October 12, 2022

Steven D. Pearson, MD, MSc
Institute for Clinical and Economic Review
14 Beacon Street, Suite 800
Boston, MA 02108

Submitted by email to: lshea@icer.org

Re: ICER's Assessment of Treatments for Atopic Dermatitis: 12-month update

Dear Dr. Pearson,

LEO Pharma appreciates the opportunity to provide further evidence in response to ICER's 12-month assessment update of the final Evidence Report "JAK Inhibitors and Monoclonal Antibodies for the Treatment of Atopic Dermatitis: Effectiveness and Value" dated August 17, 2021.

Tralokinumab safety, efficacy, and patient-reported outcomes (PRO) data have been recently published in adult and adolescent patients with moderate-to-severe atopic dermatitis (AD).

ECZTEND is an ongoing 5-year extension trial evaluating long-term safety and efficacy of tralokinumab.[1] In the 2-year interim analysis, tralokinumab was well tolerated with a safety and efficacy profile comparable to the parent trials.[1,2,3] Participants in ECZTEND on tralokinumab (N=1174) had an exposure-adjusted rate of 237.8 adverse events (AEs)/100 patient-years exposure with AE incidence comparable to or lower than parent trials.[1,2,3] Additional 3-year interim data supports the 2-year data. In the 3-year analysis, adverse events of special interest (AESI) including conjunctivitis, were observed at rates similar to or lower than in the parent

[1] Blauvelt A, et al. Long-term 2-year safety and efficacy of tralokinumab in adults with moderate-to-severe atopic dermatitis: Interim analysis of the ECZTEND open-label extension trial. J Am Acad Dermatol. 2022 Oct;87(4):815-824.
[2] Simpson EL, et al. Safety of Tralokinumab in Adult Patients With Moderate-to-Severe Atopic Dermatitis: Pooled Analysis of Five Randomized, Double-blind, Placebo-controlled Phase 2 and Phase 3 Trials. Br J Dermatol. 2022 Sep 9.
[3] Wollenberg A, et al. Conjunctivitis in adult patients with moderate-to-severe atopic dermatitis: results from five tralokinumab clinical trials. Br J Dermatol. 2022 Mar;186(3):453-465. Epub 2021 Nov 28.

trials with new safety signals detected.[4,5] Improvements on clinical and PRO endpoints were also seen over 3 years.[6]

At 3 years, 9 of 10 patients achieved at least one of the clinically relevant outcomes of EASI ≤ 7, pruritus NRS ≤ 4, or DLQI ≤ 5, representing mild/no AD; approximately 60% achieved clinically meaningful outcomes by all three measures.[6] The response rates were maintained over time with patients having EASI ≤ 7 for more than 80% of visits during the 3 years of treatment.

Additional efficacy and PRO analyses have also been conducted in ECZTRA 3 and showed tralokinumab+optional TCS provided progressive and sustained improvements in efficacy endpoints and PROs, with 70.2% achieving EASI75 and a 59.4% improvement in worst daily pruritus at week 32.[7] In an analysis of ECZTRA 1, 2, and 3, tralokinumab demonstrated early and clinically meaningful improvements on the pruritus NRS, the eczema-related sleep NRS, the DLQI, and POEM total score at Week 16.[8] In a one-year subset analysis of North American patients enrolled in ECZTRA 1, 2, and 3, efficacy and safety at Weeks 16 and 52 were similar and comparable to the non-Northern American population.[9]

Lastly, LEO would also like to make ICER aware of newly available 1 year data from ECZTRA 6, the pivotal trial of patients of age 12-17 with moderate-to-severe AD, that demonstrated

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[4] Blauvelt, et al. Long term Efficacy of Tralokinumab in More Than 1400 Moderate-to-Severe Atopic Dermatitis Patients Treated for up to 42 Months: An Interim Analysis of ECZTEND. Poster presented at the American Academy of Dermatology Annual Meeting (AAD), 2022.
[5] Reich K, et al. Tralokinumab demonstrated a consistent safety profile with up to 42 months of treatment in moderate-to-severe atopic dermatitis: including adverse events of special interest. Oral presentation at European Academy of Dermatology and Vereneology (EADV), 2022.
[6] Warren RB, et al. 3 years of tralokinumab treatment provides long-term disease control as demonstrated by clinically meaningful outcomes in moderate-to-severe atopic dermatitis. Oral presentation at the European Academy of Dermatology and Venereology (EADV) Congress 2022.
[7] Silverberg JI et al. Tralokinumab plus topical corticosteroids as needed provides progressive and sustained efficacy in adults with moderate-to-severe atopic dermatitis over a 32-week period: an ECZTRA 3 post-hoc analysis. Am J Clin Dermatol. 2022;23:547–559.
[8] Simpson EL, et al. Patient-oriented measures for phase 3 studies of tralokinumab for the treatment of atopic dermatitis (ECZTRA 1, 2, and 3). Ann Allergy Asthma Immunol. 2022 Jul 14:S1081-1206(22)00592-0. Epub ahead of print.
[9] Blauvelt, A, et al. Tralokinumab Efficacy and Safety, with or without Topical Corticosteroids, in North American Adults with Moderate-to-Severe Atopic Dermatitis: A Subanalysis of Phase 3 Trials ECZTRA 1, 2, and 3. Dermatol Ther (Heidelb) (2022).

tralokinumab is safe and efficacious in adolescents on clinical and PRO measures.[10,11,12,13,14] The frequency of conjunctivitis was found to be low and similar to placebo.[15]

LEO Pharma would like to thank ICER for the opportunity to submit this additional evidence.

Sincerely,

*Ami Claxton, MS, PhD*

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Ami Claxton, MS, PhD
Director, Health Economics and Outcomes Research, US Medical Affairs
LEO Pharma

[10] Paller AS, et al. Efficacy and safety of tralokinumab in adolescents with moderate-to- severe atopic dermatitis: results of the phase 3 ECZTRA 6 trial. SKIN. 2022;6:s29.
[11] Wollenberg A, et al. Efficacy and safety of tralokinumab in adolescents with moderate-to-severe atopic dermatitis: results of the phase 3 ECZTRA 6 trial. Oral presentation at the European Society for Pediatric Dermatology (ESPD) Congress 2022.
[12] Paller AS, et al. The Impact of Tralokinumab on Quality Of Life and School in Paediatric Patients Aged 12–17 Years with Atopic Dermatitis: Results from the Phase 3 ECZTRA 6 Trial. Poster presentation at the International Symposium on Atopic Dermatitis (ISAD) 2022.
[13] Soong A, et al. Tralokinumab treatment substantially improves patient-reported outcomes in adolescents with moderate-to-severe atopic dermatitis at 16 weeks. ePoster presentation at the Western Society for Allergy, Asthma and Immunology (WSAAI) 2022.
[14] Wollenberg A, et al. Safety of tralokinumab in paediatric patients aged 12–17 with moderate-to-severe atopic dermatitis: results from the phase 3 ECZTRA 6 trial. Oral presentation at the European Academy of Dermatology and Venereology (EADV) Congress 2022.
[15] Wollenberg A, et al. Conjunctivitis in adolescent patients aged 12–17 with moderate-to-severe atopic dermatitis treated with tralokinumab up to Week 52: results from the phase 3 ECZTRA 6 trial. ePoster presentation at the International Symposium on Atopic Dermatitis (ISAD) 2022.

National Eczema Association

October 5, 2022

Steven D. Pearson, MD, MSc
Institute for Clinical and Economic Review
14 Beacon Street, Boston, MA 02108

Re: ICER's Atopic Dermatitis Review: 12 Month Follow-up

Dear Dr. Pearson,

The National Eczema Association (NEA) appreciates the opportunity to provide further evidence in response to the Institute for Clinical and Economic Review's (ICER) 12-month assessment update for atopic dermatitis (AD).

NEA would like to make stakeholders aware of new real-world data that illustrates the burdens of out-of-pocket costs on AD patients and caregivers. Notable highlights include:

- 42% of Americans living with AD spend $1,000 or more out-of-pocket (OOP) every year to manage their eczema; 8.5% spend more than $5,000[1].
- Nearly 1 in 4 individuals with AD (24.5%) indicated that OOP expenses related to AD had a significant or devastating impact on their personal or family finances[2].
- Individuals with AD who have a higher degree of moderate, significant, or devastating financial burden were more likely to have increased AD severity, poorer control of their condition, more days spent actively flaring and more visits to their healthcare provider[2].
- Atopic dermatitis severity and spending more time managing AD were strongly associated with higher overall disease burden[3].
- Black individuals with AD were significantly more likely to report OOP costs for prescription medications both covered and not covered by insurance, emergency room visits and outpatient laboratory testing[4].

We would like to thank ICER for the opportunity to submit additional evidence.

Sincerely,

Julie Block
NEA President and CEO

[1] Smith Begolka W, Chovatiya R, Thibau IJ, Silverberg JI. Financial Burden of Atopic Dermatitis Out-of-Pocket Health Care Expenses in the United States. *Dermatitis*. 2021 Oct 1;32(1S):S62-70.
[2] Chovatiya R, Begolka WS, Thibau IJ, Silverberg JI. Impact and Associations of Atopic Dermatitis Out-of-Pocket Health Care Expenses in the United States. *Dermatitis.* September 27, 2021 doi: 10.1097/DER.0000000000000795
[3] Elsawi R, Dainty K, Smith Begolka W, Barta K, Butler L, Capozza K, Eftekhari S, Tullos KZ, Wu W, Drucker AM. The Multidimensional Burden of Atopic Dermatitis Among Adults National Results From a Large National Survey. *JAMA Dermatol*. 2022;158(8):887-892. doi:10.1001/jamadermatol.2022.1906
[4] Chovatiya R, Begolka WS, Thibau IJ, Silverberg, JI. Financial burden and impact of atopic dermatitis out-of-pocket healthcare expenses among black individuals in the United States. *Arch Dermatol Res* **314,** 739-747 (2022). https://doi.org/10.1007/s00403-021-02282-3