

1 **SUPPLEMENTARY APPENDIX**

2 *Table 1. Summary of the evidence matrix used in the study.*

Domain	Criterion	Summary of evidence
Need for intervention	Disease severity	Dry eye disease (DED) is a chronic, multifactorial ocular surface disorder characterised by tear film instability and inflammation. While not directly affecting life expectancy, it induces significant ocular morbidity, presents potential vision-threatening complications, and substantially impairs both patient quality of life and daily functioning.
	Size of the affected population	DED represents a significant global health burden, with prevalence rates ranging from 5% to 50% internationally and 11% to 30% within Europe. Epidemiological data indicate that the disease is heavily skewed towards older demographics and female populations; however, a notable epidemiological shift reveals a rising incidence among younger age groups.
	Unmet needs	Current unmet clinical needs in DED encompass more efficacious and well-tolerated therapies, enhanced drug delivery systems, and a more rapid onset of action for ciclosporin-based formulations. Furthermore, there remains a critical requirement for standardised diagnostic tools and biomarkers, alongside patient-centred approaches that address quality of life, treatment adherence, and healthcare accessibility.
Type of benefit of intervention	Type of therapeutic benefit	There is currently no cure for DED, and available treatments mainly provide symptomatic relief without addressing underlying inflammation. In this context, ciclosporin-based therapies have demonstrated benefits in improving tear production, reducing ocular surface damage, and targeting the inflammatory component of the disease.
Knowledge about intervention	Quality of evidence	Robust clinical evidence from randomised, double-masked, vehicle-controlled, multicentre trials establishes the therapeutic efficacy and safety profile of ciclosporin-based interventions in the adult DED population. Data from these cohorts reveal statistically significant improvements in objective ocular parameters, namely tear secretion and ocular surface integrity, alongside acceptable tolerability. The studies were considered methodologically robust, with clearly defined endpoints and appropriate statistical analyses, supporting the validity and clinical relevance of the findings.
	Expert consensus/clinical practice guidelines	In accordance with the updated, phenotype-based management paradigm established in the TFOS DEWS III consensus report, the administration of ciclosporin is indicated upon clinical confirmation of inflammation or immune dysregulation acting as the definitive pathophysiological driver.

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