Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed following prior chemotherapy (review of NICE technology appraisals 162 and 175): *Exploring the sensitivity of the incidence of febrile neutropenia to the estimated incremental cost-effectiveness ratio (ICER)*

This document was prepared by the NICE technical team and verified by the Assessment Group.

Background

The Assessment Group included the incidence of febrile neutropenia for docetaxel from the TAILOR trial (3.85%) in its economic model comparing erlotinib with docetaxel in the **EGFR-TK mutation-negative population**. The manufacturer of erlotinib suggested that incidence of febrile neutropenia for docetaxel in the TAILOR trial is low compared with other trials, for example, INTEREST (≈10%) and JMEI (≈13%), and may be because of the TAILOR trial including a weekly docetaxel regimen (not used in English clinical practice). The Assessment Group considered that the lower rate of febrile neutropenia in the TAILOR trial was because of increased clinical awareness of the adverse reactions associated with docetaxel (compared with past clinical practice), and that adverse reactions are better managed and more frequently avoided. During the consultation of the Assessment Report, the manufacturer commented that it considered a pooled estimate of febrile neutropenia (and for all other adverse reactions) to be the most plausible (compared with an estimate from a single trial).

Incidence of febrile neutropenia

During NICE technology appraisal 162 (erlotinib), NICE commissioned the Decision Support Unit (DSU) to consider evidence on several parameters in relation to docetaxel. The DSU carried out a systematic review and meta-analysis of the probability of febrile neutropenia associated with docetaxel. Thirteen studies were identified and a random effects meta-analysis was conducted. The pooled, random effect meta-analysis estimate for the proportion of patients who experience one or more episodes of febrile neutropenia on docetaxel was 5.95% (95% CI 4.22 to 8.31). The mean number of febrile neutropenia episodes were estimated to be 1.4 per patient.

Cost per episode

The Assessment Group noted that the Decision Support Unit's cost of febrile neutropenia has been updated for current NHS Reference Costs 'PA45Z Febrile neutropenia with malignancy' (from £2,286 per episode to £5,048 per episode).

Table 1: Incremental cost-effectiveness results when varying the incidence of febrile neutropenia in the Assessment Group's economic model for the comparison of erlotinib and docetaxel in the EGFR-TK mutation-negative population (cost per episode of febrile neutropenia = £5,048)

Rate of febrile neutropenia (docetaxel arm)	Docetaxel (DOC)		Erlotinib (ERL)		Incremental costs (£)	Incremental QALYs	ICER (DOC compared with ERL)
	Total costs (£)	Total QALYs	Total costs (£)	Total QALYs			
1.07% (AG lower limit)[1]	13,861	0.5949	14,049	0.4863	-188	0.1086	Dominant
3.85% (AG base case)[1]	15,702	0.5939	14,049	0.4863	1,653	0.1076	£15,359
5.95% (NICE DSU)[2]	17,096	0.5931	14,049	0.4863	3,047	0.1068	£28,520
8.28% (AG upper limit)[1]	18,637	0.5922	14,049	0.4863	4,588	0.1060	£43,297

Table 2: Incremental cost-effectiveness results when varying the incidence of febrile neutropenia in the Assessment Group's economic model for the comparison of erlotinib and docetaxel in the EGFR-TK mutation-negative population (cost per episode of febrile neutropenia = £2,286)

Rate of febrile neutropenia (docetaxel arm)	Docetaxel (DOC)		Erlotinib (ERL)		Incremental costs (£)	Incremental QALYs	ICER (DOC compared with ERL)
	Total costs (£)	Total QALYs	Total costs (£)	Total QALYs			
1.07% (AG lower limit)[1]	13,474	0.5949	14,049	0.4863	-575	0.1086	Dominant
3.85% (AG base case)[1]	14,307	0.5939	14,049	0.4863	258	0.1076	£2,400
5.95% (NICE DSU)[2]	14,939	0.5931	14,049	0.4863	890	0.1068	£8,328
8.28% (AG upper limit)[1]	15,637	0.5922	14,049	0.4863	1,588	0.1060	£14,983

References:

1. Greenhalgh J, Bagust A, Boland A et al. (2013). Erlotinib and gefitinib for treating non-small cell lung cancer that has progressed following prior chemotherapy (review of NICE technology appraisals 162 and 175). The Liverpool Reviews and Implementation Group, University of Liverpool.
2. Wailoo A, Sutton A, Morgan A (2009). The risk of febrile neutropenia in patients with non-small-cell lung cancer treated with docetaxel: a systematic review and meta-analysis. *British Journal of Cancer* **100**: 436-441.