EE225

Economic Modeling of Topical and Systemic Treatments for Atopic Dermatitis: A Structured Literature Review

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Background and Objectives

- Atopic dermatitis (AD) poses a substantial burden on healthcare systems due to its significant patient-burden, with direct and indirect costs to both payers and patients.[1]
- The objective of this structured literature review is to explore economic models assessing the cost-effectiveness of AD treatments, with a focus on the challenges and methodologies associated with economic modeling for topical interventions in order to inform future economic models and healthcare decision making.

Methods

- Searches were conducted across select health technology assessment (HTA) body websites including the Canadian Agency for Drugs and Technologies in Health (CADTH) and Institut national d'excellence en santé et en services sociaux (INESSS) in Canada, the National Institute for Health and Care Excellence (NICE) in the UK, the Institute for Clinical and Economic Review (ICER) in the U.S., the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia, and the Haute Autorité de Santé (HAS) in France, since inception up to November 2023.
- HTA evaluations focusing on topical or systemic/biologic therapies in AD were included in the review.
- Critical features of model design, data inputs, assumptions, and limitations were analyzed to provide a comprehensive understanding of the economic models used in assessing the cost-effectiveness of AD treatments.

Results

Description of Included HTA Evaluations

- Only three HTA reviews were found for mild to moderate AD topical treatments between years 2004 and 2018,[2-4] compared with fifteen HTA reviews for moderate to severe AD systemic/biologic therapies between 2017 and 2023[5-15] (**Table 1**).
- All biologic/systemic therapy economic analyses (n = 15/15)[5-19] used single cohort analyses, while a subset of topical treatment reviews (n = 2/3)[2,3] used two separate cohorts for adults and children (**Table 1**).

Results Continued…

Economic Modeling Characteristics

- Economic evaluations used various methodologies, including cost-effectiveness (utilizing Markov modeling,[2,5,9,18] microsimulation,[3] and semi-Markov modeling[2,4,6-8,10-15,19]), and cost minimization[4,13,17] (**Figure 1a**).
- Analysis time horizons varied, with longer-term horizons deemed suitable for pediatric analysis and for capturing the chronic waxing and waning nature of AD. Short-term horizons were considered appropriate for mild cases, focusing on fast symptom relief and immediate treatment outcomes (**Figure 1b**). In topical evaluations, pediatric analysis time horizon ranged from 15 weeks[4] to 15 years,[2] and for adults it ranged from 27 weeks[4] to 5 years.[3]
- Health states varied based on treatment responses, definitions and disease severity influencing patients transitions (**Figure 2a**). Economic modeling for topical treatments modeled health states based on treatment response (n = 2)[2,3] and disease progression (n = 3).[2-4]
- Model cycle lengths were shorter for topical treatment analyses (4 weeks)[2-4] compared with biologic/systemic therapies (4 months to 1 year).[5-19]
- Health state utilities were informed by trial data or by literature sources, using various utility measures (**Figure 2b**). Topical models used separate utility estimates sourced from the literature for adults and children, presuming twice-daily applications.[2,3] Due to differences in sample populations, mapping methods, and severity definitions, this approach was considered unfavorable.[2,3]
- Treatment durability in cost effectiveness analyses varied and were limited to economic evaluation of systemic/biologic therapies (n = 14/17). Majority of these analyses assumed potential efficacy waning (n = 11/14),[5-7,9-12,14-16,19] while two assumed maintained efficacy (n = 2/14),[8,18] and one was unclear.[3]

Key Modeling Limitations and Gaps

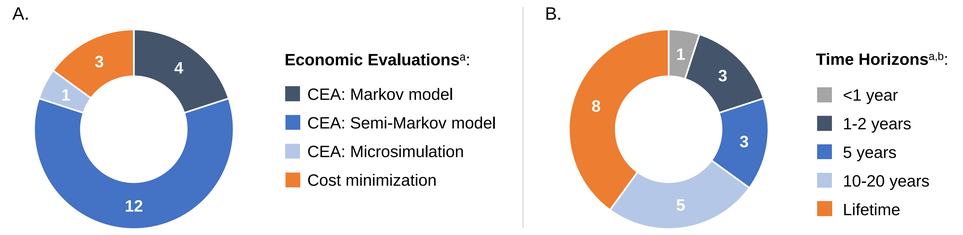
- Estimates of topical treatment use and cost were uncertain, requiring calculative assumptions based on affected body surface area, volume of drug per administration, treatment utilization during trial, or claims data, which may be inconsistent with real world use.
- Comparing efficacy of topical treatments is challenging in indirect treatment comparisons due to differences in size of baseline risk such as likelihood of response on vehicle.
- Key modeling gaps included uncertain long-term treatment efficacy, efficacy of subsequent treatments after failure of initial therapy, estimates of disease progression, the duration of drug use, the differences in drug usage between mild and moderate AD patients, long-term discontinuation, adherence, and incorporating AD resolution.

Table 1: Summary of HTA Economic Assessments for Topical and Biologic/Systemic Treatments in Atopic Dermatitis (N = 18)

AD Severity	Treatment	HTA Body (Year) Submission Number	Treatment Type — Drug Class	Population	Comparators
Mild to Moderate	Tacrolimus and Pimecrolimus	NICE (2004) TA82[2]	Topical TCI	≥2 years ≥18 years	TCS and/or emollients
	Crisaborole	CADTH (2018) SR0570[3]	Topical PDE4I	≥2 years ≥18 years	TCS or TCIs
	Crisaborole	PBS/PBAC (2018) NR[4]	Topical PDE4I	≥2 years	Pimecrolimus for the face and eyelids and emollients and moisturizers for the rest of the body
Moderate to Severe	Dupilumab and Crisaborole[a]	ICER (2017) NR[5]	Systemic/ biologic mAb IL-inhibitor (IL-4 and IL-13) and Topical PDE4I	≥18 years	Emollients
	Dupilumab	HAS (2018) CT16605[6]	Systemic/ biologic mAb IL-inhibitor (IL-4 and IL-13)		TCS and/or emollients
	Dupilumab	NICE (2018) TA534[7]			TCS and/or emollients
	Dupilumab	INESSS (2018) NR[8]			TCS or TCIs
	Dupilumab	PBS (2020) NR[9]			Standard of care, include concomitant TCS ± TCI therapy for flaring Cyclosporin
	Dupilumab	CADTH (2020) SR0636[10]		≥12 years	Basket of TCS, TCIs, PDE4I, oral antihistamines
	Dupilumab	INESSS (2021) NR[11]		6-11 years	TCS or TCIs
	Abrocitinib, Tralokinumab, or Upadacitinib	NICE (2022) TA814[12]	Systemic/ biologic JAK inhibitor and mAb IL-inhibitor (IL-13)	≥18 years	Dupilumab or Baricitinib
	Tralokinumab	CADTH (2022) SR0787[13]	Systemic/ biologic mAb IL-inhibitor (IL-13)	≥12 years	Dupilumab
	Upadacitinib	CADTH (2022) SR0685[14]	JAK inhibitor		Basket of emollients, low-to-mid potency TCS, rescue therapy
	Upadacitinib	INESSS (2022) NR[15]			Dupilumab and standard topical treatments (emollients, high-potency TCS and rescue treatments)
	Abrocitinib	CADTH (2023) SR0686[16]			SoC: Basket of TCS, TCIs, PDE4I, oral antihistamines; Dupilumab + SoC; Cyclosporine + SoC; or Methotrexate + SoC
	Abrocitinib	INESSS (2023) NR[17]			Upadacitinib
	Abrocitinib, Baricitinib, Tralokinumab, or Upadacitinib	ICER (2023) NR[18]	Systemic/ biologic JAK inhibitor and mAb IL-inhibitor (IL-13)	≥18 years	Dupilumab or emollients
Severe	Dupilumab	HAS (2021) CT19060[19]	Systemic/ biologic mAb IL-inhibitor (IL-4 and IL-13)	6-11 years	TCS and/or emollients

[a]ICER economic evaluation was limited to dupilumab use for moderate-to-severe AD.
Abbreviations: AD = atopic dermatitis, BSA = body surface area, CADTH = Canadian Agency for Drugs and Technologies in Health, HAS = Haute Autorité de Santé, HTA = health technology assessment, IL = interleukin, INESSS = Institut national d'excellence en santé et en services sociaux, JAK = Janus kinase, mAb = monoclonal antibody, NICE = National Institute for Health and Care Excellence, NR = not reported, PBS/PBAC = Pharmaceutical Benefits Scheme/Pharmaceutical Benefits Advisory Committee, PDE4I = phosphodiesterase 4 inhibitor, SoC = standard of care, TCI = topical calcineurin inhibitor, TCS = topical corticosteroid.

Figure 1: Economic Evaluations Approaches and Time Horizons Considered for AD Treatments: (A) Types of Economic Evaluations by HTA Bodies; (B) Variability in Time Horizons in Models



[a]PBS (2018) considered cost minimization and Markov cohort model for the evaluation of Crisaborole, both with a 5-year time horizon.
[b]In 2004, NICE considered multiple analyses with different model time horizons: 1 year for Pimecrolimus, 14 years for Tacrolimus, and 27 weeks for adults and 15 weeks for children for both TCIs. Similarly, CADTH's (2018) review included a 15-year time horizon for children and a 1-year time horizon for adults. HAS (2021) review included a 6-year primary and 10-year secondary analyses for dupilumab in children.
Abbreviations: AD = atopic dermatitis, CEA = cost effective analysis.

Figure 2: Variability in Treatment Responses and Utility Measures in AD HTA Reviews: (A) Treatment Responses; (B) Utility Measures

Abbreviations: AD = atopic dermatitis, DCD = disease-controlled days, DLQI = Dermatology Life Quality Index, EASI = Eczema Area and Severity Index, EQ-5D = EuroQol-5 Dimension, HTA = health technology assessment, HUI2 = Health Utilities Index Mark 2, IGA = Investigator's Global Assessment, SCORAD = SCORing Atopic Dermatitis.

Conclusions

- This review highlights the scarcity of HTA assessments and economic models for standard topical treatments in AD (e.g., TCS,TCI, and PDE4I), compared with systemic/biologics treatments in AD in the past 20 years.
- Variations in economic analysis methodologies included modeling approaches, single- versus multiple-cohort analyses, time horizons, health states, and severity definitions.
- There is a clear need for a more nuanced focus on the economic assessment of topical treatments due to the number of innovative topical therapies being investigated for reimbursement in AD.
- Future economic analyses should prioritize addressing methodological challenges and data gaps to improve decision-making in AD treatment.

References

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