tralokinumab (Adbry™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO247

Description

Tralokinumab (Adbry) is a subcutaneous fully human monoclonal antibody of interleukin-13 (IL-13).

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
tralokinumab (Adbry)	150 mg prefilled syringe	Moderate-to-Severe Atopic Dermatitis	**First Month:** 6 syringes/28 days **Maintenance:** 4 syringes/28 days *300 mg (2 syringes)/28 days may be considered for patients under 100 kg who achieve clear skin*

Initial Evaluation

I. **Tralokinumab (Adbry)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a dermatologist or allergist; **AND**
   C. The medication prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat atopic dermatitis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant); **AND**
   D. A diagnosis of **moderate-to-severe atopic dermatitis** when the following are met:
      1. Body surface area (BSA) involvement of at least 10%; **OR**
         i. Involves areas of the face, ears, hands, feet, or genitalia; **AND**
      2. Treatment with at least **TWO** of the following groups has been ineffective or not tolerated, or **ALL** are contraindicated:
         i. Group 1: topical corticosteroids of at least medium/moderate potency (e.g., clobetasol, betamethasone, halobetasol)
         ii. Group 2: topical calcineurin inhibitors (e.g., tacrolimus ointment, pimecrolimus cream)
         iii. Group 3: topical PDE-4 inhibitor (crisaborole [Eucrisa]); **AND**

3. Treatment with dupilumab (Dupixent) has been ineffective, contraindicated, or not tolerated.

II. Tralokinumab (Adbry) is considered investigational when used for all other conditions, including but not limited to:
   A. Asthma or COPD
   B. Nasal polyps
   C. Pediatric or adolescent atopic dermatitis
   D. Ulcerative colitis
   E. Alopecia areata

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. The medication prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat atopic dermatitis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant); **AND**
IV. Member has exhibited improvement or stability of disease symptoms (e.g., improvement in IGA score from baseline, BSA involvement, pruritis symptoms)

Supporting Evidence

I. Atopic dermatitis (AD), also known as atopic eczema, is an inflammatory skin condition most frequently occurring in pediatric patients. It manifests with pruritis, dry skin, crusting, and serous oozing causing chronic scratching which leads to blister formation, skin thickening (lichenification), fissuring, or lesions. This condition is associated with elevated serum IgE and it is often a comorbid condition with asthma and allergic conditions.
II. Treatments for mild-to-moderate AD include topical corticosteroids (TCS), topical calcineurin inhibitors (TCI), phototherapy, and/or crisaborole (Eucrisa) – a PDE4 inhibitor. Symptomatic treatments include oral and topical antihistamines and sleep aids for nighttime pruritus. Treatment choice between these products is dependent on severity, location, and other patient specific factors (e.g., allergies, age)

III. Treatment for moderate-to-severe disease not amenable to topicals includes systemic immunosuppressants (e.g., corticosteroids, cyclosporine, methotrexate, azathioprine, mycophenolate mofetil) and dupilumab (Dupixent), a biologic IgG4 that is FDA-approved for pediatrics and adults as a biologic option for moderate-to-severe AD. Currently, there are no head to head trials evaluating safety and/or efficacy differences or superiority between tralokinumab (Adbry) and other therapies. Dupilumab (Dupixent) has an established safety and efficacy profile for the treatment of atopic dermatitis and is approved down to six years of age.

IV. Tralokinumab (Adbry) was evaluated in three randomized, double-blind, placebo-controlled, Phase III trials. Two as monotherapy (ECZTRA 1 and ECZTRA 2) and one in addition to topical corticosteroids (ECZTRA 3). Medication was administered as a 600 mg loading dose on day 0, followed by 300 mg every two weeks or placebo. In ECZTRA 1 and 2: at 16 weeks, responders continued on and were re-randomized to continue 300 mg every two weeks, change to 300 mg every four weeks, or placebo. In ECZTRA 3: at 16 weeks responders were re-randomized to tralokinumab (Adbry) every two or four weeks. All patients included in the trials were adults, and safety and efficacy in adolescent and pediatric patients is unknown. Patients included in the trials had moderate-to-severe AD (IGA 3-4) with BSA of at least 10% and had insufficient response to topical therapies. The majority had utilized several topical therapies, systemic immunosuppressants and phototherapy. Patients in ECZTRA 3 (6%) had history of use of dupilumab (Dupixent), and patients in ECZTRA 1 and 2 did not have a history of use.

V. Tralokinumab (Adbry) showed positive outcomes in all three trials with regard to morbidity, symptom control, and quality of life parameters via proportion of patients with an IGA of 0 or 1, proportion of patients meeting EASI 75, SCORAD change, change in NRS score from baseline, DLQI, and in ECZTRA 3 – TCS utilization - further details on measurement tools are provided in the appendix below.

VI. ECZTRA 1 and 2: When responders of therapy were re-randomized to tralokinumab (Adbry) every two weeks, every four weeks, or placebo, the majority of patients on every two-week therapy maintained response, while there was a nonsignificant difference in response maintained between the every-two-week and placebo arms for maintenance in ECZTRA 1. This was attributed to patients being counted as non responders if any other therapy (e.g., TCS) was utilized. Additionally, many of those that were transitioned to placebo maintained response out to week 52. There was a difference seen in maintenance of response in ECZTRA 2 vs. placebo.

VII. ECZTRA 3: Those that did not achieve the endpoints at week 16 were allowed to continue therapy, of those patients, 30.5% met IGA 0/1 and 55.8% met EASI 75 at week 32. Additionally, after re-randomization to tralokinumab (Adbry) every two weeks or every four weeks, 90% and 78% of patients maintained IGA 0/1, respectively, and 92.2% and 90.8% of patients maintained EASI 75, respectively.

VIII. The overall incidence of adverse events (AE) was similar to placebo in clinical trials. Common AE (>5%): AD, URTI, skin infection, pruritus, headache, and conjunctivitis. Eye disorders are notable AE for tralokinumab (Adbry) as there was more URI (up to 3% greater) and conjunctivitis (up to

5% greater) seen in tralokinumab (Adbry) then in placebo. In addition, there were also eight cases of keratoconjunctivitis and keratitis compared to the one case seen on placebo. These AE's are seen similarly for dupilumab (Dupixent). Skin infections overall, as well as those that required systemic treatment, were greater in the placebo group. A long-term extension trial evaluating safety (EZTEND) is expected to be complete in September 2021.

Investigational or Not Medically Necessary Uses

I. Tralokinumab (Adbry) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Asthma or COPD
   B. Nasal polyps
   C. Pediatric or adolescent atopic dermatitis
   D. Ulcerative colitis
   E. Alopecia areata

Appendix

Outcomes Key		
Name	**Explanation**	**Use and Significance**
IGA: Investigators Global Assessment Scale	Five-point scale assesses AD severity: 0-4, 0 is clear and 4 is severe. Decrease in score indicates improvement of AD signs and symptoms.	-Used for clinical trials -Clinically important difference is a 1-point change
EASI: Eczema Area and Severity Index	Scale assesses severity and extent of AD, 0-72 points. EASI 75 = 75% improvement from baseline. Measures 4 characteristics: erythema, infiltration/papulation, excoriations, lichentification, each on a scale of 0-3. These have different weight for each of the four body regions and are summed.	-Used for clinical trials -Clinically important difference is a 7-point change
SCORAD: Scoring Atopic Dermatitis	Tool used to evaluate severity and extent of AD. Assesses 3 components: BSA, severity, and symptoms. Extent is assessed as a percentage of each defined body area and reported as a sum. Maximum score is 100% for extent. The severity of six symptoms is assessed using a four-point scale: erythema, swelling, oozing/crusting, excoriation, skin thickening/lichentification, dryness. Severity has a maximum score of 18 points. Symptoms are recorded on a scale of 0-10, where 10 is the worst score imaginable. Entire score has a maximum of 103, higher scores=more severe condition.	-Used in clinical trials -Clinically important difference is a ~9 point change.
NRS: Pruritus Numerical Rating Scale	Tool used by patients to report the intensity of their itch. A scale of 0-10: 10 being worst itch imaginable. Often measured as a weekly average of the peak daily pruritus, tracked throughout a trial.	-Used in clinical trials -Clinically importance difference is 3-4 points.
DLQI: Dermatology Life Quality Index	Tool used widely in dermatology.	-Sometimes used in practice.

	10 item questionnaire, assesses 6 aspects: feelings, activities, leisure, work/ school performance, personal relationships, treatment. Max score per question is 3. DLQI is calculated by summing of scores for a maximum of 30. 0-1: no effect, 21-30: extremely large effect.	-Clinically important difference is 2-7-point change.

References

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2. Silverberg JI, Toth D, Bieber T, Alexis AF. Tralokinumab plus topical corticosteroids for the treatment of moderate-to-severe atopic dermatitis: results from the double-blind, randomized, multicentre, placebo-controlled phase III ECZTRA 3 trial. Br J Dermatol. 2020 Sep 30. doi: 10.1111/bjd.19573. Epub ahead of print. PMID: 33000503.
3. American Academy of Dermatology – Guidelines of Care for the Management of Atopic Dermatitis (2014). Available at: https://www.aad.org/member/clinical-quality/guidelines/atopic-dermatitis
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5. Clinical Review Report: Dupilumab (Dupixent): (Sanofi-Aventis Canada Inc.): Indication: Moderate-to-severe atopic dermatitis (AD) [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2018 Jul. Appendix 5, Validity of Outcomes Measures. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539234/
6. Dupixent [Prescribing Information]. Regeneron Sanofi Genzyme. Tarrytown, NF. January 2021.

Policy Implementation/Update:

Action and Summary of Changes	Date
Added requirement that Adbry will not be used in combination with other biologic or non-biologic specialty medications to initial criteria	10/2022
Policy update to prefer Dupixent	05/2021
Policy created	02/2021