T-DM1 for treating HER2-positive, unresectable locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane

Addendum following a Patient Access Scheme

Produced by	School of Health and Related Research (ScHARR), The University of Sheffield
Authors	Matt Stevenson, ScHARR, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA
Correspondence to	Matt Stevenson, ScHARR, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA

Date completed	19/06/2014

Introduction

This report has been produced following the agreement of a patient access scheme (PAS) related to T-DM1. The PAS is in the form of a simple discount, the value of which is commercial in confidence ([redacted]).

This report repeats the base case analyses conducted by the Evidence Review Group (ERG) and the accompanying univariate sensitivity analyses, which were Tables 26 and 27 in the original ERG report. No further analyses or critique of the manufacturer's submission are presented and readers are referred to the original ERG report for additional information.

Revised results post PAS.

To thwart attempts at backward calculation of the agreed PAS discount, the ICERs for T-DM1 have been marked as commercial in confidence

ERG Base Case Results

Table 1: Incorporation of variation in patients' weight and body surface area to calculate drug dosage

Technologies	Totals			Incrementals			
	Costs (£)	LYG	QALYs	Costs (£)	LYG	QALYs	ICER (Cost per QALY gained)
Capecitabine	£13,628	1.94	1.07				
Vinorelbine	£19,540	1.94	1.07				Dominated
Trastuzumab and capecitabine	£39,249	2.28	1.32				Dominated
Trastuzumab and vinorelbine	£46,211	2.28	1.32				Dominated
Lapatinib and capecitabine	£33,821	2.56	1.47	£20,193	0.63	0.40	£50,620
T-DM1	[redacted]	3.24	1.95	[redacted]	0.68	0.49	[redacted]

Univariate sensitivity analysis undertaken by the ERG

The incremental cost per QALYs from the ERG's univariate sensitivity analyses are shown within Table 2. Vinorelbine monotherapy and trastuzumab in combination with vinorelbine have been removed from the table for ease of reading, since these treatment options are always dominated by capecitabine monotherapy and trastuzumab in combination with capecitabine respectively.

Table 2: Univariate sensitivity analysis undertaken by the ERG

Analysis **(BCV= Base case value)**	**Capecitabine**	**Trastuzumab and capecitabine**	**Lapatinib and capecitabine**	**T-DM1**
Base case	-	Dominated	£50,620	[redacted]
PFS supportive care cost £86.91 (BCVx2) £21.73 (BCVx0.5)	-	 Dominated Dominated	 £54,146 £48,857	[redacted] [redacted]
Post-progression supportive care cost BCVx2: variable between comparators from £117-£129	-	Dominated	£52,228	[redacted]
Treatment dose Including wastage - planned Excluding wastage - actual Excluding wastage - planned	-	 Dominated Dominated Dominated	 £51,961 £50,192 £51,760	[redacted] [redacted] [redacted]
Trastatuzumab and capecitabine vs T-DM1 HR PFS 1.48 (Upper CrI)	-	Extendedly dominated	£50,620	[redacted]
Trastatuzumab and capecitabine vs T-DM1 HR OS 1.60 (Upper CrI)	-	£20,786	Extendedly dominated	[redacted]
Capecitabine vs T-DM1 HR PFS 0.89 (Upper CrI)	-	Dominated	£57,962	[redacted]
Capecitabine vs T-DM1 HR OS 1.30 (Upper CrI)	[redacted]	Dominated	Dominated	[redacted]
PFS utility: Same values as lapatinib and capecitabine in all arms TH3RESA trial (0.71 T-DM1, 0.69 comparators)	 - -	 Dominated Dominated	 £51,727 £54,102	[redacted] [redacted]
Progressed utility 0.7 (BCV +0.2)	-	Dominated	£44,226	[redacted]

Analysis **(BCV= Base case value)**	**Capecitabine**	**Trastuzumab and capecitabine**	**Lapatinib and capecitabine**	**T-DM1**
Base case	-	Dominated	£50,620	[redacted]
PFS extrapolation KM+Weibull tail Weibull	 - -	 Dominated Dominated	 £46,646 £47,110	[redacted] [redacted]
OS extrapolation KM+Weibull tail Weibull	 - -	 Dominated Dominated	 £91,952 £90,025	[redacted] [redacted]
PFS & OS extrapolation - Weibull	-	Dominated	£89,433	[redacted]
Discount rate (costs & outcomes) 6% 0%	 - -	 Dominated Dominated	 £52,852 £47,412	[redacted] [redacted]
Time horizon - 5 years	-	Dominated	£60,284	[redacted]
PFS & OS of T-DM1 equivalent to lapatinib and capecitabine after week 72 and 96 respectively	-	Dominated	£50,620	[redacted]
Cost of AEs (BCVx2)	-	Dominated	£51,146	[redacted]
Fixed dose subcutaneous trastuzumab administration	-	Dominated	£50,620	[redacted]

All of these analyses result in an incremental cost per QALY gained for T-DM1 compared with lapatinib in combination with capecitabine in excess of [redacted]. The ICER associated with lapatinib in combination with capecitabine compared with capecitabine does not fall below £44,000.