



Injectable Atopic Dermatitis Agent(s) Prior Authorization with Quantity Limit Criteria Program Summary

This prior authorization applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Injectable Atopic Dermatitis Agent(s) Prior Authorization (PA) program is to ensure that patients prescribed therapy meet the selection requirements defined in product labeling and/or clinical guidelines and/or clinical studies. The PA defines appropriate use as the Food and Drug Administration (FDA) labeled indication or as supported by guidelines and/or clinical evidence.

TARGET DRUGS

Dupixent® (dupilumab)

QUANTITY LIMIT TARGET DRUG- RECOMMENDED LIMIT

Brand (generic)	GPI	Multisource Code	Quantity Limit
Dupixent (dupilumab) 300 mg/2 mL pre-filled syringe (pack of 2)	9027302000E520	M, N, O, Y	1 carton of 2 syringes per 28 days*

* The recommended dose of Dupixent for adult patients is an initial loading dose of 600 mg (two 300 mg injections) subcutaneously, followed by 300 mg given every other week for maintenance

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Injectable Atopic Dermatitis Agent(s) will be approved when the following criteria are met:

Initial Criteria

1. ONE of the following:

- a. There is documentation that the patient is currently being treated with the requested agent (starting on samples is not approvable)
OR
- b. The prescriber states the patient is using the requested agent (starting on samples is not approvable) AND is at risk if therapy is changed
OR
- c. The patient has the diagnosis of moderate-to-severe atopic dermatitis and ALL of the following:
 - i. ONE of the following:
 1. The patient has at least 10% body surface area involvement
OR
 2. The patient has involvement of the palms and/or soles of the feet
AND
 - ii. The patient is at least 18 years old or older
AND
 - iii. The prescriber is a specialist in the area of the patient's diagnosis or the prescriber has consulted with a specialist in the area of the patient's diagnosis (e.g., dermatologist, allergist)
AND
 - iv. ONE of the following:

1. The patient has tried and failed a systemic immunosuppressant for atopic dermatitis within the last 180 days (e.g., methotrexate, azathioprine, CellCept, cyclosporine)
OR
2. The patient has tried and failed at least a mid- potency topical steroid AND a topical calcineurin inhibitor (e.g., pimecrolimus, tacrolimus) for maintenance therapy (At least one must be within the last 180 days; the other may be in the last 999 days)
OR
3. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a mid- potency topical steroid AND a topical calcineurin inhibitor

AND

v. ONE of the following:

1. The patient has failed short-term use of at least a high potency topical steroid or oral steroids for the treatment of flares in the past 365 days
OR
2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a high potency topical steroid AND an oral steroid for short-term use. *Will accept that the patient has face/neck, skin folds, intertriginous, and/or genital area involvement for topical steroids

OR

- d. The patient has another FDA approved indication

AND

2. If the patient has a diagnosis of moderate-to-severe atopic dermatitis then BOTH of the following:

- a. The prescriber has documented the patient's current pruritus and other symptom severity (e.g., erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification)

AND

- b. The patient will continue with topical emollients as a component of maintenance treatment to aid in the prevention of flares

AND

3. The patient does not have an FDA labeled contraindication to therapy with the requested agent

AND

4. ONE of the following:

- a. The quantity requested is less than or equal to the program quantity limit

OR

- b. The quantity (dose) requested is within FDA approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength

Length of Approval: 6 months

Renewal Criteria

1. The patient has been previously approved for therapy through Prime Therapeutics Prior Authorization Review process

AND

2. If the patient has moderate-to-severe atopic dermatitis, then BOTH of the following

- a. The patient has a reduction or stabilization from baseline in at least ONE of the following:

- i. Affected body surface area
- ii. Flares
- iii. Pruritus, erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification

AND

- b. The patient will continue with topical emollients as a component of maintenance treatment to aid in the prevention of flares

AND

- 3. The patient does not have an FDA labeled contraindication to therapy with the requested agent

AND

- 4. ONE of the following:
 - a. The quantity requested is less than or equal to the program quantity limit
 - OR**
 - b. The quantity (dose) requested is within FDA approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength

Length of Approval: 12 months

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

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FDA APPROVED INDICATIONS AND DOSAGE¹

FDA Indication: Dupixent is indicated for the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.

Dosing: The recommended dose of Dupixent for adult patients is an initial dose of 600 mg (two 300 mg injections) subcutaneously, followed by 300 mg given every other week.

Dupixent can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.

CLINICAL RATIONALE

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, pruritic inflammatory dermatosis affecting up to 25% of children and 2–3% of adults. AD follows a relapsing course, and is associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and/or asthma. Onset is most common between 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by age 5. While the majority of affected individuals have resolution of disease by adulthood, 10 to 30% do not, and a smaller percentage first develop symptoms as adults. AD has a complex pathogenesis involving genetic, immunologic, and environmental factors, which lead to a dysfunctional skin barrier and dysregulation of the immune system. Clinical findings include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification. These clinical findings vary by patient age and chronicity of lesions. Pruritus is a hallmark of the condition that is responsible for much of the disease burden borne by patients and their families. Typical patterns include facial, neck and extensor involvement in infants and children; flexure involvement in any age group, with sparing of groin and axillary regions.²

American Academy of Dermatology guidelines (AAD, 2014) suggest application of moisturizers should be an integral part of the treatment of patients with AD as there is strong evidence that their use reduces disease severity and need for pharmacologic intervention. The AAD indicates that moisturizers should be part of the regimen for moderate and severe disease. They are also an important component of maintenance treatment and prevention of flares. Moisturizers are therefore a cornerstone of AD therapy and should be included in management plans.³ Two studies have shown that daily moisturizer use can lengthen the time to first flare, compared to no treatment.²

The AAD recommends topical corticosteroids for patients who fail to respond to good skin care and regular use of emollients alone. Proactive, intermittent use of topical corticosteroids as maintenance therapy (1-2 times/wk) on areas that commonly flare is recommended to help prevent relapses and is more effective than use of emollients alone. Monitoring by physical exam for cutaneous side effects during long-term, potent steroid use is suggested. Proactive, once to twice weekly application of mid-potency TCS for up to 40 weeks has not demonstrated adverse events (e.g., purpura, telangiectasia, striae, focal hypertichosis, acneiform/rasacea-like eruptions, skin atrophy) in clinical trials.³ It is suggested that patients with acute flares use super high or high potency topical corticosteroids for up to two weeks and then replace these with lower potency preparations until the lesions resolve.⁸

Topical calcineurin inhibitors (TCIs) (e.g., pimecrolimus, tacrolimus) are recommended by the AAD and are effective for acute and chronic treatment. They are particularly useful in selected clinical situations: e.g., recalcitrance to steroids; for sensitive areas (face, anogenital, skin folds); for steroid-induced atrophy; and when there is long-term

uninterrupted topical steroid use. TCIs are recommended for use on actively affected areas as a steroid-sparing agent. Proactive, intermittent use of TCIs as maintenance therapy (2-3 times per week) on areas that commonly flare is recommended to help prevent relapses while reducing need for topical corticosteroids, and is more effective than use of emollients alone. Concomitant use of a topical corticosteroid with a TCI may be recommended. Rare cases of malignancy (skin cancer, lymphoma) have been reported with TCIs, although a causal relationship has not been established. Interim analyses of ongoing, 10-year surveillance studies to address these concerns have not found evidence of increased malignancy rates relative to that expected in the general pediatric population.³

A meta-analysis (2016; 12 RCTs) compared calcineurin inhibitors (n = 3492) vs. corticosteroids (n = 3462) in treatment of atopic dermatitis. Calcineurin inhibitors and corticosteroids had similar rates of improvement of dermatitis (81% vs 71%; p = 0.01) and treatment success (72% vs 68%; p = 0.04). There were no differences in atrophy, skin infections, or adverse events that were serious or required discontinuation of therapy.⁴

Dupilumab was FDA approved through two randomized, double blind, placebo-controlled phase 3 trials (SOLO 1 and SOLO 2). All patients in both trials were at least 18 years old, had chronic AD (according to American Academy of Dermatology Consensus Criteria Eichenfield 2014) that had been present for at least 3 years, and had ≥10% body surface area (BSA) involvement at the screening and baseline visits. Additionally, all patients had a documented recent history (within 6 months before the screening visit) of inadequate response to treatment with topical medications or whom topical treatments are otherwise medically inadvisable. The primary outcome measure in both trials was proportion of patients with both IGA (Investigator Global Assessment) 0 to 1 (on a 5-point scale) and a reduction from baseline of ≥2 points at week 16. There were several secondary endpoints included. Some examples include: proportion of patients with Eczema Area and Severity Index (EASI) -75 (≥75% improvement from baseline) at week 16, percent change from baseline to week 16 in pruritus numerical rating scale (NRS), change from baseline to week 16 in % BSA, and changes in quality of life, anxiety, and depression.

The manufacturer reports the following results from SOLO 1 and SOLO 2. In SOLO 1, the primary outcome (an IGA of 0-1 and a reduction of ≥2 points from baseline at week 16) occurred in 85 patients (38%) who received dupilumab every other week and in 83 (37%) who received dupilumab weekly, as compared with 23 (10%) who received placebo (P<0.001 for both comparisons with placebo). The results were similar in SOLO 2, with the primary outcome occurring in 84 patients (36%) who received dupilumab every other week and in 87 (36%) who received dupilumab weekly, as compared with 20 (8%) who received placebo (P<0.001 for both comparisons). In addition, in the two trials, an improvement from baseline to week 16 of at least 75% on the Eczema Area and Severity Index was reported in significantly more patients who received each regimen of dupilumab than in patients who received placebo (P<0.001 for all comparisons). Dupilumab was also associated with improvement in other clinical end points, including reduction in pruritus and symptoms of anxiety or depression and improvement in quality of life.⁵⁻⁷

REFERENCES

1. Dupixent prescribing information. Regeneron. March 2017.
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3. Eichenfield L, Tom W, Berger T, et al. Guidelines of care for the management of atopic dermatitis. Section 2. Management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol 2014;71(1):116-32.
[http://www.jaad.org/article/S0190-9622\(14\)01257-2/pdf](http://www.jaad.org/article/S0190-9622(14)01257-2/pdf).
4. J Am Acad Dermatol. 2016;75(2):410-419.e3.

5. Study of Dupilumab (REGN668/SAR231893) Monotherapy Administered to Adult Patients With Moderate-to-Severe Atopic Dermatitis (SOLO 1). NCT02277743. ClinicalTrials.gov.
6. Study of Dupilumab (REGN668/SAR231893) Monotherapy Administered to Adult Patients With Moderate-to-Severe Atopic Dermatitis (SOLO 2). NCT02277769. ClinicalTrials.gov.
7. Simpson, Eric, et al. Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis. N Engl J Med 2016; 375:2335-2348. December 15, 2016. DOI: 10.1056/NEJMoa1610020.
8. UpToDate. Treatment of atopic dermatitis (eczema). Last updated March 27, 2017.

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