brepocitinib (Lisraya™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO348

Description

Brepocitinib (Lisraya) is an orally administered dual selective tyrosine kinase 2/Janus kinase 1 (TYK2/JAK1) inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
brepocitinib (Lisraya)	Dermatomyositis in adults	30 mg tablets	30 tablets/30 days

Initial Evaluation

I. **Brepocitinib (Lisraya)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with a rheumatologist, dermatologist, or a neurologist; **AND**
   B. Medication is not used in combination with other Janus kinase (JAK) Inhibitors, intravenous immune globulins (IVIg) (e.g. Octagam), or monoclonal antibodies (e.g. rituximab, adalimumab, tocilizumab, etc.); **AND**
   C. A diagnosis of **dermatomyositis**; **AND**
      1. Documented presence of one or more characteristic dermatomyositis cutaneous manifestations (e.g., heliotrope rash, Gottron's papules, or Gottron's sign); **AND**
      2. Documented active skin disease (e.g., Cutaneous Dermatomyositis Disease Area and Severity Index - Activity Score [CDASI-A] ≥ 6, or new worsening lesions, erythema, edema, ulceration, tenderness); **AND**
      3. Documented inflammatory myopathy demonstrated by at least <u>two</u> of the following:
         a. Proximal muscle weakness documented on physical examination or Manual Muscle Testing (MMT-8) ≤142
         b. Elevated muscle enzymes (e.g., CK, aldolase, AST, ALT, or LDH)
         c. Muscle Magnetic Resonance Imaging (MRI) or Electromyography (EMG) findings consistent with inflammatory myopathy
         d. Muscle biopsy consistent with dermatomyositis or inflammatory myopathy
         e. Myositis-specific autoantibody associated with dermatomyositis (e.g., anti-Jo-1, anti-TIF1y, anti-NXP2, anti-Mi2, anti-MDA5, anti-SAE); **AND**
      4. Provider attestation that alternative causes of muscle weakness, inflammatory myopathies, and connective tissue diseases have been appropriately evaluated,

and no other alternative diagnosis better explains the member's clinical presentation; **AND**

5. Inadequate response, contraindication, or intolerance to:
   i. Systemic corticosteroids (e.g., prednisone, prednisolone); **AND**
   ii. At least one conventional immunosuppressive agent (e.g., methotrexate, azathioprine, mycophenolate mofetil, tacrolimus) or anti-malarial (e.g., hydroxychloroquine); **AND**
   iii. Intravenous Immune Globulin (IVIg)*

**Please note: medications notated with an asterisk may require additional review.*

II. Brepocitinib (Lisraya) is considered investigational when used for all other conditions, including but not limited to:
   A. Non-infectious uveitis
   B. Cutaneous sarcoidosis
   C. Lichen planopilaris
   D. Amyopathic dermatomyositis (ADM)
   E. Adermatopathic dermatomyositis (dermatomyositis sine dermatitis), immune-mediated necrotizing myopathy (IMNM), polymyositis (PM), inclusion body myositis (IBM)

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. Provider attestation that the member has demonstrated clinical benefit as evidenced by improvement or stabilization of disease symptoms in one or more of the following: muscle strength, cutaneous manifestations, physical functioning, corticosteroid reduction, or physician global assessment; **AND**

IV. Medication is not used in combination with other Janus kinase (JAK) Inhibitors, intravenous immune globulins (IVIg) (e.g. Octagam) or monoclonal antibodies (e.g. rituximab, adalimumab, tocilizumab, etc.)

Supporting Evidence

I. Brepocitinib (Lisraya) is FDA approved for the treatment of adults with dermatomyositis (DM). It is a first-in-class selective dual Tyrosine kinase 2 (TYK2)/Janus kinase (JAK) 1 inhibitor. Tyrosine kinase 2 and JAK1 are intracellular kinases that play a role in cytokine-mediated immune signaling and reduce downstream signaling of pro-inflammatory cytokines, including those present in DM.

II. Dermatomyositis is a complex multisystem autoimmune disease requiring specialized assessment of cutaneous and muscular disease activity, management of immunosuppressive therapies, and monitoring for complications such as interstitial lung disease and malignancy. Rheumatologists, dermatologists, and neurologists may be best positioned to diagnose and manage these patients.

III. Concomitant use of brepocitinib (Lisraya) with other JAK inhibitors, intravenous immunoglobulin (IVIG), biologic immunomodulators, and other specialty immunosuppressive agents was prohibited in the pivotal clinical trial; therefore, the safety and efficacy of these combination regimens have not been established. Concurrent use with other targeted immunomodulatory therapies may increase the risk of additive immunosuppression and serious infections, including opportunistic and latent infections. In addition, JAK inhibitors are associated with risks of serious infection, malignancy, major adverse cardiovascular events (MACE), thrombosis, and mortality. Given the lack of clinical evidence and the potential for additive toxicity, concurrent use of brepocitinib (Lisraya) with other JAK inhibitors, biologics, or specialty immunosuppressive therapies is not recommended. Similar restrictions against use with other JAK inhibitors, biologic immunomodulators, and potent immunosuppressants appear in the prescribing information of multiple currently marketed JAK inhibitors.

IV. European League Against Rheumatism/American College of Rheumatology 2017 (EULAR/ACR) classification criteria help to distinguish DM from other idiopathic inflammatory myopathies by taking into account age at onset, cutaneous manifestations, and presence and characteristics of muscle weakness (see figure 1 in the appendix).

V. Patients with pathognomonic cutaneous manifestations of DM can be classified accurately using the 2017 EULAR/ACR classification criteria. While the EULAR/ACR criteria facilitate diagnosis based on characteristic skin findings, clinicians frequently incorporate additional diagnostic modalities to support diagnostic certainty and evaluate disease extent. The diagnosis of DM is therefore typically based on a combination of clinical presentation, laboratory findings, imaging studies, electrophysiologic testing, serologic markers, and, when indicated, histopathologic evaluation. Diagnostic modalities that may be used to support the diagnosis of DM include:

- Clinical evaluation: In addition to comprehensive medical history and physical examination, providers assess characteristic manifestations such as symmetrical muscle weakness involving the shoulders and hip muscles, as well as pathognomonic cutaneous findings. This can include assessments such as MMT-8 and Cutaneous Dermatomyositis Disease Area and Severity Index Activity (CDASI-A) score, if available in practice.
- Laboratory testing: Blood tests are commonly obtained to evaluate alternative diagnoses and assess for evidence of muscle inflammation. Elevations in muscle enzymes, including creatine kinase (CK), aldolase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH), may support the diagnosis; however, normal or abnormal laboratory results alone neither confirm nor exclude DM.
- Skin and muscle biopsies: Histopathologic evaluation can provide supportive evidence for dermatomyositis (DM) and may be particularly useful in diagnostically

challenging cases. However, characteristic skin biopsy findings are not present in all patients, and histopathologic changes may be absent despite clinically evident disease. Therefore, skin biopsy results should be interpreted within the context of the overall clinical presentation, and negative findings do not exclude the diagnosis. In contrast, muscle biopsy remains the gold standard for histopathologic confirmation of DM. The hallmark muscle biopsy finding is perifascicular atrophy, characterized by the presence of atrophic, degenerating, and regenerating muscle fibers distributed along the periphery of the fascicle. Perifascicular atrophy typically involves both type 1 and type 2 muscle fibers, may affect two to ten layers of fibers, and strongly supports a diagnosis of DM, even in the absence of significant inflammatory infiltrates.

- Electromyogram (EMG): Although EMG is not included in the 2017 EULAR/ACR classification criteria, it may provide evidence of inflammatory myopathy and can be useful when the diagnosis remains uncertain or when muscle involvement is subtle.
- Magnetic resonance imaging (MRI): MRI can identify muscle edema and inflammation and may help detect subclinical muscle involvement. MRI findings are supportive but are not independently diagnostic of DM.
- Myositis-specific and myositis-associated autoantibodies: Autoantibody testing can provide important diagnostic and prognostic information. Certain antibodies are strongly associated with DM and specific disease phenotypes. While positive antibody results may strengthen diagnostic confidence, negative results do not exclude the diagnosis.

VI. To test brepocitinib's (Lisraya) effects on both skin and muscle, participants in the VALOR study were required to have active skin and muscle disease at baseline (CDASI-A ≥6 and MMT-8 score ≤142). While MMT-8 is currently gold standard for assessing muscle weakness and activity in DM, there are limitations to this assessment and providers may choose to evaluate muscle weakness in different ways.

VII. Dermatomyositis (DM) is a rare and serious systemic autoimmune disease with significant morbidity. Many patients require prolonged corticosteroid use and experience inadequate response to conventional immunosuppressants. The VALOR trial enrolled patients with dermatomyositis who had persistent active disease despite prior treatment with established standard-of-care therapies. Eligible patients were required to have an inadequate response to at least one conventional treatment, including systemic corticosteroids, conventional immunosuppressant agents, or intravenous immunoglobulin (IVIg). In addition, participants were receiving oral corticosteroids and were typically treated with at least two dermatomyositis-directed therapies (which may have included corticosteroids), such as methotrexate, azathioprine, mycophenolate mofetil, mycophenolic acid, leflunomide, sulfasalazine, or hydroxychloroquine. These study requirements support restricting brepocitinib (Lisraya) use to patients who have demonstrated inadequate response to conventional therapies prior to treatment initiation.

VIII. The current treatment paradigm most commonly includes steroids, methotrexate, azathioprine, mycophenolate, tacrolimus, antimalarials, IVIg, and rituximab. Systemic corticosteroids remain

first-line therapy for DM, but due to the substantial toxicity associated with prolonged steroid use, conventional steroid-sparing immunosuppressive agents such as methotrexate, azathioprine, mycophenolate mofetil, and tacrolimus have long served as foundational treatments and are frequently recommended early in the treatment course. Treatment escalation typically occurs only after inadequate response, intolerance, or contraindication to conventional therapies.

IX. Methotrexate, azathioprine, mycophenolate mofetil, and tacrolimus are well-established immunomodulatory therapies with extensive long-term safety experience, established monitoring recommendations, and continued use as standard-of-care treatments across autoimmune diseases. Although each agent carries known risks, many serious toxicities are uncommon, predictable, and detectable through routine laboratory and clinical monitoring, allowing for management through dose adjustment or treatment discontinuation when necessary. Methotrexate remains a commonly utilized first-line steroid-sparing therapy in dermatomyositis; clinically significant hepatotoxicity is relatively uncommon at the low weekly doses used for autoimmune disease, most liver enzyme elevations are mild and reversible, and methotrexate pneumonitis is a recognized but relatively rare adverse event. Azathioprine's risks of myelosuppression and hepatotoxicity are well characterized and routinely managed through laboratory surveillance, while mycophenolate mofetil is generally regarded as having a favorable tolerability profile, with gastrointestinal adverse effects occurring more commonly than serious organ toxicity. Tacrolimus is associated with known risks such as nephrotoxicity, neurotoxicity, hypertension, and drug interactions; however, these toxicities are generally predictable, routinely monitored through renal function assessment, blood pressure monitoring, and, when appropriate, drug-level monitoring, and much of the safety concern stems from higher-dose transplant experience rather than the doses commonly used in autoimmune disease. Overall, available evidence does not support broadly characterizing these conventional immunosuppressants as uniformly unsafe or inappropriate for step therapy in otherwise eligible patients; however, patients with documented contraindications, intolerance, or clinically significant adverse effects would meet the contraindication/intolerance provisions of the policy.

X. Antimalarials (typically hydroxychloroquine) are an established and commonly used treatment for the cutaneous manifestations of DM. Although their efficacy is generally more modest than that of systemic immunosuppressants, hydroxychloroquine has historically been recommended as an initial systemic treatment option for cutaneous manifestations of DM because of its safety profile, low cost, and evidence of benefit in reducing inflammatory skin lesions. Multiple reviews and treatment algorithms for DM include hydroxychloroquine or other antimalarials as first-line or early-line therapy before escalation to more advanced immunomodulatory therapies.

XI. Step therapy through IVIg (e.g., Octagam) is appropriate because IVIg has demonstrated efficacy in both muscle and skin manifestations of dermatomyositis and has an established role in standard clinical practice. The FDA approval of IVIg for adult dermatomyositis was supported by the Phase III ProDERM trial, which demonstrated significantly greater clinical improvement among IVIg-treated patients compared with placebo, including improvements in overall disease activity and cutaneous disease manifestations. Infusion-related reactions, headaches, and flu-like symptoms may occur with IVIg treatment; however, these events are generally manageable

and do not preclude therapy in most patients. Documented severe infusion reactions or intolerance may satisfy the policy's intolerance requirement. Personal preference alone does not establish medical necessity to bypass therapies with established efficacy in dermatomyositis. Intravenous immunoglobulin has demonstrated significant improvements in disease activity in a Phase 3 randomized trial and is currently FDA-approved specifically for adult dermatomyositis. Therefore, failure, contraindication, or intolerance to IVIg is required prior to escalation to brepocitinib (Lisraya).

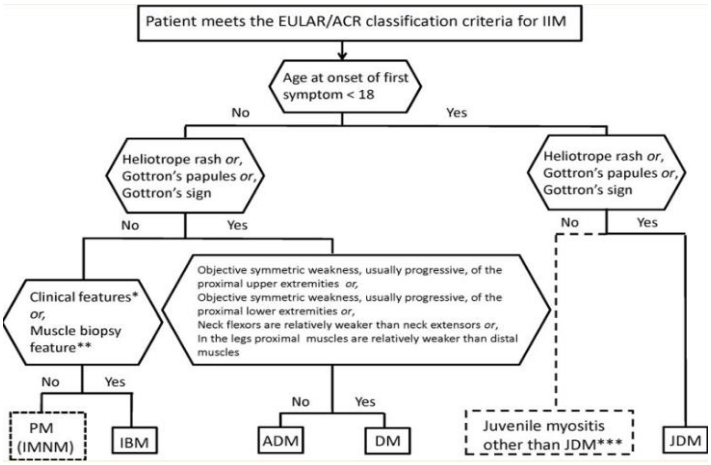
Investigational or Not Medically Necessary Uses

I. Brepocitinib (Lisraya) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Non-infectious uveitis
      i. A Phase 2 randomized, double-masked, dose-ranging study is currently ongoing to evaluate the clinical safety and efficacy of oral brepocitinib (Lisraya) in participants with active intermediate, posterior, or pan non-infectious uveitis (NCT05523765). Safety and efficacy in the treatment of non-infectious uveitis have not yet been established and is considered experimental and investigational.
   B. Cutaneous sarcoidosis
      i. A Phase 2/3 randomized, double-blind, placebo-controlled, dose-ranging study to evaluate the clinical safety and efficacy of oral brepocitinib (Lisraya) in participants with cutaneous sarcoidosis is ongoing (NCT06978725). Safety and efficacy in the treatment of cutaneous sarcoidosis have not yet been established and is considered experimental and investigational.
   C. Lichen planopilaris
      i. A Phase 2/3 randomized, double-blind, placebo-controlled study to evaluate the clinical safety and efficacy of oral brepocitinib (Lisraya) in participants with lichen planopilaris is ongoing (NCT07532603). Safety and efficacy in the treatment of lichen planopilaris have not yet been established and is considered experimental and investigational.
   D. Amyopathic dermatomyositis (ADM)
      i. A prospective, 12-week, open-label, single-arm study comprised of individuals with refractory skin disease characteristic of dermatomyositis with no to minimal muscle involvement is ongoing (NCT06433999). Safety and efficacy in the treatment of skin-predominant or amyopathic dermatomyositis have not yet been established and is considered experimental and investigational.
   E. Adermatopathic dermatomyositis (dermatomyositis sine dermatitis), immune-mediated necrotizing myopathy (IMNM), polymyositis (PM), inclusion body myositis (IBM)
      i. Safety and efficacy in the treatment of adermatopathic dermatomyositis have not yet been established and is considered experimental and investigational. Patients without characteristic dermatomyositis-associated cutaneous findings should not be presumed to have dermatomyositis solely on the basis of inflammatory

myopathy. The absence of hallmark skin manifestations raises consideration of alternative idiopathic inflammatory myopathy subtypes, including IMNM, PM, and IBM. These conditions have distinct diagnostic criteria and management strategies, and the available clinical evidence for brepocitinib (Lisraya) does not extend to these populations. Because efficacy data are currently limited to dermatomyositis, treatment of IMNM, PM, IBM, or other non-dermatomyositis inflammatory myopathies with brepocitinib (Lisraya) is considered experimental/investigational.

Appendix

I. Figure 1: EULAR/ACR Classification Criteria



Lundberg IE, Tjärnlund A, Bottai M, et al. 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups.

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Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	11/2026