Cost-Effectiveness of the PPARγ Modulator N-acetyl-GED-0507-34-LEVO (NAC-GED 5%) versus benzoyl peroxide-adapalene for moderate-to-severe acne

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BACKGROUND

> Acne vulgaris is a highly prevalent dermatology condition, and the 8th most common disease worldwide, affecting approximately 85% of persons aged 12 to 25. It can substantially impact an individual's quality of life, self-esteem, and psychological well-being. Cost-effective treatments help make acne management more accessible to a wider range of patients. Acne management often requires long-term treatment and follow-up. Cost-effective treatments can reduce the financial burden on individuals and healthcare systems, making it more sustainable to provide care to a larger number of patients.

OBJECTIVE

> This study explored the potential cost-effectiveness and associated economically justifiable price (EJP) of N-acetyl-GED-0507-34-LEVO (NAC-GED 5%) versus benzoyl peroxide (BPO)+adapalene and other available treatments for moderate-to-severe acne vulgaris from the perspective of the United Kingdom's (UK) National Healthcare Services (NHS).

METHODS

> An early decision-analytic model (see Figure 1) was developed based on a previous cost-effectiveness analysis (CEA) by Mavranezouli et al. (2022)[1] that informed the National Institute for Health and Care Excellence (NICE) guidelines for acne management.

> The early CEA of NAC-GED 5% was based on Phase II randomized clinical trial (RCT) results[2] and was designed to estimate health outcomes and costs related to acute acne treatment. Except for oral isotretinoin, all the treatments included in the CEA are assumed to be administered over 3 months for acute treatment, followed by maintenance treatment for 1 month. The model considered a 1-year time horizon and evaluated the cost-effectiveness of NAC-GED 5% compared to BPO+adapalene and other available treatments in patients aged 9 years and above.

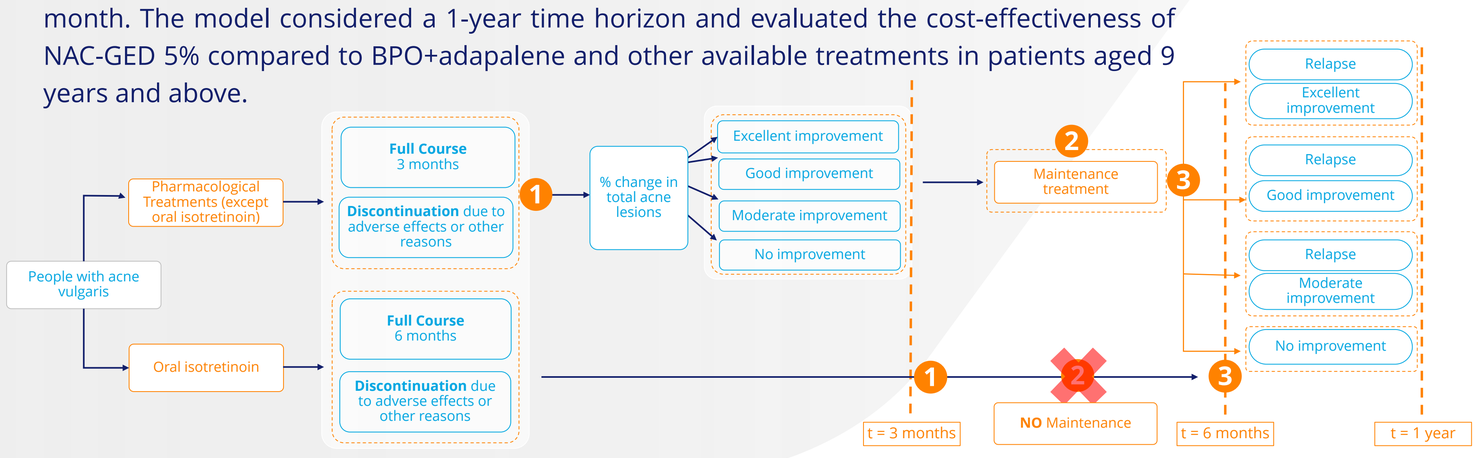


Figure 1: Schematic diagram of the economic model structure

> Relative effects on efficacy were measured as a percentage change in total acne lesion count from baseline (%CFB), discontinuation due to any reason, and discontinuation due to side effects, and were obtained from the NICE-informed CEA model that was based on the source network meta-analysis (NMA) based on Phase III results of applicable treatments. Since NAC-GED 5% was not included in the NMA undertaken by the NICE, the relative efficacy of NAC-GED 5% in relation to adapalene was assumed to be equal to the absolute efficacy from the clinical trial, and the assumption was tested in a sensitivity analysis. Hence, it is a naïve comparison.

> Three scenarios were explored based on the efficacy, and the corresponding utilities were leveraged from the NICE-established CEA model (See Table 1).

> The base case analysis was conducted from the National Health Service (NHS) perspective in the UK and included treatment costs, such as drug costs, administration, and monitoring, other health service resource use costs associated with managing the disease (e.g., GP visits, hospital admissions), and costs of managing adverse events caused by treatment. Intervention resource use was leveraged from the NICE-informed CEA model while the unit costs were obtained from national sources and other published literature.

> Expert interviews validated the model's inputs, assumptions, and results. The EJP for NAC-GED 5% was calculated to meet the willingness-to-pay (WTP) threshold of £20,000 per quality-adjusted life year (QALY).

Acne Health State	Perceived Improvement	Moderate-to-severe Acne
Health states relating to %CFB		
71.26%–100% reduction in acne lesions	Excellent	0.94
53.14%–71.26% reduction in acne lesions	Good	0.87
28.20%–53.14% reduction in acne lesions	Moderate	0.79
< 28.20% reduction or any % increase in acne lesions	None	0.72
Other health states		
Baseline (start of model)	NA	0.72
Reduction in utility due to intolerable side effects	NA	−0.07

Table 1: Relationship between percentage change in total acne lesion count from baseline, perceived acne improvement and utility value.

RESULTS

> Based on the WTP of £20,000 per QALY, an EJP of **£59 per tube** was calculated for **NAC-GED 5% relative to BPO+adapalene**. Over the one-year time horizon, at this EJP, treatment with NAC-GED 5% was associated with a **total cost of £181 per month**. NAC-GED 5% was found to be **cost-effective relative to the majority of topical and oral monotherapies and topical treatment combinations.** NAC-GED 5% yielded **comparable incremental utility relative to clindamycin** but resulted in a higher incremental cost of treatment at the calculated EJP.

> **NAC-GED 5%** demonstrated **incremental utility relative to low-dose oral isotretinoin (<120 mg/kg),** mainly due to a **quicker onset of action** and **enhanced tolerability**, reflected in its **lower relative discontinuation rates.** Hence, **NAC-GED 5%** was found to be **cost-effective relative to low-dose oral isotretinoin.**

> **At the calculated EJP, NAC-GED 5% yielded incremental cost relative to high-dose oral isotretinoin (>120 mg/kg) mainly due to a higher drug cost**, and a higher proportion of on-treatment patients reflected in its **lower relative discontinuation rates.** However, **high-dose oral isotretinoin** exhibited **incremental utility gain attributing to its superior efficacy.**

> The **deterministic sensitivity analysis** (Figure 3) demonstrated that, as expected, the **key driver** of the incremental cost-effectiveness ratio (ICER) was the **efficacy of NAC-GED 5%** which varied between moderate and excellent improvement (the base case assumed good improvement). The other factors driving the ICER were the **discontinuation rates for BPO+adapalene, followed by the good improvement utility**.

Figure 2 : Cost-effectiveness plane

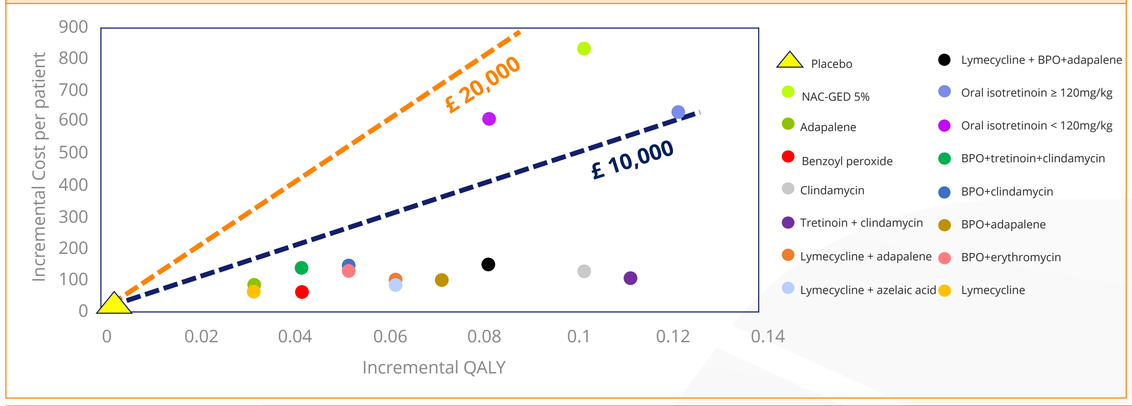
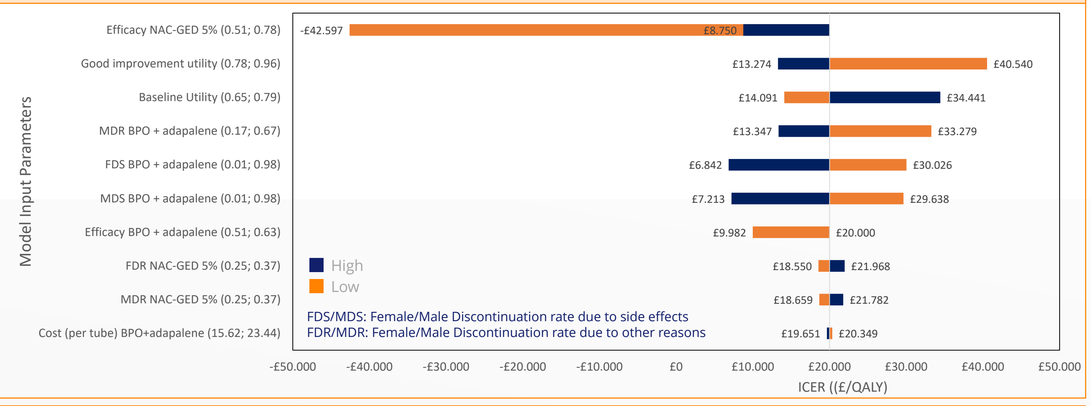


Figure 3: Tornado Plot (ICER) Base case: NAC-GED 5% vs BPO+Adapalene



LIMITATIONS:	> Lack of head-to-head trial results	> Naïve comparison on relative efficacy of NAC-GED 5% vs adapalene	> Short time horizon (1 year)	> The impact of scarring is excluded from this analysis due to lack of comparable evidence across treatment options

CONCLUSION

> This early CEA examined the relative cost-effectiveness of NAC-GED 5%, based on Phase II[2] RCT results, relative to a range of treatment options for moderate-to-severe acne vulgaris. NAC-GED 5% showed favorable results in acne improvement and cost-effectiveness, with good efficacy and lower discontinuation rates implying better tolerability, as compared to BPO+adapalene as well as low-dose oral isotretinoin. The efficacy of NAC-GED 5% needs to be confirmed in a Phase III RCT.

> It is unlikely that the efficacy of all treatment options considered in this analysis will be evaluated in a head-to-head Phase III RCT. Therefore, there is a need to update the existing indirect treatment comparison (ITC) by including the results from NAC-GED 5% upcoming Phase III RCT to compare acne management treatments and enhance the accuracy of future cost-effectiveness assessments.

> Although widely used as an objective endpoint in clinical trials, %CFB might inadequately capture utility in different health states of the disease. Patients with mild-to-moderate acne benefit more from small %CFB improvements compared to those with severe acne, as the latter may still have a significant number of lesions even after 'excellent' %CFB reduction and are at higher risk of scarring. Future economic models should aim to incorporate the consequences of scarring for the quality of life of acne vulgaris patients.

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