

Determining value and the contribution of ciclosporin-based therapies in dry eye disease: a European expert MCDA pilot study

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ABSTRACT

Introduction: Dry eye disease (DED) is a multifactorial, immune-mediated inflammatory condition affecting the ocular surface and lacrimal glands. Multiple ciclosporin-based therapies with different formulations are currently available in Europe, although clear guidance on their optimal use remains limited. The aim of this study was to determine the main unmet needs and the current management landscape of ciclosporin-based therapies, from the perspective of clinical experts using multi-criteria decision analysis (MCDA).

Methods: A systematic literature review was conducted to gather evidence for each of the MCDA framework criteria. An international expert panel of seven clinical specialists in DED from four European countries independently weighted the criteria and scored the non-comparative criteria in the evidence matrix. Results were presented and discussed in a group online session.

Results: DED is a highly prevalent, chronic inflammatory disease associated with significant visual and functional burden. Its management is not uniform and often involves a stepwise approach. Recent ciclosporin-based treatment alternatives address some unmet needs; however, others—such as the need for greater standardization of diagnostic tools and improved objective markers of inflammation—remain to be addressed. Highest importance was assigned to Efficacy/effectiveness (4.7 ± 0.5), Quality of evidence (4.7 ± 0.5), and Safety/tolerability (4.6 ± 0.5) criteria, highlighting the relevance of treatment-related outcomes in clinical decision-making.

Conclusions: The expert opinion, based on MCDA, enabled the identification of key value drivers and unmet needs in the current management of DED based on ciclosporin-based therapies. These early insights may contribute to promoting future work to support informed, evidence-based decision-making.

Keywords: Ciclosporin, Dry eye disease, Multi-criteria decision analysis

Introduction

According to the TFOS DEWS II definition (1), dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by a loss of tear film homeostasis,

accompanied by ocular symptoms, in which tear film instability, hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play key aetiological roles.

The most recent TFOS DEWS III report (2) classifies DED into aqueous-deficient and evaporative forms, which frequently coexist, with increasing recognition of mixed disease and the role of neurosensory abnormalities as key contributors to disease heterogeneity. Symptoms are widely varied, including vision-related impairment and ranging from irritation and a foreign body sensation to more severe manifestations such as visual fatigue and corneal ulcers, all of which can markedly impair patients' quality of life (1,3).

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In Europe, DED affects approximately 11–30% of the population. It is more prevalent among women, and its incidence increases with age (2,4,5). However, a 2025 study conducted in Spain reported a 22.5% prevalence of DED symptoms among young adults aged 18–29 years, highlighting that DED is not limited to older populations (6).

Traditionally, management of DED has followed a stepwise approach, in which patients progressed through sequential levels of therapy according to disease severity. This strategy typically began with environmental modifications, lid hygiene, and first-line use of artificial tears. In moderate to severe cases, particularly when initial measures prove insufficient, treatment escalated to anti-inflammatory agents such as topical corticosteroids and topical ciclosporin (7).

Following the publication of the recent TFOS DEWS III report (2), the therapeutic paradigm has shifted towards an aetiology-driven model. The current management approach focuses on identifying each patient's specific disease drivers (such as tear film instability, meibomian gland dysfunction or aqueous deficiency, among others) and selecting targeted interventions accordingly.

Among the immunomodulators that may be necessary in DED non-responsive to conventional approaches, long-term application of topical ciclosporin is often acknowledged as an appropriate option, alongside other anti-inflammatory agents such as lifitegrast. Ciclosporin is a calcineurin inhibitor that suppresses T-cell activation by inhibiting interleukin-2 production, thereby reducing ocular surface inflammation and contributing to the restoration of tear film stability and symptom relief (8). In the updated therapeutic framework proposed by TFOS DEWS III, ciclosporin is recommended when inflammation or immune dysregulation is identified as a primary disease driver (2). Several topical ciclosporin A (CsA) formulations are available globally for the management of DED, thereby expanding the therapeutic options available to clinicians. However, market- and region-specific obstacles exist, such as limitations in cost reimbursement, pricing, different decision-making processes, and evaluation of clinical indication, all influencing medical professionals' pharmacological management of DED.

Multi-Criteria Decision Analysis (MCDA) provides a methodological framework for determining what represents value in a given medical condition. It allows consideration of all criteria relevant to healthcare decision-making in a transparent, systematic manner, and from the perspective of key stakeholders. MCDA methodology is already being used internationally to support decision-making across various healthcare contexts (9–11).

The aim of this pilot study was to apply MCDA methodology to guide discussion, identify key unmet needs, and determine what represents value in the current landscape of ciclosporin-based therapies in DED from the perspective of European experts.

Methods

Study design

The study was designed following published good methodological practices (12,13) on the field-tested 'Evidence and

Value: Impact on Decision Making' (EVIDEM) MCDA framework (version 4.0) (11). The EVIDEM framework stimulates structured reflection from stakeholders through a set of 13 quantitative criteria grouped into five domains (CORE Model), regarding the need for intervention (three criteria), the comparative outcomes of the intervention (three criteria), the type of benefit of the intervention (two criteria), the economic consequences of the intervention (three criteria), and the knowledge about the intervention (two criteria). Additionally, the EVIDEM framework includes seven generic criteria to tailor the framework to the context of decision-making (contextual tool).

For the purpose of this pilot study, the framework was adapted as follows. The quantitative criterion type of preventive benefit was excluded, as it was not considered applicable to DED. In addition, all contextual criteria (Mandate and scope of healthcare system, population priorities and access, common goal and specific interests, environmental impact, system capacity and appropriate use of intervention, political, historical & cultural context, and opportunity costs and affordability) were omitted, as they are country-specific and therefore not applicable to the study's pan-European scope.

The proposed modifications were reviewed, discussed, and accepted by all the experts. The resulting adapted MCDA EVIDEM framework used in our pilot study ultimately comprised 12 quantitative criteria, with their subcriteria, as shown in Table 1.

Panel design and MCDA methodology training

The expert panel consisted of seven ophthalmologists, experts in DED, from four European countries (one from France, three from Germany, one from Spain, and two from the United Kingdom). Participants were selected as key opinion leaders in the management of DED within their respective countries, being prominent members of the scientific community, authors of publications on the subject, and investigators in DED clinical trials.

As part of the study, an online training session was conducted in May 2025, providing a detailed explanation of MCDA methodology and its interpretation.

Literature review and evidence matrix generation

A systematic literature review was conducted between March and April 2025 to retrieve relevant information for each of the MCDA framework criteria assessed. Evidence was obtained from major biomedical literature databases (PubMed/Medline and Cochrane), including articles published in English or Spanish, with no time restrictions. It was complemented with information obtained from grey literature sources, including Google Scholar, clinical practice guidelines, and the official websites of scientific societies and European healthcare evaluation bodies. Selection of studies to be included in the literature review was conducted based on predetermined inclusion and exclusion criteria (Table 2).

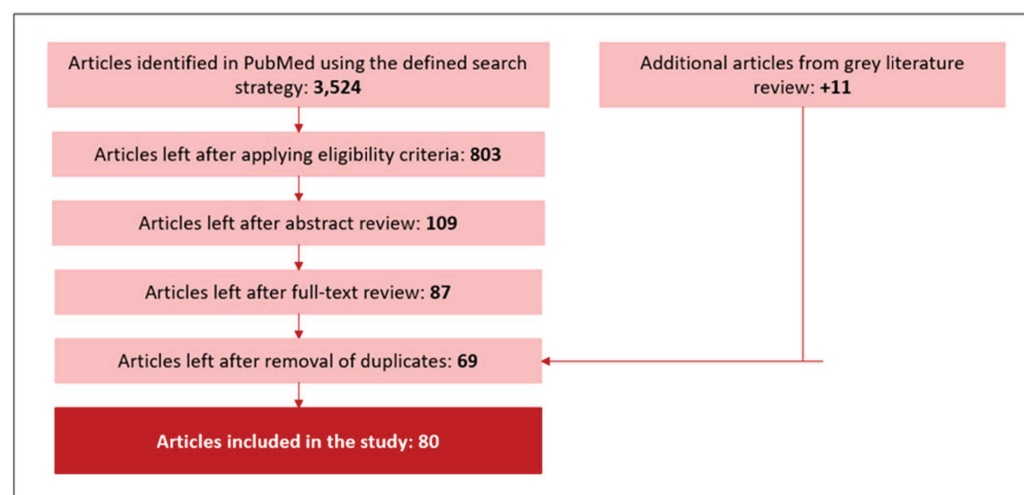
Retrieved publications were screened in two phases: abstract review and full-text review. Articles not meeting the predefined eligibility criteria were excluded at each stage. After removing duplicates, 80 documents that met the eligibility criteria were included in the literature review (Fig. 1).

TABLE 1 - Adapted MCDA EVIDEM framework used in this pilot study

QUANTITATIVE CRITERIA	
Criteria	Subcriteria
NEED FOR INTERVENTION	
Disease severity	• Effect of disease on life expectancy • Effect of disease on morbidity (includes disability and function) • Effect of disease on patients' quality of life
Size of affected population	• Prevalence • Incidence
Unmet needs	• Unmet needs in efficacy • Unmet needs in safety • Unmet needs in patient-reported outcomes • Patient demand
COMPARATIVE OUTCOMES OF INTERVENTION	
Comparative efficacy/ effectiveness	• Magnitude of health gain • Percentage of the target population expected to obtain the health gain • Onset and duration of health gain
Comparative safety /tolerability	• Adverse events • Serious adverse events • Fatal adverse events • Short-term safety • Long-term safety • Tolerability
Comparative patient-reported outcomes (PROs)	• Improvement in health-related quality of life • Convenience/ease of use/mode of administration
TYPE OF BENEFIT OF INTERVENTION	
Type of therapeutic benefit	• Symptom relief • Clinical course modification (disease interruption/progression slowing) • Cure or life prolongation
ECONOMIC CONSEQUENCES OF INTERVENTION	
Comparative cost consequences: cost of intervention	• Net cost of intervention • Acquisition cost • Implementation/ maintenance cost
Comparative cost consequences: other medical costs	• Impact on primary care expenditures • Impact on hospital care expenditures • Impact on long-term care expenditures
Comparative cost consequences: other non-medical costs	• Impact on productivity • Financial impact on patients • Costs to the wider social care system
KNOWLEDGE ABOUT INTERVENTION	
Quality of evidence	• Validity • Relevance • Completeness of reporting • Type of evidence
Expert consensus / clinical practice guidelines	<i>NOTE: No subcriteria are applicable in this criterion</i>

TABLE 2 - Eligibility criteria for studies to be included in the literature review

Inclusion criteria	Exclusion criteria
- Articles related to DED and the EVIDEM framework criteria. - Articles on studies involving adult patients. - Articles published in peer-reviewed journals. - Articles reporting randomized controlled trials. - Systematic reviews and meta-analyses. - Observational studies (cohort, case-control, cross-sectional). - Articles published in English or Spanish. - Articles available in full text.	- Duplicate articles. - Articles that mention DED but focus on other pathologies. - Articles on studies involving pediatric or adolescent patients. - Articles related to animal studies or in vitro research. - Case reports, editorials, and opinion pieces. - Articles published in languages other than English or Spanish. - Articles not available in full text.

**FIGURE 1** - PRISMA flow diagram of study selection.

The retrieved information was organized in a descriptive, summarised, and structured way and used to populate the MCDA framework criteria (shown in Table 1) organized within the evidence matrix. This was later reviewed and validated by one of the participating experts.

Criteria weighting

Weights represent the trade-off between criteria. Experts were instructed to assign weights to each of the 12 criteria of the MCDA framework to express their individual perspective on their relative importance.

A direct rating scale (DRS) was used, where each participant assigned a relative weight per criterion using a non-hierarchical simple 5-point scale (1 = lowest relative importance, 5 = highest relative importance) (11). Subcriteria within each criterion were assessed qualitatively.

The weighting exercise was distributed by email to all participants, and each criterion was independently weighted by the expert panel in May 2025.

Matrix scoring

The scoring exercise, including the evidence matrix, was distributed by email and completed independently by each participant in May 2025, prior to group discussion of results.

Evidence matrix scoring was performed only for the six non-comparative criteria (disease severity, size of the affected population, unmet needs, type of therapeutic benefit, quality of evidence, and expert consensus/clinical practice guidelines), while the six comparative criteria (efficacy/effectiveness, safety/tolerability, patient-reported outcomes, cost of intervention, other medical costs, and non-medical costs) were excluded from the exercise.

This approach was selected because the objective of the study was to capture expert perspectives on ciclosporin-based therapies as a therapeutic class in the management of DED, rather than to evaluate or compare specific products. Therefore, comparative criteria were not considered applicable within the scope of this study.

As per the weighting exercise, the six non-comparative criteria were rated on an ordinal scale ranging from 0 to 5, with higher values indicating greater perceived contribution of value. Experts were instructed to score each criterion individually, based on both the information provided in the evidence matrix and their own experience and judgment.

Validation of the completed exercises was carried out to ensure that all criteria were weighted and scored correctly, accompanied by the corresponding rationale behind the scoring.

Data analysis

Individual weighting and scoring results from each participant were collected, transferred to a common database, and analyzed using Microsoft Excel software. Descriptive analyses were performed to calculate the mean, median, minimum, and maximum values and standard deviations for both weights and scores corresponding to each framework criterion.

Discussion meeting

An online expert group discussion was held in June 2025 with all study participants to present and discuss the weighting and scoring results and the reasoning behind the weights/scores of each criterion.

During the session, experts took turns explaining the rationale behind their assessments, sharing their perspectives, and engaging in an open discussion with the rest of the group.

During the session, experts were given the opportunity to modify their scores if their opinion changed after considering the contributions and perspectives shared by their colleagues (re-scoring). However, no changes to the scores/weights were made.

Results

Criteria weighting

Participants assigned the highest weights to the Efficacy/effectiveness of treatment (4.7 points $\pm$ 0.5 SD), Quality of evidence for treatment (4.7 points $\pm$ 0.5 SD), and Safety/tolerability of treatment (4.6 points $\pm$ 0.5 SD) criteria. During the discussion, experts indicated that these treatment-related aspects were key characteristics of a “good” therapy in DED. Participants highlighted the strength and robustness of the available evidence as important considerations both for clinicians when selecting treatments and for health authorities when evaluating and approving new products. Efficacy and safety were considered particularly relevant by the experts for current ciclosporin-based therapies, as participants indicated that the decision to prescribe a new formulation largely depends on its proven effectiveness, rapid onset of action, and tolerability profile. Ciclosporin represents a standard-of-care treatment in DED not controlled by artificial tears alone (4). Early initiation of anti-inflammatory therapy in patients

with DED is recommended to break the vicious cycle of pathophysiology (4). Developing an effective delivery system for ciclosporin has posed significant challenges. New alternatives (i.e., NCELL (14) and NovelEyeSol (15)) have recently become available, presenting advantages with regard to bio-availability of the active ingredient versus emulsion formulations (16). Several experts reported that, in their experience, long-term adherence to treatment among DED patients is often limited if the patient perceives that symptomatic relief does not occur early enough and side effects, such as stinging upon instillation, reduce tolerability. In this context, preservative-free formulations were viewed favourably by the experts, as preservatives may further compromise ocular surface integrity and negatively affect tolerability in susceptible patients, particularly during long-term treatment.

The lowest weights were assigned to the criteria Non-medical costs (3.3 points $\pm$ 0.8 SD), Type of therapeutic benefit (3.3 points $\pm$ 0.8 SD) and Other medical costs (3.4 points $\pm$ 0.8 SD). Some experts indicated that, although costs are relevant to both patients and payers, they considered them secondary to clinical outcomes when determining therapeutic value. Similarly, the type of therapeutic benefit was regarded by the experts as less important than the overall efficacy outcomes in terms of symptom relief and improvements in vision.

Detailed criteria weighting results are shown in Figure 2.

Several criteria showed higher dispersion values (i.e., showing differences in weighting among the participating experts): Unmet needs, Size of the affected population, Type of therapeutic benefit, and the three economic criteria (Cost of intervention, Other medical costs, and Non-medical costs).

Regarding unmet needs (4.1 points $\pm$ 1.2 SD), experts who assigned greater weight to this criterion justified their scoring by indicating that widely available existing treatments (e.g., artificial tears) primarily address symptoms rather than the underlying cause of the disease. These experts highlighted the need for greater availability and use of therapies targeting the pathophysiological mechanisms driving DED (e.g., ciclosporin-based therapies), with adequate safety and efficacy for long-term use. In contrast, other experts considered this criterion less relevant, given the existence of current ciclosporin-based treatments with a good bioavailability profile and in line with clinical practice guideline recommendations that, in their view, adequately address the main clinical manifestations of the disease. Among the unmet needs identified by the experts were the availability of reliable biomarkers

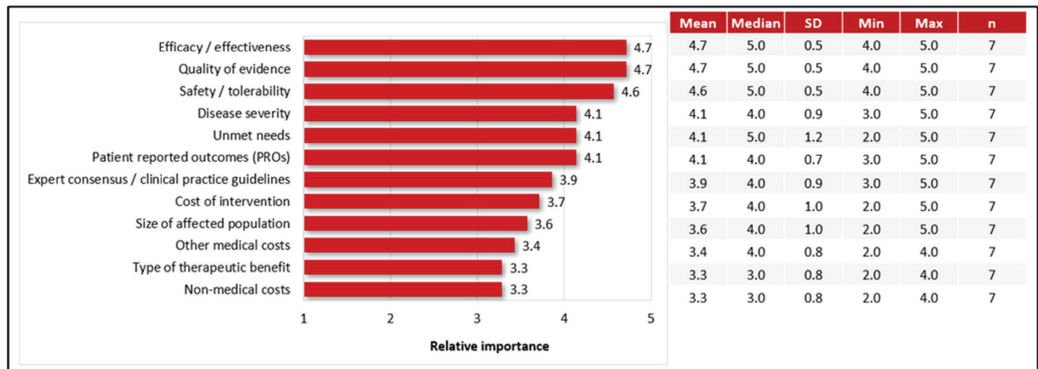


FIGURE 2 - Quantitative criteria weighting results. SD = standard deviation; Min = minimum; Max = maximum; n = number of experts.

of inflammation to guide treatment decisions, assess therapeutic response, and monitor disease progression. The need for clear clinical and molecular criteria to reliably stratify patients according to disease severity was also highlighted by the experts.

Differences in experts’ weighting were also observed for the criterion Size of the affected population (3.6 points ± 1.0 SD). Some experts highlighted the high prevalence of DED (affecting 11-30% of the population in Europe (4)) and noted that, in their view, current lifestyle factors are contributing to its increasing occurrence among younger patients. These experts considered the large number of patients to represent a substantial burden on healthcare systems, as DED often requires long-term follow-up, repeated consultations, and continuous treatment adjustments (17,18). They also noted that the variability in disease presentation and severity within such a broad patient population complicates diagnosis and standardization of care across clinical settings. However, other experts assigned less importance to this criterion, noting that the proportion of patients with severe forms of the condition remains relatively small. Experts also highlighted the importance of managing the disease from its early stages to prevent and/or slow down disease progression.

Similarly, views diverged on the Type of therapeutic benefit (3.3 points ± 0.8 SD). For some experts, aspects such as symptom relief and improvements in visual function were key drivers of what represents value in DED, as they considered these outcomes relevant to better adherence and long-term treatment persistence. Others, however, placed less emphasis on these symptomatic outcomes, prioritizing instead broader measures of clinical efficacy, such as the ability of a therapy to modify disease progression or to address underlying inflammatory mechanisms. In this respect, experts viewed favourably the availability of new treatment alternatives aimed at slowing or preventing disease progression.

Finally, substantial variation across experts was also noted for the economic criteria – namely, Cost of intervention (3.7 points ± 1.0 SD), Other medical costs (3.4 points ±

0.8 SD), and Non-medical costs (3.3 points ± 0.8 SD). Experts who assigned lower weights to these criteria indicated that, in their view, cost considerations play a secondary role when clinical outcomes are clearly favourable. Conversely, those who attributed higher importance to economic criteria considered costs to be particularly relevant both for patients and health authorities. These experts noted that, for patients, high treatment costs can hinder long-term adherence and persistence, negatively impacting outcomes, while for health authorities they may represent a significant barrier to granting access to new therapies.

Matrix scoring

Scores obtained for the disease-related criteria and the non-comparative treatment-related criteria are presented in Figures 3 and 4, respectively.

DED was considered a severe disease (4.0 points ± 0.6 SD), with experts highlighting its impact on vision, quality of life, and work productivity. It was also viewed as highly prevalent and growing (3.9 points ± 1.2 SD), with experts noting the associated challenges for long-term management. Experts highlighted numerous unmet needs (4.3 points ± 0.8 SD), including the lack of clear clinical and molecular criteria to distinguish between moderate and severe forms of DED and the absence of reliable biomarkers of inflammation.

New ciclosporin-based therapies were considered to potentially provide a meaningful therapeutic benefit (3.3 points ± 0.8 SD), with experts highlighting their potential to reduce ocular surface inflammation and slow disease progression. The quality of the evidence was rated as high (3.9 points ± 0.7 SD), with experts highlighting the availability of robust clinical data for recently introduced ciclosporin-based therapies. The use of ciclosporin-based therapies was viewed as broadly aligned with current expert recommendations and clinical practice guidelines (3.1 points ± 2.0 SD), although expert opinions varied regarding treatment initiation and duration.

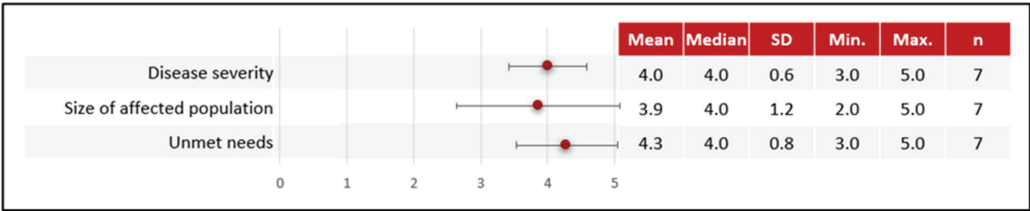


FIGURE 3 - Disease-related criteria scoring results. SD = standard deviation; Min = minimum; Max = maximum; n = number of experts. The dots represent the mean scores.

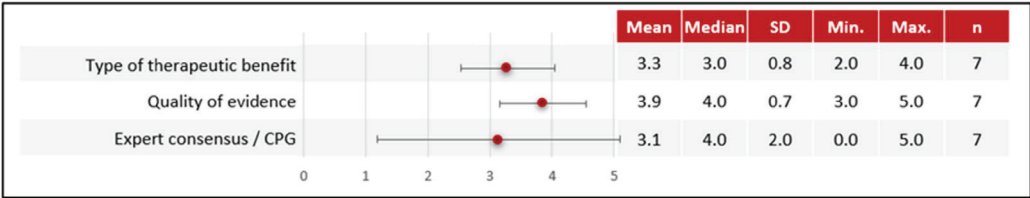


FIGURE 4 - Non-comparative treatment-related criteria scoring results. SD = standard deviation; Min = minimum; Max = maximum; n = number of experts. The dots represent the mean scores.



Discussion

Drawing on the insights from this pilot study, the expert panel emphasized several key aspects regarding the burden and clinical impact of DED. Although DED does not directly reduce life expectancy, experts considered it a severe disease due to its substantial impact on vision, quality of life, work productivity, and overall daily functioning. As a complex, chronic, and progressive inflammatory condition, DED is associated with persistent ocular surface inflammation that can cause corneal and conjunctival damage. In its more advanced stages, this ongoing inflammation may lead to irreversible structural alterations, serious corneal complications, and ultimately impaired vision (19). While severe cases account for only a small proportion of the overall patient population, DED is highly prevalent, largely driven by modern lifestyle factors, and is increasingly affecting younger individuals (6). Therefore, early diagnosis and management are crucial to prevent and/or slow down disease progression (20,21). From a clinical perspective, improving corneal and conjunctival staining is essential to control disease progression and prevent long-term ocular surface damage (2). Consequently, treatments with a rapid onset of action are particularly valued, as early control of underlying inflammation is critical for improving both signs and symptoms (2).

Consistent with current literature, multiple unmet needs remain in the management of moderate-to-severe DED (22–24). These include the absence of treatments with an optimal tolerability profile and a faster onset of action than current options. Evidence from real-world clinical practice with current ciclosporin-based therapies suggests that tolerability may be better than that reported in clinical trials and that the onset of action may be shorter in some patients. Nevertheless, further improvements are necessary to optimize patient experience and treatment outcomes (25,26). Additional unmet needs include the need for greater standardization of diagnostic tools and improved objective markers of inflammation (27,28). Although ocular surface inflammation is recognized as a key feature of DED, no reliable biomarkers are currently available to guide treatment decisions, assess therapeutic response, or monitor disease progression. The need for clear clinical and molecular criteria to stratify patients by disease severity was also highlighted by the experts, as current distinction between moderate and severe DED remains insufficiently standardized.

Another critical unmet need involves patient adherence, which remains suboptimal due to the delayed onset of action of ciclosporin-based emulsion therapies. In this context, innovative formulations that enhance targeted ciclosporin penetration and offer a faster onset of action are viewed favourably, as they may improve early symptom control and contribute to sustained treatment adherence. Furthermore, preservative-free formulations minimize potential interference with the therapeutic effects of the active substance and are associated with better tolerability.

Despite the widespread use of topical ciclosporin A, clear criteria for initiating therapy are currently lacking, and treatment duration remains highly variable in clinical practice. These findings, aligned with the recent TFOS DEWS III report (2), underscore the expert panel's call for future consensus

documents to harmonize definitions and standardize clinical practice across Europe.

According to clinical practice guidelines, ciclosporin is recommended when inflammation or immune dysregulation is identified as a primary disease driver (2); furthermore, new formulations have recently been approved in Europe (14,15,29). However, comparing their efficacy and safety/tolerability profiles remains difficult due to substantial heterogeneity in study designs and patient populations. Experts agreed that topical ciclosporin A offers potential therapeutic benefit in slowing or preventing disease progression. Nonetheless, additional real-world data and broader clinical experience with new ciclosporin-based products are required to adequately assess their long-term therapeutic value. According to expert opinion, tolerability plays a crucial role in adherence, as pain and discomfort at the instillation site are recognized as major factors influencing long-term use.

Clinical evidence on patient-reported outcomes (PROs) remains limited, hindering comparisons between available products. Improvements in symptoms—such as ocular dryness and the frequency of episodes of dryness flares—are particularly relevant to patients' quality of life. Furthermore, both patient adherence and treatment effectiveness are heavily influenced by tolerability. Hence, the choice of formulation should be carefully weighed. Finally, treatment cost represents another critical factor influencing patient long-term adherence, as lower costs may facilitate better compliance by enabling patients to maintain therapy in the long term.

One of the main strengths of this study lies in the use of the MCDA methodology, which enabled each criterion to be systematically evaluated in a transparent and objective way. MCDA is a globally standardized tool for expert panels to unify criteria on disease management and the prioritization of unmet needs (13). Utilizing a standardized, healthcare-specific, reflective, and deliberative MCDA framework—such as EVIDEM—presents a robust foundation for developing models tailored to specific diseases and national regulatory contexts (11,30).

The exchange of opinions among experts further enriched individual analyses and assessments. However, this pilot study also presents certain limitations, including the relatively small number of experts involved, as reported in similar studies (11,31,32). The small panel size was intentionally chosen to facilitate in-depth discussion and exchange of perspectives, allowing for a more comprehensive exploration of the different value criteria and identifying areas of discrepancy across experts that could represent an opportunity for future work in reaching consensus. On the other hand, the limited number of experts, representing four European countries, may not fully capture the diversity of clinical perspectives and practice patterns across Europe and therefore limits the representativeness of the findings to a broader pan-European context. The results should therefore be interpreted as exploratory and as reflecting the perspectives of the participating expert panel.

Drug evaluation and decision-making frameworks across Europe closely align with Multi-Criteria Decision Analysis (MCDA/EVIDEM) methodology (10,11). These processes entail synthesizing scientific evidence through systematic literature reviews, assessing multiple criteria for drug appraisal,

and drafting technical reports to guide final decision-making. Crucially, ethical considerations underpin both the evaluation phase and the subsequent decision-making process. Nevertheless, certain limitations persist. Future initiatives encompassing a broader expert panel and integrating the perspectives of additional stakeholders – including patients, healthcare evaluators, and payers – are warranted to validate and extend the insights from this pilot study, thereby fostering a comprehensive understanding of value definitions in DED. This methodological approach is well-documented in the literature; prior studies have either adopted a single-stakeholder perspective, focusing strictly on patients (33–36) or evaluation agencies (37–40), or employed a multidisciplinary, multi-stakeholder MCDA framework that simultaneously incorporates patients, physicians, and other key actors.

Furthermore, because the limited availability of published literature may have constrained the current findings, these outcomes should be re-evaluated as new evidence becomes available.

The field of ophthalmology offers robust methodological precedents that closely align with our current analysis of DED. An example is the multiple stakeholder MCDA in diabetic macular oedema management (MULTIDEX-DME) study (41), evaluating DME treatments across multiple regions, including Italy and Spain. Similar to ours, the study structured its value framework into sequential phases of criteria prioritization and alternative scoring.

As the most widespread MCDA framework in health technology assessment (HTA), EVIDEM is routinely adapted (42). This customization allows global criteria to fit the specific funding regulations and healthcare delivery contexts of different countries or distinct technologies. In our study, the core components of the original EVIDEM framework required only minor adjustments to ensure broader applicability across participants from different European countries. These modifications were primarily confined to the Contextual Tool, thereby preserving the integrity of the MCDA Core Model, which remains the central focus for drug value assessment. Specifically, the Contextual Tool was refined by removing the contextual criteria deemed irrelevant due to the inherent variations in clinical guidelines, healthcare goals, and political landscapes across European countries. Similar adaptations have been reported in the literature (43).

Ultimately, this tailored framework provides a valuable initial tool for identifying the key drivers of decision-making regarding DED treatments.

Conclusions

To our knowledge, this pilot study represents the first application of MCDA methodology to ascertain what represents value in DED from the perspective of European clinical experts, in particular considering current ciclosporin-based treatment options. The reflective MCDA methodology enabled the identification and weighting of key criteria driving clinical practice management of DED, grounded in the latest available scientific evidence.

Furthermore, these findings identify critical areas to guide and foster future collaborative initiatives, ultimately contributing to better-informed decision-making in DED management.

Disclosures

Conflict of Interest: SA has received honoraria from AbbVie, Santen, Théa, Nordic Pharma, Bausch and Lomb, Holostem, Nanomedics, Sun Pharma, Medicom Healthcare, Sifi, Alcon, and Dompé. FF has received honoraria from Brill, Amgen, Kowa, Holostem, Novartis, and Sun Pharma. ML has received honoraria from AbbVie, Alcon, Allergan, Alfa Intes, Bausch & Lomb, Biotest, DMG, Dompé, Horus / Dulcis, KOL, Marinomed, MSD, Nordic, Novaliq, Novartis, Pol Pharma, Quantel, Santen, Shire, Sifi, Sun Tarsus Topivert, and Théa. EMM has received honoraria from Alfa Intes Industria Terapeutica Splendore, DMG, Kala Ophthalmics, Sanofi, Shire, Sun Pharma, SIFI, Viatris, Bausch + Lomb, GSK, Alcon/Novartis, Dompé farmaceutici, Novaliq, Santen, Théa Pharma, TRB-Chemedica, and VISUfarma. SS has received honoraria from Bausch+Lomb, SUN Pharma, Bayer, Nordic Pharma, Santen, Tarsus Pharmaceutical, Inc., Dompé, Alcon. PS has received honoraria from URSAPHARM Arzneimittel GmbH, Bausch + Lomb, SUN Pharma, AbbVie, Amgen, Sanofi, GlaxoSmithKline, and Théa Pharma. JMBdC has received honoraria from AbbVie, Alcon, Allergan, Alfa Intes, Angelini, Bausch & Lomb, Brill, Dompé, Farmamix, Horus, KOL, Nordic Pharma, Novaliq, Novartis, Pol Pharma, Santen, Shire, Sifi, Sun Pharma, Tarsus, and Théa. All authors received honoraria from Sun Pharma for their participation in this study.

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