Response to Consultee and NICE comments

Comment	Response
1. Acquisition costs of ESAs	Thank you.
2. Biosimilars	Amendments made to clarify which products are biosimilars and definition of this within Section 2 of the report, see p44.
3. Assessment of clinical effectiveness	Thank you.
4. Assessment of cost-effectiveness	Thank you.
5. Factual inaccuracies	
Wording re the dosing (i) Page 43, Table 3, Section 2.4.2.1. Dose increase for darbepoetin alfa: “4 wks Hb increase <1 g/dl dose is doubled 4.5 µg/kg SC QW” The label for darbepoetin alfa does not specify dose increase due to lack of response.1 We recommend the removal of this statement. (ii) Page 72, Section 4.2.2.2. For darbepoetin alfa the licensed weight-based, starting dose is 2.25 µg/kg in a once-weekly dose or 6.75 µg/kg once every three weeks. The maximum dose is 4.5 µg/kg per week. For darbepoetin alfa, the licensed weight-based starting dose is 2.25 µg/kg in a once-weekly dose or 6.75 µg/kg once every three weeks. 1 We recommend the removal of the statement regarding maximum dose.	(1) The wording re the dosing of darbepoetin alfa has been revised in accordance with the SmPC. i. Page 43, Table 3, Section 2.4.2.1 – re dose increase I have changed this text to not specified ii. Page 72, Section 4.2.2.2 – the statement regarding the maximum dose has been removed.
Pages 73, 745; Tables 11, 12, 31, 62, 63, 65, 66, 67; Figures 30, 31; Appendices D, G Pages 71, 121, 179 ; Tables 10, 13, 32, 33, 37; Figures 2, 3, 4, 8, 13, 18, 20, 79, 89, 90, 98, 109, 111; Appendix C Reference: Del Mastro L, Venturini M, Lionetto R, Garrone O, Melioli G, Pasquetti W, et al. Randomized phase III trial evaluating the role of erythropoietin in the prevention of chemotherapy-induced anaemia. Journal of Clinical Oncology 1997;15(7):2715–21 is referred to as ‘’Del	(2) The Del Mastro reference is indeed a single reference as pointed out; we have amended the report to ensure all citations refer to the correct publication year. [[Del Mastro, L., M. Venturini, R. Lionetto, O. Garrone, G. Melioli, W. Pasquetti, M. R. Sertoli, G. Bertelli, G. Canavese, M. Costantini and R. Rosso (1997). "Randomized phase III trial evaluating the role of erythropoietin in the prevention of chemotherapy-induced anemia." J Clin Oncol 15: 2715-2721.]] These

Mastro 1997" (first set of page references) and "Del Mastro 1999'' (second set of references) Since this is a single reference, we recommend that it is referenced as such in the AR.	changes are marked in track changes in the attached document. The Stata outputs (forest plots [random and fixed effects]; and meta-regression plots) have also been updated to reflect this change (not marked as track changes). The p values in the text for metaregression Pages affected: **TEXT:** p69, p71, p79, p86, p100, p118, p121, p167, p172, p174, p180, p452 **FIGURES: Main doc:** 2 (p86), 3 (p90), 4 (p91), 8 (p101), 11 (just p111), 13 (p118), 15 (just p127), 18 (p139), 20 (p142), 21 (just p145), 25 (just p199). **Appendix L**: 78 (p679), 79 (p680), 87 (p689), 88 (p690), 89 (p691), 90 (p692), 97 (p699), 98 (p700), 109 (p711), 111 (p713).
From NICE to PenTAG via email 28th Feb: The total number of patients in the summary of the OS results (last paragraph, page 120) is different from the number quoted in the table of malignancy outcomes (page 125).	Section 4.2.6.2.2 Overall survival has been double checked. OS data were available from 21 studies (reported in 23 publications) including 5,054 participants. The text in the report has been updated, p117. (FYI, for reasons reported in the second para p117 the number of studies included in the meta-analysis is 18). The number of participants reported in the Summary at the bottom of p120 (818/2,317 and 744/2,137) has been checked and this is correct. The total number of participants included in the meta-analysis should be 4,454 and Table 22 (p125). This has been updated in the report, p125.
From NICE to PenTAG via email 28th Feb: Could you please indicate the total number of trials that were included in the subgroup described as 'closer to licence', that is with baseline Hb levels of ≤ 11 g/dl. Table 28, page 154 of the report only shows the number of trials for each outcome of this subgroup, without indicating what the total number is.	Start dose and incl Hb ≤11 g/dl, 14 trials make up this group: Abels 1993, Aravantinos, 2003; Boogaerts, 2003; Dammacco, 2001, Hedenus, 2002; Hedenus, 2003; Kotasek, 2003; Kurz, 1997; Littlewood 2001; Osterborg 2002, 2005; Silvestris, 1995; Tjulandin, 2010; Tjulandin, 2011; Vansteenkiste, 2002 [[Please note that some of the studies may been split into subsets e.g. Abels 1993, cisplatin and

	non-cisplatin; Tjulandin, 2010, theta and beta. Also note that Osterborg is one trial reported in two publications 2002 (main trial results) and 2005 (follow-up data)]]. We have added a table into the report summarising this information see Table 28 (p152). This table provide a summary for overall and for the "close to license" subgroups; i.e. start dose only; start dose only and incl Hb ≤11 g/dl; and start dose only, incl Hb ≤11 g/dl, and target Hb level ≤13 g/dl.
From NICE to PenTAG via email 28th Feb: The text describing the PSA for the OS scenario 1 (first paragraph, page 353) is identical to the text describing the PSA for the OS scenario 2 (first paragraph, page 359).	Page 359, Section 7.2.6.2.2, first para: The text has been changed to: "The scatter plot shows that changing the baseline OS function has not had a significant impact on the considerable uncertainty regarding incremental QALYs (see also Table 97)."
5. Other	
Author list and acknowledgments	P1, alteration to title for one member of the team (Linda Long)
Table 10, p69 and Appendix G, p653 and p656;	Osterborg 2005, reports survival data; Osterborg 2002 reports other efficacy and safety outcomes