

## Lifetime cost-effectiveness simulation of exenatide once-weekly in type 2 diabetes: evidence from the EXSCEL trial

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**Background and aims:** The Exenatide Study of Cardiovascular Event Lowering (EXSCEL) assessed the effect of branded exenatide 2mg once-weekly (EQW) vs placebo added to usual care in 14,752 patients with type 2 diabetes (T2D), with or without previous cardiovascular disease. This pragmatic, randomized, double-blind, placebo-controlled, event-driven trial demonstrated a statistically non-significant reduction in major adverse cardiovascular events and a nominally significant reduction in all-cause mortality with allocation to EQW. We assessed the lifetime cost-effectiveness of EQW added to usual care, compared with usual care alone.

**Materials and methods:** Medical resource use and EuroQol 5-Dimension (EQ-5D) data were collected throughout the study. Within-trial results were extrapolated to a lifetime horizon using the UKPDS Outcomes Model version 2 after accounting for missing within-trial data. Cost-effectiveness was evaluated separately for US and UK settings, with costs assessed from a healthcare perspective and outcomes measured by quality-adjusted life-years (QALYs). The base case analyses extrapolated the 9% annual discontinuation rate observed in the trial forward for the first 10 years of the extrapolated period. In the US setting, a 23.1% discount on the wholesale acquisition price of branded EQW was applied. Further analyses were performed using pre-specified patient sub-groups and assuming patients who were still receiving EQW at the end of the trial remained on branded EQW during lifetime.

**Results:** Branded EQW plus usual care was estimated to gain 0.151 QALYs ( $p < 0.001$ ) over a lifetime horizon at an additional cost of USD34,410 ( $p < 0.001$ ) per patient, compared with usual care in a US setting. The incremental cost-effectiveness ratio (ICER) was estimated as USD230,429/QALY (base case; Table). In a UK setting, the estimated net gain was 0.141 QALYs ( $p < 0.001$ ) at an additional cost of GBP4,566 ( $p < 0.001$ ) with an ICER of GBP32,782/QALY. The base case ICERs exceeded the standard cost-effectiveness thresholds of USD100,000 and GBP20,000 per QALY, respectively. However, the ICERs for different sub-groups were found to be considerably lower, with an ICER of USD88,608 for patients enrolled in US sites and an ICER of GBP16,319 for patients aged 65 years and older in the UK setting.

**Conclusion:** Branded EQW added to usual care was associated with greater QALY gain and additional costs compared with usual care alone during a lifetime. The base case ICERs exceeded standard cost-effectiveness thresholds. However, EQW was cost-effective in specific sub-groups of the trial population, such as patients enrolled in US sites and (in the UK setting) patients aged 65 years and older.

Table 1: Lifetime cost-effectiveness of exenatide once-weekly vs placebo – base case, sensitivity and sub-group analyses

	n	US			UK		
		Additional costs (SE) [USD]	Additional QALYs (SE)	ICER (95% CI) [USD/QALY]	Additional costs (SE) [GBP]	Additional QALYs (SE)	ICER (95% CI) [GBP/QALY]
Base case (accounting for discontinuation of EQW)	EQW: 7,356 Plac: 7,396	34,410 (616)	0.151 (0.018)	230,429 (173,110 to 287,749)	4,566 (252)	0.141 (0.017)	32,782 (24,580 to 40,984)
All patients remaining on treatment during lifetime horizon	EQW: 7,356 Plac: 7,396	41,955 (719)	0.162 (0.018)	262,895 (204,574 to 321,215)	6,328 (259)	0.150 (0.017)	42,596 (32,791 to 52,400)
Patients enrolled in US sites	EQW: 1,567 Plac: 1,597	35,151 (1,451)	0.402 (0.046)	88,608 (68,211 to 109,006)	#	#	#
Age ≥65 years	EQW: 2,964 Plac: 2,975	31,220 (953)	0.270 (0.028)	116,704 (93,734 to 139,675)	4,020 (413)	0.249 (0.025)	16,319 (11,895 to 20,742)
Patients with cardiovascular history at baseline	EQW: 5,394 Plac: 5,388	31,758 (747)	0.163 (0.020)	197,589 (150,833 to 244,346)	4,106 (319)	0.154 (0.018)	26,923 (19,899 to 33,947)

EQW: exenatide once-weekly, Plac: placebo, SE: standard error, USD: US dollars, GBP: British pound, QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.  
# The sample size of patients enrolled in UK sites was too small to estimate robust results for this sub-group.

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