Evaluating the Impact of Different Payment Models on the Cost-Effectiveness and Budget Impact of Cell and Gene Therapies: Eladocagene Exuparvovec as a Case Study

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Background and objectives

- Cell and gene therapies (CGTs) may benefit patients with severe or rare diseases; however, they face numerous challenges in market access and reimbursement due to high upfront costs and limited clinical evidence. Managed Entry Agreements (MEAs) have emerged as a key negotiation tool to address these challenges.
- Eladocagene exuparvovec, a gene therapy for Aromatic L-Amino Acid Decarboxylase (AADC) deficiency, was selected as a case study based on available clinical data and UK access. This therapy offers a one-time treatment with the potential for durable improvement in motor function.

The objective is to evaluate the impact of different payment models (selected based on literature and feasibility) on the cost-effectiveness and budget impact results.

Methods

Economic modelling:

- A state-transition model was built to assess health outcomes, QALYs and costs for patients with AADC deficiency, comparing eladocagene exuparvovec with best supportive care from a UK payer perspective.
- The model included five motor milestone health states (Figure 1) and was populated using literature.
- A cohort of 30 patients, reflecting the clinical trial population, entered the model at age 4 in the “No motor function” state.
- A lifetime horizon was applied
- Cycle length: 6 months for the first 84 months, followed by annual cycles thereafter.
- Discount rate: 1.5% per year for both costs and QALYs, , in line with NICE’s non-reference-case guidance.
- A five-year Budget Impact Model (BIA) was also developed, aligned with the CEA structure and using the same clinical and economic evidence base.

Figure 1. Model state diagram

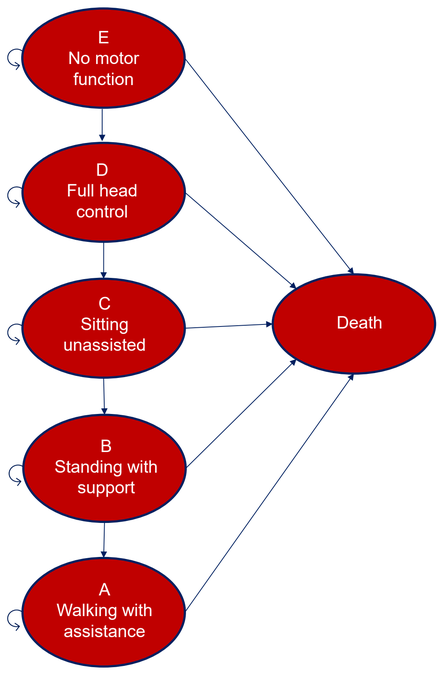


Figure 2. The selected payment models for the case study

Outcome-based payment
- Reimbursement is based on patients' outcomes at month 54
- 50% of gene therapy price will be paid for patients who reach the “sitting” health state, 75% for “standing with support”, and the full price for “walking with assistance”

Annuity payment model
- Reimbursement is performed on an annuity basis with an interest rate (1.5%)
- Full price is being paid in instalments.

Outcome-based instalments
- A first payment of 20% of gene therapy cost is paid for all patients
- Instalments payment over the next 4 years based on the outcome (10% “sitting”, 20% “standing and walking with support” each.

Payment models were selected based on a scoping review performed according to PRISMA guidelines. Selection criteria included frequency of use in Europe and the UK, suitability for one-time, high-cost, long-term therapies, and feasibility within the cost-effectiveness and budget impact models.

Results

CEA

- Eladocagene exuparvovec led to higher costs but substantial gains in life-years and QALYs compared with best supportive care in the base-case up-front payment model (see Table 1). It was not cost-effective.
- Across payment models, **outcome-based and mixed approaches improved cost-effectiveness** relative to upfront payment.
- The **annuity payment model**, although spreading payments over time, resulted in a **higher ICER** than the base-case up-front model due to additional interest costs.
- ICERs remained above common thresholds across all payment models, **though linking payments to outcomes and spreading costs improved cost-effectiveness.**

Table 1. Summary of discounted cost-effectiveness results for three alternative payment models

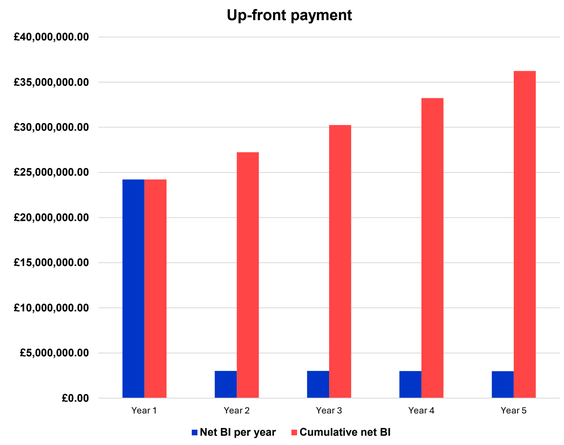
Payment Model	Total Costs gene therapy	Total Costs (BSC)	Incremental Costs	Incremental QALYs	ICER (£/QALY)
Up-front payment	£105.9M	£10.1M	£95.8M	364	**£278,365**
Outcome-based	£60.9M	£10.1M	£50.8M	364	**£147,541**
Annuity	£107.2M	£10.1M	£97.1M	364	**£282,302**
Outcome-based instalments	£58.3M	£10.1M	£48.2M	364	**£139,987**

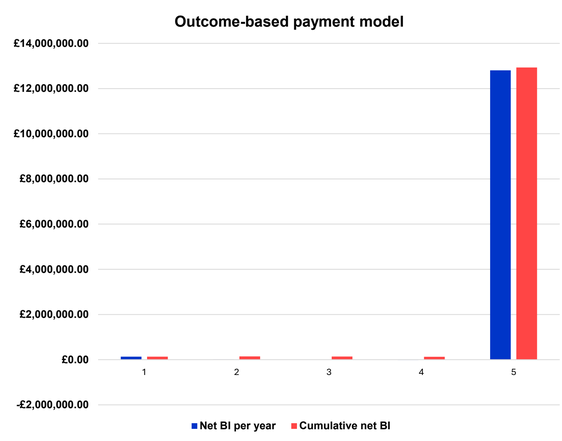
BIA

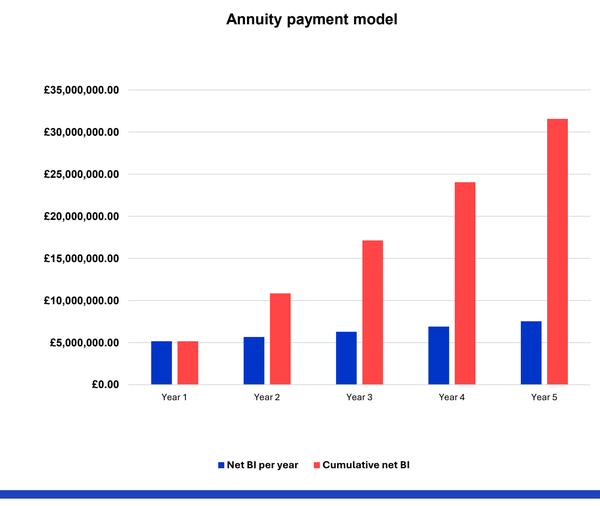
- **Upfront payment:** £24.2 million in Year 1, above NHS affordability threshold.
- **Outcome-based model:** Deferred most costs to Year 5 (£12.8 million).
- **Annuity model:** £5.2 million in Year 1, highest 5-year total (£31.6 million).
- **Mixed model:** £5 million in Year 1, total £15 million.

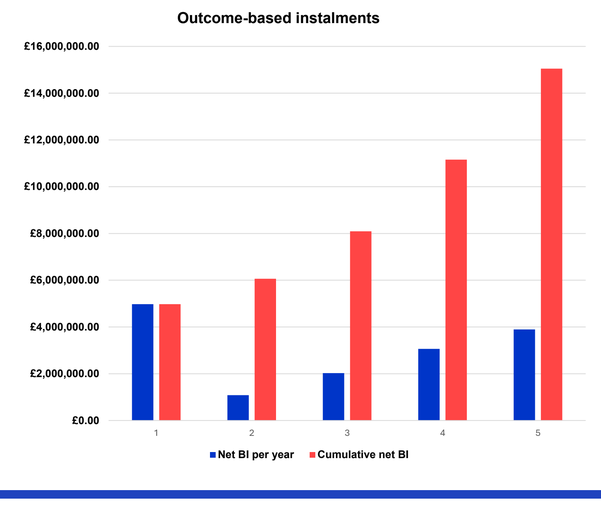
Overall, outcome-based and staged models eased early budget pressure, with annuity and mixed models offering the best balance (Figure 3).

Figure 3. The net budget impact and cumulative budget impact per different payment models









Conclusion

- This case study found the outcome-based instalments model to be the most favourable in terms of **financial sustainability** and **payer value**. It balances the **interests of both payers and manufacturers**.
- Although ICERs remained above common thresholds, these findings demonstrate that innovative payment models can influence the economic evaluation of CGTs and **should be considered in reimbursement planning.**

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