tralokinumab-ldrm (Adbry™)

Policy # 00796
Original Effective Date: 07/11/2022
Current Effective Date: 07/10/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of tralokinumab-ldrm (Adbry™)‡ for the treatment of atopic dermatitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for tralokinumab-ldrm (Adbry) will be considered when the following criteria are met:

Initial:

- Patient has a diagnosis of moderate to severe atopic dermatitis; AND
- Patient is 18 years of age or older; AND
- Patient has had chronic atopic dermatitis for at least 6 months; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has atopic dermatitis involvement estimated to be ≥ 10% of the body surface area (BSA) according to the prescribing physician; AND
  *(Note: This specific patient selection criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has tried and failed (e.g., intolerance or inadequate response) at least ONE prescription GENERIC topical corticosteroid, unless there is clinical evidence or patient history that suggests the use of ONE prescription GENERIC topical corticosteroid will be ineffective or cause an adverse reaction to the patient; AND

- Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC tacrolimus ointment OR GENERIC pimecrolimus cream, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Requested drug is NOT being used in combination with JAK (janus kinase) inhibitors (e.g., upadicitinib [Rinvoq®]‡, ruxolitinib [Opzelura™]‡, abrocitinib [Cibinqo®]‡) or monoclonal antibodies (e.g., dupilumab [Dupixent®]‡) typically used to treat atopic dermatitis.

Continuation:

- Patient has received an initial authorization; AND
- Patient has received at least 6 months of therapy with the requested drug; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has been adherent to the requested drug and other medications for the condition being treated; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has had a clinically meaningful beneficial response to Adbry therapy as compared to their baseline status (before Adbry therapy) as evidenced by TWO or more of the following:
  - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
  - Reduction in the frequency or intensity of pruritus
  - Reduction in the frequency of disease exacerbations/flares
  - Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
  - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.); AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT being used in combination with JAK (janus kinase) inhibitors (e.g., upadicitinib [Rinvoq], ruxolitinib [Opzelura], abrocitinib [Cibinqo]) or monoclonal antibodies (e.g., dupilumab [Dupixent]) typically used to treat atopic dermatitis; AND

- If the patient is below 100 kg and has achieved clear or almost clear skin after 24 weeks of treatment with a 300 mg every 2 weeks dosage, a dosage of 300 mg every 4 weeks must be attempted. If the patient has tried and failed the 300 mg every 4 weeks dosage, the 300 mg every 2 weeks dosage will be approved.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of tralokinumab-ldrm (Adbry) when any of the following criteria are NOT met to be **not medically necessary**:**

- Patient has had chronic atopic dermatitis for at least 6 months
- Patient has atopic dermatitis involvement estimated to be ≥ 10% of the body surface area (BSA) according to the prescribing physician
- For continuation requests: Patient has received at least 6 months of therapy with the requested drug
- For continuation requests: Patient has been adherent to the requested drug and other medications for the condition being treated
- For continuation requests: Patient has had a clinically meaningful beneficial response to Adbry therapy as compared to their baseline status (before Adbry therapy) as evidenced by TWO or more of the following:
  - Reduction in disease severity (e.g., erythema, dryness, edema/papulation, excoriations, lichenification, oozing/crusting)
  - Reduction in the frequency or intensity of pruritus
  - Reduction in the frequency of disease exacerbations/flares
  - Reduction in the BSA with atopic dermatitis involvement (a 20% reduction in percent BSA involved over baseline)
  - Improvement in overall patient quality of life (e.g., improved sleep, less depression or anxiety, etc.)
- For continuation requests: If the patient is below 100 kg and has achieved clear or almost clear skin after 24 weeks of treatment with a 300 mg every 2 weeks dosage, a dosage of 300 mg every 4 weeks must be attempted.

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of tralokinumab-ldrm (Adbry) when the patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary****).

Background/Overview

Adbry is an interleukin-13 antagonist indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Adbry is supplied as a 150 mg/mL solution in a single-dose prefilled syringe. The recommended dosage of Adbry is 600 mg given subcutaneously, followed by 300 mg given subcutaneously every other week. A dosage of 300 mg given subcutaneously every 4 weeks may be considered for patients below 100 kg who achieve clear or almost clear skin after 16 weeks of treatment.

Atopic Dermatitis

There are various treatment options for atopic dermatitis, including first line agents such as topical corticosteroids (many of which are in generic form) and topical immunomodulatory agents such as generic tacrolimus and generic pimecrolimus. For those that are refractory to topical therapies, systemic immunomodulatory agents are an option for therapy. Adbry has not yet been integrated into the American Academy of Dermatology guidelines at the time of this publication.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Adbry is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Trial Background

The efficacy of Adbry was assessed in three randomized, double-blind, placebo-controlled trials (ECZTRA 1, ECZTRA 2, and ECZTRA 3). Efficacy was assessed in a total of 1,934 subjects 18 years of age and older with moderate-to-severe atopic dermatitis (AD) not adequately controlled by topical medication(s). Disease severity was defined by an Investigator's Global Assessment (IGA) score ≥ 3 in the overall assessment of AD lesions on a severity scale of 0 to 4, an Eczema Area and Severity Index (EASI) score ≥16 on a scale of 0 to 72, and a minimum body surface area (BSA) involvement of ≥10%.

In all three trials, subjects received subcutaneous injections of Adbry 600 mg or placebo on Day 0, followed by 300 mg every other week or placebo for 16 weeks. Responders were defined as achieving an IGA 0 or 1 ("clear" or "almost clear") or EASI-75 (improvement of at least 75% in EASI score from baseline) at Week 16.

To evaluate maintenance of response in the monotherapy trials (ECZTRA 1 and ECZTRA 2), subjects responding to initial treatment with Adbry 300 mg every other week were re-randomized to Adbry 300 mg every other week, Adbry 300 mg every 4 weeks or placebo every other week for another 36 weeks following first dose administration. Subjects randomized to placebo in the initial treatment period who achieved a clinical response at Week 16 continued to receive placebo every other week for another 36 weeks. Non-responders at Week 16, and subjects who lost clinical response during the maintenance period were placed on open-label treatment with Adbry 300 mg every other week and optional use of topical corticosteroids.

In the combination therapy trial (ECZTRA 3), subjects received either Adbry 300 mg every other week with topical corticosteroids or placebo with topical corticosteroids and as needed topical calcineurin inhibitors (TCI) until Week 16. Subjects in the Adbry 300 mg with topical corticosteroids

group who achieved clinical response at Week 16 were re-randomized to Adbry 300 mg every other week with topical corticosteroids or Adbry every 4 weeks with topical corticosteroids for another 16 weeks following first dose administration. Subjects in the placebo with topical corticosteroids group who achieved clinical response at Week 16 continued on placebo with topical corticosteroids for another 16 weeks. Subjects who did not achieve clinical response at Week 16 received Adbry 300 mg every other week for another 16 weeks. A mid-potency topical corticosteroid (i.e., mometasone furoate 0.1% cream) was dispensed at each dosing visit. Subjects were instructed to apply a thin film of the dispensed topical corticosteroid as needed once daily to active lesions from Week 0 to Week 32 and were to discontinue treatment with topical corticosteroids when control was achieved. An additional, lower potency topical corticosteroid or TCI could be used at the investigator's discretion on areas of the body where use of the supplied topical corticosteroid was not advisable, such as areas of thin skin.

Response at Week 16
All three trials assessed the primary endpoints of the proportion of subjects with an IGA 0 or 1 at Week 16 and the proportion of subjects with EASI-75 at Week 16. In ECZTRA 1, 16% of the Adbry subjects achieved an IGA of 0 or 1 vs. 7% in the placebo group. In ECZTRA 2, 21% of the Adbry subjects achieved an IGA of 0 or 1 vs. 9% in the placebo group. In ECZTRA 3, 38% of the Adbry + topical corticosteroids subjects achieved an IGA of 0 or 1 vs. 27% in the placebo + topical corticosteroids group. In ECZTRA 1, 25% of the Adbry subjects achieved EASI-75 vs. 13% in the placebo group. In ECZTRA 2, 33% of the Adbry subjects achieved an EASI-75 vs. 10% in the placebo group. In ECZTRA 3, 56% of the Adbry + topical corticosteroids subjects achieved an EASI-75 vs. 37% in the placebo + topical corticosteroids group.

Maintenance Period
In ECZTRA 1, 179 Adbry 300 mg every other week responders (IGA 0/1 or EASI-75) were re-randomized (and dosed) at Week 16 to Adbry 300 mg every other week (68 subjects), Adbry 300 mg every 4 weeks (76 subjects) or placebo (35 subjects). Among these subjects, 39 subjects in Adbry 300 mg every other week arm, 36 subjects in Adbry 300 mg every 4 weeks arm and 19 subjects in placebo arm were IGA 0/1 responders at Week 16. Maintenance of IGA 0/1 response at Week 52 was as follows: 20 subjects (51%) in the every other week arm, 14 subjects (39%) in the every 4 weeks arm and 9 subjects (47%) in the placebo arm. Among the re-randomized subjects, 47 subjects in Adbry 300 mg every other week arm, 57 subjects in Adbry 300 mg every 4 weeks arm and 30 subjects in placebo arm were EASI-75 responders at Week 16. Maintenance of EASI-75 response at

Week 52 was as follows: 28 subjects (60%) in the every other week arm, 28 subjects (49%) in the every 4 weeks arm and 10 subjects (33%) in the placebo arm.

In ECZTRA 2, 218 Adbry 300 mg every other week responders (IGA 0/1 or EASI-75) were re-randomized (and dosed) at Week 16 to Adbry 300 mg every other week (90 subjects), Adbry 300 mg every 4 weeks (84 subjects) or placebo (44 subjects). Among these subjects, 53 subjects in the Adbry 300 mg every other week arm, 44 subjects in the Adbry 300 mg every 4 weeks arm and 26 subjects in the placebo arm were IGA 0/1 responders at Week 16. Maintenance of IGA 0/1 response at Week 52 was as follows: 32 subjects (60%) in the every other week arm, 22 subjects (50%) in the every 4 weeks arm and 6 subjects (23%) in the placebo arm. Among the re-randomized subjects, 76 subjects in the Adbry 300 mg every other week arm, 69 subjects in the Adbry 300 mg every 4 weeks arm and 40 subjects in the placebo arm were EASI-75 responders at Week 16. Maintenance of EASI-75 response at Week 52 was as follows: 43 subjects (57%) in the every other week arm, 38 subjects (55%) in the every 4 weeks arm and 8 subjects (20%) in the placebo arm.

In ECZTRA 3, 131 Adbry 300 mg every other week + topical corticosteroids responders (IGA 0/1 or EASI-75) were re-randomized (and dosed) at Week 16 to Adbry 300 mg every other week + topical corticosteroids (65 subjects) or Adbry 300 mg every 4 weeks + topical corticosteroids (66 subjects). Among these subjects, 45 subjects in Adbry 300 mg every other week + topical corticosteroids arm and 46 subjects in Adbry 300 mg every 4 weeks + topical corticosteroids arm were IGA 0/1 responders at Week 16. Maintenance of IGA 0/1 response at Week 32 was as follows: 40 subjects (89%) in the every other week arm and 35 subjects (76%) every 4 weeks arm. Among the re-randomized subjects, 65 subjects in Adbry 300 mg every other week arm and 62 subjects in Adbry 300 mg every 4 weeks arm were EASI-75 responders at Week 16. Maintenance of EASI-75 response at Week 32 was as follows: 60 subjects (92%) in the every other week arm and 56 subjects (90%) in the every 4 weeks arm.

References

1. Adbry [package insert]. Leo Pharma. Madison, New Jersey. Updated January 2022.

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Current Effective Date: 07/10/2023
06/02/2022 Medical Policy Committee review
06/08/2022 Medical Policy Implementation Committee approval. New policy.
06/01/2023 Medical Policy Committee review
06/14/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 06/2024

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;

B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.