0.76 per 100,000 population eligible for treatment with first-line erlotinib reflects internal assumptions regarding the proportion of NSCLC patients who will undergo EGFR testing prior to initiating a first-line treatment regimen. The manufacturer estimates that only 50% of patients will receive such testing or have a specimen sufficient for testing. The committee, however, reports that EGFR testing is now standard practice in this patient group.
- **The cost of erlotinib treatment is subject to a confidential patient access scheme.** This is based on the manufacturer's eligibility algorithm. The cost of treating a single patient for 10 months is expected to be in excess of £10,000.
- **The cost of erlotinib depends on the dose.** There are three available doses of erlotinib. The dose is reduced as appropriate by clinicians. Cost estimates reflect the recommended maximum dose of 150mg. It is not clear how many patients would be eligible for a reduced dose.
- **Erlotinib is covered by a simple discount on the Patient Access Scheme (PAS).** Gefitinib is also covered by a scheme; all patients who receive at least 3 months of treatment incur a flat charge of £12,200. The erlotinib PAS agreement is likely to be more straightforward to administer.

If you require any further information please contact me directly: Phone: [redacted], email [redacted].

Yours sincerely

[redacted]

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