Cost-effectiveness of dapagliflozin in adult patients with inadequately controlled type 1 diabetes: A health economic analyses using 24-week results from the DEPICT-1 randomised control trial

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Unmet need in type 1 diabetes

• Type 1 diabetes mellitus (T1DM) is an autoimmune disease requiring exogenous insulin that accounts for 10% of diabetes diagnoses and affects around 400,000 people in the UK [1]

• DCCT and EDIC demonstrated that optimisation of glycaemic control reduces the risk of microvascular and macrovascular complications [2-5]

• In the UK, a significant number of people do not reach glucose control targets and are consequently exposed to higher risk of avoidable and costly complications
  • Less than 10% of people with T1DM reach glucose control targets of 48 mmol/mol (6.5%) [6]
  • Less than 30% have HbA1c levels ≤59 mmol/mol (7.5%) [7]
  • Over 30% have HbA1c levels ≥75 mmol/mol (9%) [7]

• A UK study estimated that a sustained 0.4% reduction in hba1c over 25 years could save around £1bn [6]

Weight as a barrier to optimal glycaemic control

- T1DM has traditionally been associated with lean individuals [1]
- Weight gain is a common side effect of intensive insulin therapy
- The prevalence of obesity in T1DM is increasing at a faster rate than in the general population. Approximately 50% of people with T1DM are either overweight or obese [2]
- The main reported barrier to physical activity is fear of severe hypoglycaemia [1]
- SGLT-2 inhibitors have improved weight profiles in type 2 diabetes mellitus [3] and have shown promising results as an add-on to insulin in T1DM [4]

Dapagliflozin: Introduction

- Dapagliflozin is a sodium-glucose co-transporter-2 inhibitor (SGLT-2i)
- Insulin-independent mechanism of action, that acts by reducing reabsorption of filtered glucose in the kidneys
- Excretion of glucose in urine reduces bodyweight in addition to reducing HbA1c [1]
- Established therapy option in type 2 diabetes
- Will be the first SGLT-2i therapy to become available in Europe for the treatment of T1DM and is expected to be the first licensed adjunct to insulin approved in the UK, almost a century since the introduction of insulin.
Dapagliflozin: DEPICT-1

• Dapagliflozin Evaluation in Patients with Inadequately Controlled Type 1 Diabetes (DEPICT-1) was a Phase 3, double-blind placebo-controlled trial that assessed the efficacy and safety of dapagliflozin as an add-on to adjustable insulin in people with inadequately controlled T1DM

Key trial findings [1]:
• Improved glycaemic control and stability (0.42–0.45% placebo-adjusted HbA1c reduction at 24 weeks)
• Bodyweight loss (3.0–3.7% placebo-adjusted bodyweight reduction at 24 weeks)
• Reduction in insulin dose (8.8–13.2% placebo-adjusted reduction in total insulin dose at 24 weeks)
• Without increasing hypoglycaemia
• Safety profile similar to type 2 diabetes with the exception of a small increase in ketone-related events

Objectives

• The study objective was to estimate the cost-effectiveness of dapagliflozin (10 mg or 5 mg) as an add-on to insulin for people with T1DM

• Intervention: dapagliflozin (10 mg or 5 mg) as add-on to insulin
• Comparator: insulin therapy alone (placebo)
• Population: adults with T1DM that is inadequately controlled by insulin alone
• Setting/perspective: UK healthcare payer
• Time horizon: lifetime
• Discounting: 3.5% per annum

• Efficacy and safety data: 24-week results from DEPICT-1 [1]
Cost-effectiveness methods: Model structure

- Cardiff Type 1 Diabetes Model
- Published and validated [1,2]
- Patient-level simulation that predicts incidence of:
  - Retinopathy
  - Nephropathy
  - Neuropathy
  - Cardiovascular disease
  - Hypoglycaemia
  - Diabetic ketoacidosis
  - Treatment-related adverse events
  - Mortality


Cost-effectiveness methods: Model inputs

UK pricelists & literature [1,2]
- Therapy
- Adverse events
- Hypoglycaemia
- Diabetic ketoacidosis
- Long-term complications

DCCT/EDIC, other epidemiological studies & UK-specific life-tables
- Complication risk
- Mortality risk
- HbA1c natural history (+0.045% annually)

Trial specific (DEPICT-1) [4]
- Biomarker changes
- Discontinuation rates
- Adverse event rates
- Hypoglycaemic episodes
- Diabetic ketoacidosis events

Inputs broadly consistent with NICE T1DM guidelines [1]

Cost-effectiveness results: Base case

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Dapagliflozin 10 mg</th>
<th>Incremental</th>
<th>Dapagliflozin 5 mg</th>
<th>Incremental</th>
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</thead>
<tbody>
<tr>
<td><strong>Cost</strong></td>
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<td>£47,987</td>
<td>£5,485</td>
<td>£47,766</td>
<td>£5,264</td>
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<tr>
<td><strong>QALY</strong></td>
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<td>10.75</td>
<td>0.40</td>
<td>10.73</td>
<td>0.38</td>
</tr>
<tr>
<td><strong>Life year</strong></td>
<td>15.65</td>
<td>15.86</td>
<td>0.21</td>
<td>15.85</td>
<td>0.21</td>
</tr>
</tbody>
</table>

**ICER:** £13,792

**ICER:** £13,706

Cost drivers

![Diagram showing cost drivers](image)

QALY drivers

![Diagram showing QALY drivers](image)

Approximate contribution to incremental QALYs versus placebo

Cost-effectiveness results: Sensitivity analysis

Scenario (10 most influential)

![Diagram showing sensitivity analysis for Dapagliflozin 10 mg](image)

![Diagram showing sensitivity analysis for Dapagliflozin 5 mg](image)

69% cost-effective at £20,000 per QALY gained

67% cost-effective at £20,000 per QALY gained
Conclusions

• Based on 24-week results from DEPICT-1, this analysis suggests that at commonly applied UK willingness-to-pay thresholds, dapagliflozin would be a cost-effective adjunct to insulin for people with T1DM whose insulin regimen does not provide sufficient glycaemic control

• Improved glycaemic control is expected to lead to improved patient outcomes and associated cost-offsets; while additional QALY gains may be achieved via weight loss and the avoidance of additional hypoglycaemia events associated with dapagliflozin

Further considerations

• In DEPICT-1, dapagliflozin was associated with reduced insulin dose after adjusting for weight [1] which may be associated with additional cost-offsets not captured in this analysis

• Long-term efficacy and safety: dapagliflozin was well tolerated and reductions in HbA1c and bodyweight were maintained over the 28-week extension period of DEPICT-1 [2]