

Medical Policy



Title: **Injectable Atopic Dermatitis Agent(s)**

➤ **Prime Therapeutics will review Prior Authorization requests**

Prior Authorization Form:

<https://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6512KS-INAD.pdf>

Link to Drug List (Formulary):

http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

Professional

Original Effective Date: April 5, 2017
 Revision Date(s): April 5, 2017;
 August 15, 2017; October 1, 2018;
 November 19, 2018
 Current Effective Date: November 19, 2018

Institutional

Original Effective Date: April 5, 2017
 Revision Date(s): April 5, 2017;
 August 15, 2017; October 1, 2018;
 November 19, 2018
 Current Effective Date: November 19, 2018

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact [Blue Cross and Blue Shield of Kansas Customer Service](#).

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

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 Agent

- **Dupixent®** (dupilumab)

FDA Approved Indications and Dosage¹

Agent	Indication	Dosing
Dupixent® (dupilumab) subcutaneous injection	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 Add-on maintenance treatment in patients with moderate to severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma	Atopic dermatitis: Initial dose of 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week Asthma: Initial dose of 400mg (two 200 mg injections) followed by 200 mg given every other week OR Initial dose of 600 mg (two 300 mg injections) followed by 300 mg given every other week

POLICY**Prior Authorization and Quantity Limits Criteria for Approval****Initial Evaluation**

Targeted Agent will be approved when ALL of the following are met:

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) within the past 90 days
OR
 - B. The prescriber states the patient is currently being treated with the requested agent within the past 90 days (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:
 - a. The patient has at least 10% body surface area involvement
OR
 - b. The patient has involvement of the palms and/or soles of the feet
AND
 - ii. The patient is 18 years of age or over
AND

- iii. ONE of the following:
 - a. There is documentation the patient has tried and had an inadequate response to a systemic immunosuppressant (e.g., methotrexate, azathioprine, CellCept, cyclosporine) for a minimum of 3 months
OR
 - b. There is documentation the patient has tried and had an inadequate response to BOTH a mid-potency topical steroid for a minimum of 4 weeks AND a topical calcineurin inhibitor (e.g., pimecrolimus, tacrolimus) for a minimum of 6 weeks
OR
 - c. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL systemic immunosuppressants, a mid-potency topical steroid AND a topical calcineurin inhibitor
AND
- iv. ONE of the following:
 - a. There is documentation that the patient has tried and had an inadequate response to use of a high potency topical steroid OR oral steroids for the treatment of flares for a minimum of 1 week
OR
 - b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to BOTH a high potency topical steroid AND an oral steroid. *Will accept that the patient has face/neck, skin folds, intertriginous, and/or genital area involvement for topical steroids
AND
- v. The prescriber has documented the patient's baseline pruritus and other symptom severity (e.g., erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification)
AND
- vi. The patient will continue the use of topical emollients and good skin care practices along with the requested agent
OR
- D. The patient has another FDA approved indication for the requested agent
AND
- 2. 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, immunologist)
AND
- 3. The patient does not have an FDA labeled contraindication to 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

*Note: Please approve initial loading dose

- Atopic dermatitis: 600 mg (two 300 mg injections) and 300 mg every other week maintenance dose
- Asthma: 400 mg (two 200 mg injections) followed by 200 mg maintenance dose every other week OR 600 mg (two 300 mg injections) and 300 mg every other week maintenance dose

Renewal Evaluation

1. The patient has been previously approved for the requested agent through Prime Therapeutics Prior Authorization Review process
AND
2. If the patient has a diagnosis of 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 the use of topical emollients and good skin care practices along with the requested agent
3. 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, immunologist)
AND
4. The patient does NOT have an FDA labeled contraindication to the requested agent
AND
5. 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

Brand (generic)	Quantity Per Day Limit
Dupixent (dupilumab)	
200 mg/1.14 mL pre-filled syringe	2 syringes (2.28 mL)/28 days
300mg/2 mL pre-filled syringe	2 syringes (4 mL) 28 days

RATIONALE

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, pruritic inflammatory dermatosis affecting up to 25% of children and 1-5% of adults.^{2,3} 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

Goals of treatment are to reduce symptoms (pruritus and dermatitis), prevent exacerbations, and minimize therapeutics risks. Despite its relapsing and remitting nature, the majority of patients with AD can achieve clinical improvement and disease control with nonpharmacological interventions (e.g. emollient use), conventional topical therapies (including corticosteroids and calcineurin inhibitors) and environmental and occupational modifications, when necessary.⁴ The American Academy of Dermatology guidelines 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. They are an important component of maintenance treatment and prevention of flares.⁵

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/weekly) 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/rosacea-like eruptions, skin atrophy) in clinical trials.⁵ 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.⁴ Maintenance therapy includes use of moderate to high potency topical corticosteroids or topical calcineurin inhibitors. Medium to high potency topical corticosteroids applied once daily for 2 consecutive days per week for up to 16 weeks is recommended over topical calcineurin inhibitors.⁴

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 such as, 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.

Prescribing information for Elidel® (pimecrolimus) cream indicates evaluation after 6 weeks if symptoms of AD do not improve.⁷

Phototherapy is recommended as a treatment for both acute and chronic AD in children and adults, after failure of the mentioned above. Systemic immunomodulator agents are indicated and recommended for the subset of adult and pediatric patients in whom optimized topical regimens using emollients, topical anti-inflammatory therapies, adjunctive methods, and/or phototherapy do not adequately control the signs and symptoms of disease. Photo therapy and systemic immunomodulating agents may also be used in patients whose medical, physical, and/or psychological states are greatly affected by their skin disease.⁶ Oral cyclosporine or corticosteroids are short term treatment options for moderate to severe dermatitis with rapid onset or bridging therapy. Oral cyclosporine is suggested over oral corticosteroid. AD symptoms begin to resolve as quickly with the use of cyclosporine within the first week and dramatic improvement can be seen in 8 weeks. Long term (e.g. beyond one year) use of oral cyclosporine is limited by its side effects, mainly hypertension and kidney toxicity. Oral corticosteroids are recommended for patients whom cannot use cyclosporine. Dose for corticosteroid recommended is 40 to 60 mg per day for one week then taper over the following two to three weeks. While patients are being tapered off, patients are transitioned to another immunosuppressive agent with better safety profile for long term use. Second-line systemic immunosuppressive agents include methotrexate, azathioprine, and mycophenolate mofetil. The maximum benefit of methotrexate may not be seen for several months after start of therapy. Azathioprine and mycophenolate mofetil benefits maybe seen for 6 to 8 weeks.^{3,4}

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 $\geq 10\%$ 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 trails 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 ($\geq 75\%$ 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.⁷⁻⁹

REVISIONS	
04-05-2017	Policy published in New to Market Drugs policy on 04-19-2017. Policy retro-effective to 04-05-2017.
08-15-2017	Policy published as a stand-alone policy on 07-14-2017. Effective 08-15-2017.
10-01-2018	<p>In Description section:</p> <ul style="list-style-type: none"> ▪ Converted FDA Approved Indication and Dosage information into a chart for more clarity <p>In Policy section:</p> <div style="border: 1px solid black; padding: 5px;"> <p>Summary of revisions:</p> <ul style="list-style-type: none"> • For Atopic Dermatitis – update language for prerequisites to “tried and had an inadequate response to” with minimum trial length (length of time to achieve clinical response or failure) <ul style="list-style-type: none"> ○ Systemic immunosuppressants – 3 months ○ Topical steroids – 4 weeks ○ Topical calcineurin inhibitors – 6 weeks (per Elidel label, physician should assess after 6 weeks of use) ○ Addition of intolerance / contraindication / hypersensitivity to all systemic immunosuppressants (in addition to topical prerequisites) • Addition of good skin care practices to be continued with the requested agent • Require a specialist for all indications with initial evaluation and for all requests for renewal evaluation </div> <p><u>Initial Evaluation</u></p> <ul style="list-style-type: none"> ▪ In Item 1 A and 1 B added "within the past 90 days" ▪ In Item 1B removed "using" and added "currently being treated with" ▪ In Item 1 C ii revised "at least 18year old or older" to "18 years of age or over" ▪ In Item 1 C iii a removed "failed" and "for atopic dermatitis within the last 180 days" and added "had an inadequate response to" and "for a minimum of 3 months" to read "There is documentation the patient has tried and had an inadequate response to a systemic immunosuppressant (e.g., methotrexate, azathioprine, CellCept, cyclosporine) for a minimum of 3 months" ▪ In Item 1 C iii b removed "failed" and "maintenance therapy (At least one must be within the last 180 days; the other may being the last 999 days)" and added "had an inadequate response to BOTH", "for a minimum of 4 weeks", and "for a minimum of 6 weeks" to read "There is documentation the patient has tried and had an inadequate response to BOTH a mid-potency topical steroid for a minimum of 4 weeks AND a topical calcineurin inhibitor (e.g., pimecrolimus, tacrolimus) for a minimum of 6 weeks" ▪ In Item 1 C iii c added "ALL systemic immunosuppressants" to read "The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL systemic immunosuppressants, a mid-potency topical steroid AND a topical calcineurin inhibitor" ▪ In Item 1 C iv a revised "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" to "There is documentation that the patient has tried and had an inadequate response to use

REVISIONS	
	<p>of a high potency topical steroid OR oral steroids for the treatment of flares for a minimum of 1 week"</p> <ul style="list-style-type: none"> ▪ In Item 1 C iv b removed "for short-term use" and added "BOTH" to read "The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to BOTH a high potency topical steroid AND an oral steroid" ▪ In Item 2 added "immunologist" to read "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, immunologist)" ▪ After Length of Approval added "*Note: Please approve initial loading dose of 600 mg (two 300 mg injections) ONCE along with the maintenance therapy" <p><u>Renewal Evaluation</u></p> <ul style="list-style-type: none"> ▪ In Item 2 B removed "as a component of maintenance treatment to aid in the prevention of flares" and added "and good skin care practices along with the requested agent" to read "The patient will continue the use of topical emollients and good skin care practices along with the requested agent" ▪ Added "3. 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, immunologist)" ▪ Updated the Quantity Limits chart
	Rationale section updated
	References updated
11-19-2018	<p>In Description section:</p> <ul style="list-style-type: none"> ▪ FDA Approved Indications an Dosage for Dupixent updated <p>In Policy section:</p> <ul style="list-style-type: none"> ▪ In Initial Evaluation Length of Approval Note removed "ONCE along with the" to read "*Note: Please approve initial loading dose • Atomic dermatitis: 600 mg (two 300 mg injections) ONCE along with the and 300 mg every other week maintenance dose therapy • Asthma: 400 mg (two 200 mg injections) followed by 200 mg maintenance dose every other week OR 600 mg (two 300 mg injections) and 300 mg every other week maintenance dose" ▪ In Quantity Limits table added 200 mg dose.
	References updated

REFERENCES

1. Dupixent prescribing information. Regeneron Pharmaceuticals, Inc. October 2018.
2. Eichenfield L, Tom W, Chamlin S, et al. Guidelines of care for the management of atopic dermatitis: Part 1: Diagnosis and Assessment of Atopic Dermatitis. J Am Acad Dermatol. 2014;70(2): 338–351.
3. Berger, Timothy G., MD., et al. Management of Severe Refractory Atopic Dermatitis (eczema) in Adults. UpToDate. Last updated May 3, 2018.
4. Weston, William L., MD., et al. Treatment of Atopic Dermatitis (eczema). UpToDate. Last updated April 2018.
5. 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.
6. Sidbury, Robert, MD., et al. Guidelines of Care for the Management of Atopic Dermatitis. Section 3. Management and Treatment with Phototherapy and Systemic Agents. J Am Acad Dermatol 2014; 71 (2): 327-349.

7. Elidel prescribing information. Valeant Pharmaceuticals. December 2017.
8. Study of Dupilumab (REGN668/SAR231893) Monotherapy Administered to Adult Patients With Moderate-to-Severe Atopic Dermatitis (SOLO 1). NCT02277743. ClinicalTrials.gov.
9. Study of Dupilumab (REGN668/SAR231893) Monotherapy Administered to Adult Patients With Moderate-to-Severe Atopic Dermatitis (SOLO 2). NCT02277769. ClinicalTrials.gov.
10. 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.