

## Biologic drugs for psoriatic arthritis: Revisions to the cost effectiveness analysis

### York Assessment Group

2<sup>nd</sup> February 2009

#### Introduction

This paper presents revisions to the cost-effectiveness analysis following the comments made by NICE consultees on the Assessment Group (AG) report and model of 4<sup>th</sup> December 2009.

#### Methods

The AG considered that three changes should be made to the model, in the light of the comments made by NICE consultees.

1. Abbott provided revised estimates from their RCTs of the effect of adalimumab on HAQ change for PsARC responders and non-responders. These new estimates were to four decimal places, whereas the original data provided to the AG were rounded to one decimal place. These new data have been used to generate a new evidence synthesis.
2. The AG made a mistake in the calculation of a standard error when extracting data for the evidence synthesis. This has been corrected.
3. The AG made a mistake in the calculation of the costs of adalimumab and etanercept. The costs were calculated for 12 week instead of three month periods. This has been corrected.

The AG have also run a new sensitivity analysis for patients with PsA and mild-to-moderate psoriasis. The base-case assumes that patients who fail to achieve a PsARC response at 3 months will be withdrawn from the biologic and be placed on palliative care. The new sensitivity analysis assumes that patients with PsA and mild-to-moderate psoriasis will continue on their biologic drug if they achieve either a PsARC or a PASI 75 response at 3 months.

#### Results

##### Revised estimates of HAQ change given treatment response using corrected standard errors and additional decimal places for adalimumab estimates

Patients who responded to treatment							
	Initial analysis (Table 5.15)			Revised analysis			Diff
	$\Delta$ HAQ	Credible intervals		$\Delta$ HAQ	Credible intervals		
Placebo	-0.2179	-0.3139	-0.1278	-0.2436	-0.3369	-0.1505	0.0257
Etanercept	-0.6235	-0.8153	-0.4375	-0.6304	-0.8046	-0.4548	0.0069
Infliximab	-0.6527	-0.7962	-0.5090	-0.6570	-0.7926	-0.5227	0.0043
Adalimumab	-0.4230	-0.5392	-0.2955	-0.4769	-0.5957	-0.3508	0.0539

**Revised estimates of HAQ change given treatment no-response using corrected standard errors and additional decimal places for adalimumab estimates**

Patients who did not respond to treatment							
	Initial analysis (Table 5.16)			Revised analysis			Diff
	$\Delta$ HAQ	Credible intervals		$\Delta$ HAQ	Credible intervals		
Placebo	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Etanercept	-0.185	-0.390	0.015	-0.190	-0.381	0.000	0.004
Infliximab	-0.191	-0.337	-0.046	-0.194	-0.333	-0.057	0.003
Adalimumab	-0.064	-0.188	0.065	-0.130	-0.262	-0.001	0.066

**Table 6.3 (Revised). Model parameters and assumptions used in the base-case of the York Assessment Group model. Changes are highlighted in yellow**

Description	Variable name	Mean	SE		Source / appendix
Gender male =1, female = 0	Male	1			
PsA minimum duration (years)	PSA.dur	3			
Concomitant MTX in all strategies: yes = 1, no = 0	MTX	1			
Baseline HAQ	HAQ0	1.05			Mean of RCTs (Table 5.1)
Baseline PASI	PASIO	7.5			Clinical opinion
Baseline age	Age	47			Mean of RCTs (Table 5.1)
Model time horizon years	Years	40			Clinical opinion
Discount rate (per year)	r	0.035			<sup>182</sup>
Utility function intercept	h0	0.897	0.006		A10.17
Change in utility for 1 unit change in HAQ	h1	-0.298	0.006		A10.17
Change in utility for 1 unit change in PASI	h2	-0.004	0.0003		A10.17
Interaction term HAQ PASI	h3	0	10xE-5		A10.17
Cost function intercept (per 3 month period)	c0	233			A10.15

Description	Variable name	Mean	SE		Source / appendix
Change in cost for 1 unit change in HAQ	c1	103	67		Kobelt <sup>42</sup> A10.15
3 month cost for mild-to-moderate psoriasis if uncontrolled by biologics	c2.1	198	9		Ref costs <sup>189</sup> A10.16
3 month cost for psoriasis in remission	c2.2	16	1		Hartman <sup>191</sup> A10.16
Change in HAQ while on treatment per 3 month period	HAQ1.d	0	0.02		Experts A10.11
Change in HAQ while not on treatment per 3 month period	HAQ1.w	0.018	0.007		NOAR A10.14
Rebound in HAQ in 3m after withdrawal (compared to HAQ at baseline) (Zero means 'rebound equal to initial gain')	loss.w	0	0.3		Experts A10.11
Intercept of regression of log-mortality versus age in men	ln.R.g.m	-10.25	0.046		England and Wales life table/ A10.19
Intercept of regression of log-mortality versus age in women	ln.R.g.f	-11.10	0.046		
Change in log-mortality with additional year of age in men over 40 years	a.g.m	0.094	0.0006		
Change in log-mortality with additional year of age in women over 40 years	a.g.f	0.101	0.0006		
Log withdrawal rate from biologics per year	ln.long.yr	-1.823	0.2044		Registers/A 10.12
Probability of PsARC response on placebo	p.psarc.plac	0.249	0.0384		Section 5.2
Change in HAQ given a PsARC response on placebo	HAQ.resp.plac	-0.243	0.0474		
Probability of PASI 50 response on placebo	p.pasi.50.plac	0.130	0.021		Section 5.2
Probability of PASI 75 response on placebo	p.pasi.75.plac	0.044	0.009		
Probability of PASI 90 response on placebo	p.pasi.90.plac	0.016	0.004		
Standardised mortality ratio for PSA vs general population	SMRmen	1.65			<sup>30</sup> /A10.19
	SMRwomen	1.59			

Description	Variable name	Mean	SE		Source / appendix
generalisability of trial (1=no, 2 = yes)	plac.effect	1			A10.9
rules on continuation (1 - 5)	continue	1			BSR & BAD
		Etan	Inflix	Adal	
Cost of drugs (first 3 months)	c.drug1	2495	5523	2495	BSR/A 10.13
Cost of drugs for months 4-6	c.drug2	2443	2965	2443	
Cost of drugs, subsequent three months	c.drug3	2385	2965	2385	
Probability of PsARC response on biologic	p.psarc	0.713	0.795	0.587	Section 5.2
	p.psarc_SE	0.071	0.058	0.072	
Change in HAQ in first 3 months given no PsARC response of biologic	HAQ.no.resp	-0.190	-0.194	-0.130	Section 5.2
	HAQ.no.resp_SE	0.10	0.070	0.066	
Change in HAQ in first 3 months given PsARC response of biologic	HAQ.resp	-0.630	-0.657	-0.477	Section 5.2
	HAQ.resp_SE	0.090	0.069	0.062	
Probability of PASI 50 response on biologic	p.pasi.50	0.4026	0.9128	0.7383	Section 5.2
Probability of PASI 75 response on biologic	p.pasi.75	0.1768	0.7687	0.4772	
Probability of PASI 90 response on biologic	p.pasi.90	0.0737	0.5571	0.2571	
	p.pasi.50_SE	0.0916	0.0374	0.0853	
	p.pasi.75_SE	0.0586	0.0795	0.1085	
	p.pasi.90_SE	0.0292	0.1088	0.0863	
Correlation between PASI 75 and PsARC	Rho	0.435	0.435	0.435	ADEPT <sup>52</sup> /A 10.10
	rho_SE	0.112	0.112	0.112	

**Table 6.5 (Revised) Results of the base-case analysis**

Strategy	QALY	Cost £	Inc QALY	Inc cost	ICER	PCE 20K	PCE 30K
N	5.171	42168			NA	0.472	0.309
A	6.580	68638	1.409	26470	Ex dom	0.046	0.032
E	7.001	74841	0.422	6203	17853	0.436	0.475
I	7.308	88442	0.307	13601	44326	0.046	0.184

PCE 20K/30K: Probability that the treatment is cost-effective at a threshold of £20,000/£30,000 per QALY

ICER: Incremental cost-effectiveness ratio. QALY: Quality-Adjusted Life Year

N: Palliative care, A: Adalimumab, E:Etanercept, I:Infliximab

Ex dom: Extendedly dominated

**Table 6. 6 (revised). Univariate sensitivity analyses**

Scenario	Description	Trt	QALY	Cost £	ICER	p.20	p.30
1	Base-case	N	5.171	42168	NA	0.472	0.309
1		A	6.580	68638	Ex dom	0.046	0.032
1		E	7.001	74841	17853	0.436	0.475
1		I	7.308	88442	44326	0.046	0.184
2	Rebound in HAQ is small after withdrawal (base-case =initial gain)	N	5.171	42168	NA	0.214	0.114
2		A	7.225	67710	Ex dom	0.051	0.029
2		E	7.792	73706	12035	0.609	0.521
2		I	8.188	87174	34006	0.126	0.336
3	Rapid worsening in HAQ with no treatment (upper 95% of CI)	N	3.309	44434	NA	0.358	0.187
3		A	4.967	70829	Ex dom	0.047	0.029
3		E	5.447	76985	15221	0.528	0.544
3		I	5.786	90609	40248	0.067	0.240
4	Log-PASI utility function (Abbott <sup>174</sup> )(Base-case linear)	N	4.558	42168	NA	0.459	0.308
4		A	6.001	68638	Ex dom	0.069	0.040
4		E	6.390	74841	17835	0.400	0.390
4		I	6.769	88442	35898	0.072	0.262
5	No correlation between PASI 75 and PsARC (base-case = 0.4)	N	5.171	42168	NA	0.479	0.311
5		A	6.571	68968	Ex dom	0.040	0.032
5		E	6.997	74990	17979	0.434	0.476

Scenario	Description	Trt	QALY	Cost £	ICER	p.20	p.30
5		I	7.303	88641	44558	0.047	0.181
6	RCT results fully generalisable to clinical practice (no adjustment for placebo effect)	N	5.171	42168	NA	0.451	0.282
6		A	6.637	68561	Ex dom	0.053	0.037
6		E	7.068	74752	17178	0.446	0.482
6		I	7.381	88344	43371	0.050	0.199
9	Exponential HAQ-cost function (Abbott <sup>174</sup> )(base-case linear)	N	5.171	63052	NA	0.375	0.266
9		A	6.580	82129	Ex dom	0.048	0.032
9		E	7.001	86502	12813	0.477	0.457
9		I	7.308	99045	40878	0.100	0.245
12	Inpatient treatment for uncontrolled psoriasis	N	5.171	151496	NA	0.255	0.151
12		A	6.580	165282	9787	0.114	0.055
12		I	7.308	175157	13557	0.621	0.769
12		E	7.001	178530	Dominated	0.010	0.025
13	Cost per 3 month per 1 unit change in HAQ is £183 (US data) <sup>43</sup> (Base-case £103)	N	5.171	52548	NA	0.444	0.303
13		A	6.580	77518	Ex dom	0.047	0.032
13		E	7.001	83224	16761	0.453	0.467
13		I	7.308	96562	43468	0.056	0.198
14	Change in utility per 1 unit change in HAQ is -0.45 (Wyeth <sup>152</sup> ) (base-case - 0.29)	N	0.846	42168	NA	0.312	0.203
14		A	2.905	68638	Ex dom	0.024	0.011
14		E	3.589	74841	11913	0.522	0.474
14		I	3.954	88442	37280	0.142	0.312
15	HAQ improves while on drug (lower 95% of CI) (base-case no change)	N	5.171	42168	NA	0.029	0.007
15		A	7.845	66823	Ex dom	0.075	0.023
15		E	8.492	72704	9194	0.712	0.516
15		I	8.959	86065	28635	0.184	0.454
16	High rate of withdrawal (upper 95% of CI)	N	5.171	42168	NA	0.464	0.316
16		A	6.302	62085	Ex dom	0.041	0.029
16		E	6.635	66604	16690	0.436	0.460
16		I	6.876	77323	44451	0.059	0.195
17	Low rate of withdrawal (lower 95% of	N	5.171	42168	NA	0.485	0.322

Scenario	Description	Trt	QALY	Cost £	ICER	p.20	p.30
17	CI)	A	6.891	76566	Ex dom	0.060	0.035
17		E	7.411	84811	19038	0.427	0.462
17		I	7.793	101890	44731	0.028	0.181
18	All treatments have the same probability of PsARC response at 3 months	N	5.197	41416	NA	0.472	0.312
18		A	7.104	77174	Ex dom	0.176	0.193
18		E	7.236	78115	17999	0.351	0.467
18		I	7.316	87889	122073	0.001	0.028
19	All treatments have the same probability of psoriasis responses (PASI 50, 75 and 90) at 3 months	N	5.273	41746	NA	0.418	0.275
19		A	6.722	67892	Ex dom	0.016	0.016
19		E	7.186	72834	16254	0.554	0.602
19		I	7.414	87951	66219	0.012	0.107
20	Cost of drugs as in Wyeth submission <sup>152</sup>	N	5.171	42168	NA	0.425	0.273
20		A	6.580	65847	Ex dom	0.067	0.057
20		E	7.001	71478	16015	0.505	0.614
20		I	7.308	92632	68944	0.003	0.056
22	All biologics have the same change in HAQ at 3 months for a PsARC responder	N	5.171	42168	NA	0.470	0.314
22		A	6.659	68526	17717	0.165	0.174
22		E	6.949	74920	22056	0.341	0.395
22		I	7.217	88573	50806	0.024	0.117
23	3 vials of infliximab (base-case: 4 vials)	N	5.171	42168	NA	0.423	0.259
23		A	6.580	68638	Ex dom	0.000	0.000
23		E	7.001	74841	Ex dom	0.034	0.061
23		I	7.308	76550	16809	0.543	0.680
26	Rebound to natural history after withdrawal (Base-case: rebound to initial gain)	N	5.171	42168	NA	0.983	0.687
26		A	5.846	69701	Ex dom	0.004	0.038
26		E	6.104	76145	36408	0.013	0.273
26		I	6.307	89900	67759	0.000	0.002
31	No costs of psoriasis (base-case: UK data <sup>189, 190</sup> )	N	5.171	28908	NA	0.485	0.317
31		A	6.580	56792	Ex dom	0.037	0.022
31		E	7.001	62209	18196	0.459	0.513

Scenario	Description	Trt	QALY	Cost £	ICER	p.20	p.30
31		I	7.308	77704	50499	0.019	0.148
32	Schering-Plough estimates of cost per PASI point excluding phototherapy <sup>175</sup>	N	5.171	55479	NA	0.456	0.298
32		A	6.580	80496	Ex dom	0.065	0.042
32		E	7.001	87252	17361	0.414	0.423
32		I	7.308	99438	39715	0.065	0.237
33		Schering-Plough estimates of cost per PASI point including phototherapy <sup>175</sup>	N	5.171	112633	NA	0.370
33	A		6.580	131482	13381	0.146	0.057
33	E		7.001	141118	Ex dom	0.145	0.161
33	I		7.308	146187	20188	0.339	0.545
99	The effectiveness of biologic therapy lasts no longer than 10 years, compared with palliative care	N	5.171	42168	NA	0.861	0.534
99		A	5.875	66044	Ex dom	0.017	0.038
99		E	6.130	71556	30645	0.122	0.408
99		I	6.325	83779	62746	0.000	0.020

35	Continue on biologic after 3 months if respond to <i>either</i> PsARC <i>or</i> PASI 75 (Basecase: PsARC only)	N	5.171	42168	NA	0.475	0.312
35		A	6.763	72421	Ex dom	0.078	0.040
35		E	7.006	74934	17859	0.376	0.382
35		I	7.476	92890	38194	0.071	0.266

**Table 6.7 (Revised). Cost-effectiveness of the strategies under different scenarios. Scenarios that have changed compared with the report of 4<sup>th</sup> December are highlighted**

#	Description	Adalimumab	Etanercept	Infliximab
1	Base-case	Ex Dom	<20k	>30k
2	Rebound in HAQ is small after withdrawal (base-case =initial gain)	Ex Dom	<20k	>30k
3	Rapid worsening in HAQ with no treatment (upper 95% of CI)	Ex Dom	<20k	>30k
4	Log-PASI utility function (Abbott <sup>174</sup> )(Base-case linear)	Ex Dom	<20k	>30k
5	No correlation between PASI 75 and PsARC (base-case = 0.4)	Ex Dom	<20k	>30k
6	RCT results fully generalisable to clinical practice (no adjustment for placebo effect)	Ex Dom	<20k	>30k



9	Exponential HAQ-cost function (Abbott <sup>174</sup> )(base-case linear)	Ex Dom	<20k	>30k
12	Inpatient treatment for uncontrolled psoriasis	<20k	Dom	<20k
13	Cost per 3 month per 1 unit change in HAQ is £183 (US data) <sup>43</sup> (Base-case £103)	Ex Dom	<20k	>30k
14	Change in utility per 1 unit change in HAQ is -0.45 (Wyeth <sup>152</sup> ) (base-case -0.29)	Ex Dom	<20k	>30k
15	HAQ improves while on drug (lower 95% of CI) (base-case no change)	Ex Dom	<20k	20-30k
16	High rate of withdrawal (upper 95% of CI)	Ex Dom	<20k	>30k
17	Low rate of withdrawal (lower 95% of CI)	Ex Dom	<20k	>30k
18	All treatments have the same probability of PsARC response at 3 months	Ex Dom	<20k	>30k
19	All treatments have the same probability of psoriasis responses (PASI 50, 75 and 90) at 3 months	Ex Dom	<20k	>30k
20	Cost of drugs as in Wyeth submission <sup>152</sup>	Ex Dom	<20k	>30k
22	All biologics have the same change in HAQ at 3 months for a PsARC responder	<20k	<20k	>30k
23	3 vials of infliximab (base-case: 4 vials)	Ex Dom	Ex Dom	<20k
26	Rebound to natural history after withdrawal (Base-case: rebound to initial gain)	Ex Dom	>30k	>30k
31	No costs of psoriasis (base-case: UK data)	Ex Dom	<20k	>30k
32	Schering-Plough estimates of cost per PASI point without phototherapy <sup>175</sup>	Ex Dom	<20k	>30k
33	Schering-Plough estimates of cost per PASI point with phototherapy <sup>175</sup>	<20k	Ex dom	<20k
99	The effectiveness of biologic therapy lasts no longer than 10 years, compared with palliative care	Ex Dom	20k-30k	>30k
35	Continue on biologic after 3 months if respond to either PsARC or PASI 75 (Basecase: PsARC only)	Ex Dom	<20k	>30k

(Nb. Changes to 15, 23, 33). New scenario 35 (continuation rule)

**Table 6.8 (revised). Subgroup analysis**

	Description		QALY	Cost £	ICER	PCE20k	PCE30k
10	Baseline HAQ 1.8 (BSR register <sup>184</sup> ) (Base-case 1.05)	N	2.090	46594	NA	0.528	0.350
10		A	3.397	73207	Ex dom	0.044	0.029
10		E	3.804	79431	19156	0.389	0.447
10		I	4.101	93046	45898	0.039	0.174
11	Baseline PASI 12.5 (Base-case 7.5)	N	4.810	66811	NA	0.431	0.274

11		A	6.257	90422	16310	0.115	0.057
11		E	6.661	98214	19319	0.294	0.269
11		I	7.012	107988	27778	0.160	0.400
7	Baseline PASI 12.5, and continue after 3 months only if respond to <i>both</i> PsARC & PASI 75 (base-case PsARC only)	N	4.810	66811	NA	0.399	0.246
7		E	5.315	74865	Ex dom	0.030	0.039
7		A	5.790	81637	15125	0.174	0.073
7		I	6.717	101796	21739	0.397	0.642
8	Baseline PASI 12.5, and continue after 3 months if respond to <i>either</i> PsARC or PASI 75	N	4.810	66811	NA	0.435	0.278
8		A	6.448	93601	16349	0.170	0.076
8		E	6.665	98293	21609	0.208	0.177
8		I	7.187	111940	26177	0.187	0.469
21	Baseline PASI 12.5, and annual inpatient treatment for uncontrolled psoriasis (Base-case UVB)	N	4.810	171746	NA	0.185	0.079
21		A	6.257	183184	7901	0.101	0.053
21		I	7.012	191216	10636	0.710	0.855
21		E	6.661	197741	Dom	0.004	0.013
30	Baseline PASI zero (base-case 7.5)	N	5.713	28908	NA	0.498	0.330
30		A	7.064	56792	Ex dom	0.018	0.019
30		E	7.512	62209	18512	0.471	0.549
30		I	7.752	77704	64744	0.013	0.102

**Table 6.9 (revised). Costs and QALYs of biologics used as second-line therapy for patients with mild-to-moderate skin disease if first biologic fails**

Scenario	Description	Trt	QALY	Cost	ICER assuming I was used 1 <sup>st</sup> line	ICER assuming E was used 1 <sup>st</sup> line	ICER assuming A was used 1 <sup>st</sup> line
24	Second –line biologic if first failed for inefficacy	N	5.171	42168			
24		A	5.827	54394		18652	
24		E	6.142	58783	17114		17114
24		I	6.410	68630		24406	36746
25	Second –line biologic if first failed	N	5.171	42168			

25	for adverse events	A	6.273	61430		17486	
25		E	6.597	65780	16554		16554
25		I	6.831	76205		26445	44569

NA. Therapy is not available for second-line use as failed in 1<sup>st</sup> line

## Conclusions

Etanercept is the most cost-effective intervention in the base-case for patients with PsA and mild-to-moderate skin disease. This is the same conclusion as the report of 4<sup>th</sup> December. There are minor changes to some of the sensitivity analyses.

For patients with PsA and moderate-to-severe skin disease, and who continue with biologic therapy if they achieve a response for either psoriasis or joint disease, the ICER of adalimumab versus palliative care is about £16,000 per QALY, the ICER of etanercept versus adalimumab is about £21,000 per QALY and the ICER for infliximab versus etanercept is about £26,000 per QALY. All biologics have a similar probability of being cost-effective in this sub-group at a threshold of £20,000 per QALY.

The results for patients with PsA and moderate-to-severe psoriasis differ compared with the report of 4<sup>th</sup> December, which found a higher probability that etanercept was cost-effective, and a lower probability that infliximab and adalimumab would be cost-effective.