

Trastuzumab for the treatment of HER2 positive metastatic adenocarcinoma of the stomach or gastro-oesophageal junction.

ERG revisions based on manufacturer response to ACD (05/08/2010)

The manufacturer's response to the ACD included: (i) a revised economic analysis of the licensed population and (ii) results for a subgroup of IHC3+ patients.

The ERG was requested to provide validity checks on the resubmission provided by the manufacturer. Due to the limited time available to review the resubmission, the additional work undertaken by the ERG does not constitute a formal critique of the manufacturer's resubmission and hence does not accord with the procedures and templates applied to the original submission. However, the ERG undertook a number of checks of the models to ensure the internal validity of the manufacturer's revised analyses based on the revised set of assumptions employed by the manufacturer.

In the manufacturer's response, their original model was amended to reflect the assumptions made in the ERG alternative base-case, except with regards to PFS utility. The changes by the manufacturer resulted in a new ICER estimate of £62,829 per QALY for trastuzumab (HCX) versus EOX based on the deterministic analysis. However, the mean ICER for HCX versus EOX based on the new probabilistic analysis (incorporating uncertainty surrounding the treatment effect parameters) was higher at £67,786 per QALY. For comparative purposes, the alternative base-case ICER estimate previously reported by the ERG was £66,982 for HCX versus EOX based on the results from a deterministic analysis.

The revised estimates presented by the manufacturer are based on the manufacturer's original assumptions for PFS utility which allow for improvements in QoL during PFS (both during and after treatment). The ERG has previously critiqued these assumptions in their original report. While the ERG accept that improvements in QoL during PFS are clinically plausible, the ERG does not consider it plausible that QoL during PFS would exceed that of the general population. For this reason, the ERG re-ran the revised analyses presented by the manufacturer imposing a ceiling value for PFS utility estimates which was equal to general population utility estimates.

The following tables present the revised ICER estimates from the ERG based on the main scenarios presented by the manufacturer in their response. Analyses are undertaken based on: (i) licensed population; (ii) IHC3+ subgroup – unstratified analysis; (iii) IHC3+ subgroup – stratified analysis. The results from the deterministic and probabilistic analyses are reported separately. Separate tables are also provided based on a fully incremental analysis of the ICER and for select pairwise comparisons.

1. Revised ERG economic analysis of the licensed population (including utility ceiling assumption)

Table 1a: Fully incremental analysis of the ICER (deterministic analysis)

Strategy	Mean Costs	Mean QALYs	ICER
HCX	£25,967	0.975	£63,081
HCF	£25,262	0.881	Extendedly dominated
EOX	£15,963	0.817	£49,155
ECX	£12,516	0.746	-
ECF	£14,020	0.680	Dominated

Table 1b: Pairwise comparisons of the ICER (deterministic analysis)

Strategy	ICER
HCX vs EOX	£63,081
HCX vs ECX	£58,812
HCF vs ECF	£55,833

Table 1c: Fully incremental analysis of the ICER (probabilistic analysis)

Strategy	Mean Costs	Mean QALYs	ICER
HGX	£26,040	0.976	£71,463
HGF	£25,306	0.883	<i>Extendedly dominated</i>
EOX	£16,205	0.838	£44,854
ECX	£12,627	0.758	-
ECF	£14,100	0.689	<i>Dominated</i>

Table 1d: Pairwise comparisons of the ICER (probabilistic analysis)

Strategy	ICER
HGX vs EOX	£71,463
HGX vs ECX	£61,700
HGF vs ECF	£57,621

2. Revised ERG economic analysis of the IHC3+ population (including utility ceiling assumption): unstratified analysis

Table 2a: Fully incremental analysis of the ICER (deterministic analysis)

Strategy	Mean Costs	Mean QALYs	ICER
HGX	£28,464	1.097	£49,970
HGF	£27,629	0.994	<i>Extendedly dominated</i>
EOX	£16,422	0.854	<i>Extendedly dominated</i>
ECX	£12,821	0.784	-
ECF	£14,488	0.717	<i>Dominated</i>

Table 2b: Pairwise comparisons of the ICER (deterministic analysis)

Strategy	ICER
HCX vs EOX	£49,547
HCX vs ECX	£49,970
HCF vs ECF	£47,313

Table 2c: Fully incremental analysis of the ICER (probabilistic analysis)

Strategy	Mean Costs	Mean QALYs	ICER
HCX	£28,508	1.101	£51,934
HCF	£27,679	1.001	Extendedly dominated
EOX	£16,457	0.869	£49,966
ECX	£12,859	0.797	-
ECF	£14,504	0.720	Dominated

Table 2d: Pairwise comparisons of the ICER (probabilistic analysis)

Strategy	ICER
HCX vs EOX	£51,934
HCX vs ECX	£51,468
HCF vs ECF	£46,880

3. Revised ERG economic analysis of the IHC3+ population (including utility ceiling assumption): stratified analysis

Table 3a: Fully incremental analysis of the ICER (deterministic analysis)

Strategy	Mean Costs	Mean QALYs	ICER
HCX	£29,761	1.192	£43,206
HCF	£28,636	1.084	<i>Extendedly dominated</i>
EOX	£16,671	0.871	<i>Extendedly dominated</i>
ECX	£13,107	0.806	-
ECF	£14,808	0.743	<i>Dominated</i>

Table 3b: Pairwise comparisons of the ICER (deterministic analysis)

Strategy	ICER
HCX vs EOX	£40,861
HCX vs ECX	£43,206
HCF vs ECF	£40,575

Table 3c: Fully incremental analysis of the ICER (probabilistic analysis)

Strategy	Mean Costs	Mean QALYs	ICER
HCX	£29,773	1.194	£44,490
HCF	£28,653	1.089	<i>Extendedly dominated</i>
EOX	£16,660	0.879	<i>Extendedly dominated</i>
ECX	£13,171	0.820	-
ECF	£14,791	0.745	<i>Dominated</i>

Table 3d: Pairwise comparisons of the ICER (probabilistic analysis)

<i>Strategy</i>	<i>ICER</i>
<i>HCX vs EOX</i>	£41,699
<i>HCX vs ECX</i>	£44,490
<i>HCF vs ECF</i>	£40,257