

Short note for economics of dapagliflozin post PMB

Data element 1: Hypo disutility

The ERG suggests that analyses based upon those of Currie but assuming that these only apply only for 3 months may be the most justifiable in the current context:

- 0.012 QALYs for severe
- 0.004 QALYs for symptomatic

The ERG has converted the values in the model submitted to quarterly values by dividing cells E78 and F78 of the *Utilities* worksheet by 4.

Note that CG87 applied only a 0.010 decrement per severe event based upon expert opinion.

Data element 2: Cost of pioglitazone

The manufacturer submission applies an average annual cost for pioglitazone of £414.07. Since the preparation of the submission the cost of pioglitazone has fallen sharply in both eMIMS and the NHS drug tariff. Applying the manufacturer weights for the three possible doses, the current weighted average annual cost of pioglitazone is only £112.18. The ERG has revised this within the model by changing cell C10 of the worksheet *Drug_Cost* from £414.07 to £112.18.

Data element 3: Cost of complications

There are concerns that those without complication are modelled as not incurring any costs other than the direct drug costs. The UKPDS 65 outlines annual costs of £157 and £159 in 1999 prices which when summed result in an overall cost of £316 in 1999 prices or £483 in 2011 prices. As per the ERG report the simplest means of addressing this within the DCEM structure is to subtract this amount from the costs of complications.

Table 01: Revised costs of complications

Event	Manufacturer sub.			Adjusted by £483		
	Fatal	Non-fatal	Maint.	Fatal	Non-fatal	Maint.
Ischaemic Heart Disease		£3,479	£1,149		£2,996	£666
Myocardial Infarction	£2,244	£6,709	£1,105	£1,761	£6,226	£622
Congestive Heart Failure	£3,880	£3,880	£1,360	£3,397	£3,397	£877
Stroke	£5,658	£4,103	£776	£5,175	£3,620	£293
Amputation	£13,359	£13,359	£771	£12,876	£12,876	£288
Blindness (one eye)		£1,752	£742		£1,269	£259
ESRD		£34,806	£34,806		£34,323	£34,323

The ERG has made these changes to cells C8:G14 of the Costs worksheet.

Data element 4: BMI disutility

The ERG views the 0.0061 per BMI point disutility from Baghurst et al (2005) as a more reasonable base case value than those drawn from Lane et al (2012).

Revising data elements 1-4

The above four data element revisions change the results of the modelling as outlined below. These are accompanied by summaries of the proportion of benefits that are attributable to weight changes, and the degree to which these would have to be reduced to result in ICERs of £20,000 per QALY and £30,000 per QALY.

Dual therapy: comparison with SU

Table 01: Previous dual therapy modelling versus SU

	DAPA	SU	net
QALYs	11.740	11.280	0.467
Costs	£12,904	£11,658	£1,246
ICER			£2,671

Table 02: Revised dual therapy modelling versus SU

	DAPA	SU	net
QALYs	12.407	12.289	0.118
Costs	£11,095	£9,810	£1,285
ICER			£10,925

Table 03: Revised dual therapy modelling versus SU: removing direct BMI effects upon HRQoL

	DAPA	SU	net	ICER
Costs	£11,095	£9,810	£1,285	
QALYs	12.407	12.289	0.118	£10,925
BMI impact	-0.074	-0.132	0.059	
ex BMI impact	12.481	12.422	0.059	£21,767

Revising the BMI HRQoL coefficient from -0.0061 to -0.00054 results in an ICER of £20,000 per QALY. The ICER excluding the direct BMI HRQoL impacts lies below £30,000 per QALY.

Dual therapy: comparison with DPP-IV and TZD

Table 04: Previous dual therapy modelling versus DPP-IV and TZD

	DAPA	DPP-4	net	TZD	net
QALYs	12.620	12.600	0.020	12.200	0.420
Costs	£14,733	£14,882	-£149	£14,793	-£60
ICER			Dominant		Dominant

Table 05: Revised dual therapy modelling versus DPP-IV and TZD

	DAPA	DPP-4	net	TZD	net
QALYs	13.239	13.207	0.032	13.181	0.058
Costs	£12,647	£12,778	-£131	£10,954	£1,693
ICER			Dominant		£29,001

Table 06: Revised dual therapy modelling versus DPP-4: removing direct BMI effects upon HRQoL

	DAPA	DPP-4	net	ICER
Costs	£12,647	£12,778	-£131	
QALYs	13.239	13.207	0.032	Dominant
BMI impact	-0.067	-0.076	0.008	
ex BMI impact	13.306	13.283	0.024	Dominant

Table 07: Revised dual therapy modelling versus TZD: removing direct BMI effects upon HRQoL

	DAPA	TZD	net	ICER
Costs	£12,647	£10,954	£1,693	
QALYs	13.239	13.181	0.058	£29,001
BMI impact	-0.067	-0.134	0.067	
ex BMI impact	13.306	13.315	-0.008	Dominated

Revising the BMI HRQoL coefficient from -0.0061 to -0.0085 results in an ICER of £20,000 per QALY. Revising the BMI HRQoL coefficient from -0.0061 to -0.0059 results in an ICER of £30,000 per QALY.

Triple therapy:

Table 08: Previous triple therapy modelling

	DAPA	DPP-4	net	TZD	net	GLP-1	net
QALYs	██████	11.468	██████	11.088	██████	11.689	██████
Costs	██████	£11,974	██████	£11,951	██████	£13,244	██████
ICER			Dominant		Dominant		Dominant

Table 09: Revised triple therapy modelling

	DAPA	DPP-4	net	TZD	net	GLP-1	net
QALYs	██████	12.318	██████	12.270	██████	12.348	██████
Costs	██████	£10,127	██████	£9,187	██████	£11,397	██████
ICER			Dominant		£11,090		£427k

Table 10: Revised triple therapy modelling versus DPP-4: removing direct BMI effects upon HRQoL

	DAPA	DPP-4	net	ICER
Costs	██████	£10,127	██████	
QALYs	██████	12.318	██████	Dominant
BMI impact	██████	-0.119	██████	
ex BMI impact	██████	12.436	██████	£26,781

Excluding the BMI HRQoL impact results in a point in the south west quadrant: the cost effectiveness of the DPP-4 compared to dapagliflozin is £26,781 per QALY and if the willingness to pay were £30,000 per QALY the DPP-IV would be seen as being cost effective. But revising the BMI HRQoL coefficient from -0.0061 to ██████ results in an ICER of £30,000 per QALY.

Table 11: Revised triple therapy modelling versus TZD: removing direct BMI effects upon HRQoL

	DAPA	TZD	net	ICER
Costs	██████	£9,187	██████	
QALYs	██████	12.270	██████	£11,090
BMI impact	██████	-0.167	██████	
ex BMI impact	██████	12.437	██████	Dominated

Revising the BMI HRQoL coefficient from -0.0061 to ██████ results in an ICER of £20,000 per QALY. Revising the BMI HRQoL coefficient from -0.0061 to ██████ results in an ICER of £30,000 per QALY.

Table 12: Revised triple therapy modelling versus GLP-1: removing direct BMI effects upon HRQoL

	DAPA	GLP-1	net	ICER
Costs	██████	£11,397	██████	
QALYs	██████	12.348	██████	£427,095
BMI impact	██████	-0.090	██████	
ex BMI impact	██████	12.438	██████	£252,972

Note that the above ICERs are in the south west quadrant so give the cost effectiveness of the GLP-1 versus dapagliflozin: £427k per QALY for the GLP-1 versus dapagliflozin and as a consequence the GLP-1 is not estimated to be cost effective. This also applies to the ICER for the GLP-1 excluding the BMI HRQoL impacts: it improves to £253k per QALY but the GLP-1 is still not estimated to be cost effective. In the light of this, the BMI HRQoL value cannot be revised to anything sensible that results in ICERs of £20,000 per QALY and £30,000 per QALY.

Add on to insulin: comparison with DPP-IV:

Table 13: Previous add-on to insulin modelling

	DAPA	DPP-4	net
QALYs	12.329	12.210	0.119
Costs	£17,815	£17,298	£517
ICER			£4,358

Table 14: Revised add-on to insulin modelling

	DAPA	DPP-4	net
QALYs	12.974	12.947	0.027
Costs	£16,200	£15,677	£524
ICER			£19,094

Table 15: Revised add-on to insulin versus DPP-4: removing direct BMI effects upon HRQoL

	DAPA	DPP-4	net	ICER
Costs	£16,200	£15,677	£524	
QALYs	12.974	12.947	0.027	£19,094
BMI impact	-0.054	-0.076	0.022	
ex BMI impact	13.028	13.023	0.005	£105,511

Revising the BMI HRQoL coefficient from -0.0061 to -0.0058 results in an ICER of £20,000 per QALY. Revising the BMI HRQoL coefficient from -0.0061 to -0.0034 results in an ICER of £30,000 per QALY.

Model structure - sequencing of therapies in triple therapy modelling

There were some concerns about the triple therapy modelling not modelling the triple therapies followed by insulin followed by intensified insulin. The sequences can be changed to place the triple therapies first, followed by insulin+met, followed by intensified insulin. Within the current model structure this has the effect of also changing the HbA1c switching threshold for coming off the triple therapies to 7.72% but retaining the 8.7 % for the move from insulin+met to intensified insulin.

Table 16: Revised triple therapy modelling for data elements 1-4

	DAPA	DPP-4	net	TZD	net	GLP-1	net
QALYs	██████	12.318	██████	12.270	██████	12.348	██████
Costs	██████	£10,127	██████	£9,187	██████	£11,397	██████
ICER			Dominant		£11,090		£427k

Table 17: Revised triple therapy modelling for data elements 1-4 and treatment sequencing

	DAPA	DPP-4	net	TZD	net	GLP-1	net
QALYs	██████	12.371	██████	12.316	██████	12.417	██████
Costs	██████	11,144	██████	9,690	██████	13,479	██████
ICER			Dominated		£29,251		£45,233

Note that the ICER for the comparison with the GLP-1 remains in the south west quadrant, and so is best interpreted as the cost effectiveness of the GLP-1 compared to dapagliflozin.