Interleukin-4 (IL-4) Inhibitor Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid, FlexRx Open, FlexRx Closed, GenRx Open, Gen Closed, Health Insurance Marketplace, FocusRx and KeyRx formularies.

This is a FlexRx standard and GenRx standard prior authorization.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

<table>
<thead>
<tr>
<th>FDA APPROVED INDICATIONS AND DOSAGE¹</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agent</strong></td>
<td><strong>Indication</strong></td>
</tr>
<tr>
<td>Dupixent® (dupilumab)</td>
<td>Treatment of patients 12 years of age and older 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.</td>
</tr>
</tbody>
</table>
| subcutaneous injection              | Atopic dermatitis
Adults: Initial dose of 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week
12-17 years of age:
• <60kg: Initial dose of 400 mg (two 200 mg injections) followed by 200 mg given every other week
• ≥60kg: Initial dose of 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week

Asthma
Adults: Initial dose of 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week
12-17 years of age:
Initial dose of 400 mg (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
Patients with corticosteroid-dependent asthma OR with co-morbid moderate to severe atopic dermatitis, start with initial dose of 600
**CLINICAL RATIONALE**

**Atopic Dermatitis**

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. 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.

Goals of treatment are to reduce symptoms (pruritus and dermatitis), prevent exacerbations, and minimize therapeutic 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. 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. 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. 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. 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.

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 and Protopic® (tacrolimus) ointment indicate evaluation after 6 weeks if symptoms of AD do not improve for adults and pediatrics.\textsuperscript{7,18}

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.\textsuperscript{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.\textsuperscript{3,4}

**Efficacy**

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.\textsuperscript{7-9}
The efficacy and safety of Dupixent monotherapy in adolescent subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial in 251 adolescent subjects 12 to 17 years of age, with moderate-to-severe AD and a minimum BSA involvement of ≥10%. Eligible subjects enrolled into this trial had previous inadequate response to topical medication. Subjects in the Dupixent group with baseline weight of <60 kg received an initial dose of 400 mg at Week 0, followed by 200 mg Q2W for 16 weeks. Subjects with baseline weight of ≥60 kg received an initial dose of 600 mg at Week 0, followed by 300 mg Q2W for 16 weeks. Subjects were permitted to receive rescue treatment at the discretion of the investigator. Subjects who received rescue treatment were considered non-responders. The primary endpoint was the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and at least a 2-point improvement from baseline to Week 16. Other evaluated outcomes included the proportion of subjects with EASI-75 or EASI-90 (improvement of at least 75% or 90% in EASI from baseline, respectively), and reduction in itch as measured by the Peak Pruritus NRS (≥4-point improvement).

The efficacy results at Week 16 were as follows:
- IGA 0 or 1: 24% for Dupixent and 2% for placebo
- EASI-75: 42% for Dupixent and 8% for placebo
- EASI-90: 23% for Dupixent and 2% for placebo
- Peak Pruritus NRS (≥4-point improvement): 37% for Dupixent and 5% for placebo

**Asthma**

Asthma is a chronic inflammatory disorder of the airways.\(^\text{11,13}\) It is characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation.\(^\text{11}\) Symptoms of asthma include wheezing, coughing, recurrent difficulty breathing, shortness of breath, and chest tightness.\(^\text{11,13}\) Generally, these symptoms will occur or worsen with exposure to allergens and irritants, infections, exercise, changes in weather, stress, or menstrual cycles.\(^\text{11}\) The National Asthma Education and Prevention Program (NAEPP) Expert Panel guidelines recommend the use of detailed medical history, physical examination, and spirometry to make a diagnosis of asthma. In addition, differential diagnosis of asthma should be considered.\(^\text{11}\)

Markers of asthma that is not adequately controlled in patients receiving therapy include limitation of normal activities, poor lung function with FEV1 of <80% predicted, at least 2 episodes per year of asthma exacerbations requiring oral systemic corticosteroids. More frequent and intense exacerbations (e.g. requiring urgent, unscheduled care, hospitalization, or ICU admission) indicate poorer disease control.\(^\text{11}\)

The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma.\(^\text{13}\) Long-term goals for asthma management are to achieve good control of symptoms, maintain normal activity level and to minimize the future risk of exacerbations, fixed airflow limitation and side-effects.\(^\text{12}\) IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with low dose ICS in combination with a LABA.\(^\text{13}\) Severe asthma is defined as “asthma that requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming ‘uncontrolled’ or which remains uncontrolled despite this therapy.”\(^\text{11}\) Early initiation of low dose inhaled corticosteroid (ICS) in patients with asthma has led to greater improvement in lung function than if initiation of ICS after symptoms have been present for more than 2 to 4 years.\(^\text{13}\)

GINA recommends as-needed reliever inhaler, short acting b-agonist (SABA) as Step 1. SABAs are highly effective for the quick relief of asthma symptoms. However, there is insufficient evidence for use of SABA alone for the treatment of asthma. SABA monotherapy for the
treatment of asthma should be reserved for patients with occasional daytime symptoms (less than twice a month) of short duration with no night waking and with normal lung function. Step 2 is the recommendation of treatment with ICS. At low doses, ICS reduces asthma symptoms, increases lung function, improves quality of life, and reduces the risk of exacerbations and asthma-related hospitalizations or death. Leukotriene receptor antagonists (LTRA) are less effective than ICS. Step 3 involves one or two maintenance inhalers and an as-needed reliever. Combination low dose ICS and long acting β-agonist (LABA) as maintenance treatment plus an as-needed SABA or low dose ICS with formoterol (budesonide or beclometasone) with a reliever treatment are options recommended. Step 4 involves 2 or more maintenance agents with an as-needed reliever. Combination low dose ICS with formoterol or medium dose ICS with LABA and an as-needed SABA are recommended options. Step 5 includes higher level care and/or add-on treatment. Depending on treatment options used in previous steps, long acting muscarinic antagonists (LAMA) such as tiotropium, omalizumab, or anti-interleukin-5 (mepolizumab and reslizumab) are additional pharmacologic options as add-on therapy.13

Severe Asthma Phenotype and Eosinophilic Asthma Subphenotype
Severe asthma is defined as “asthma that requires treatment with high dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming ‘uncontrolled’ or which remains ‘uncontrolled’ despite this therapy.”13 Despite the availability of multiple asthma treatments, a substantial proportion of patients with severe asthma continue to have uncontrolled disease.17 Thirty to forty percent of severe asthma patients still need regular bursts of systemic steroids to control their asthma.16 Severe asthma has a considerable amount of variability in its pattern of inflammation, and this variability causes multiple phenotypical differences that influence treatment response.13

Eosinophilic asthma is a subphenotype of severe asthma characterized by elevated sputum and blood eosinophil levels as well as increased asthma severity, atopy, late-onset disease, and steroid refractoriness.13 Several biomarkers including blood eosinophilic counts and sputum eosinophilic counts are used in diagnosing severe asthma with an eosinophilic phenotype.13 As with other severe forms of asthma, the Gold Standard/International Guidelines treatment for severe asthma, including eosinophilic asthma, is high dose ICS plus a long acting beta-2 agonist (LABA), leukotriene modifier or theophylline and/or continuous systemic corticosteroids as background therapy.13,14

Efficacy
The asthma development program included three randomized, double-blind, placebo controlled, parallel-group, multi-center trials (AS Trials 1, 2, and 3) of 24 to 52 weeks in treatment duration which enrolled a total of 2888 subjects (12 years of age and older). Subjects enrolled in AS Trials 1 and 2 were required to have a history of 1 or more asthma exacerbations that required treatment with systemic corticosteroids or emergency department visit or hospitalization for the treatment of asthma in the year prior to trial entry. Subjects enrolled in AS Trial 3 required dependence on daily oral corticosteroids in addition to regular use of high-dose inhaled corticosteroids plus an additional controller(s). In all 3 trials, subjects were enrolled without requiring a minimum baseline blood eosinophil count. In AS Trials 2 and 3 subjects with screening blood eosinophil level of >1500 cells/mL (<1.3%) were excluded. DUPIXENT was administered as add-on to background asthma treatment. Subjects continued background asthma therapy throughout the duration of the studies, except in AS Trial 3 in which OCS dose was tapered as described below.

AS Trial 1 was a 24-week dose-ranging study which included 776 subjects (18 years of age and older). DUPIXENT compared with placebo was evaluated in adult subjects with moderate to severe asthma on a medium or high-dose inhaled corticosteroid and a long acting beta agonist. Subjects were randomized to receive either 200 mg (N=150) or 300 mg (N=157) DUPIXENT every other week (Q2W) or 200 mg (N=154) or 300 mg (N=157) DUPIXENT every
4 weeks following an initial dose of 400 mg, 600 mg or placebo (N=158), respectively. The primary endpoint was mean change from baseline to Week 12 in FEV1 (L) in subjects with baseline blood eosinophils ≥300 cells/mcL. Other endpoints included percent change from baseline in FEV1 and annualized rate of severe asthma exacerbation events during the 24-week placebo controlled treatment period. Results were evaluated in the overall population and subgroups based on baseline blood eosinophil count (≥300 cells/mcL and <300 cells/mcL. Additional secondary endpoints included responder rates in the patient reported Asthma Control Questionnaire (ACQ-5) and Asthma Quality of Life Questionnaire, Standardized Version (AQLQ(S)) scores.

AS Trial 2 was a 52-week study which included 1902 subjects (12 years of age and older). DUPIXENT compared with placebo was evaluated in 107 adolescents and 1795 adult subjects with moderate-to-severe asthma on a medium or high-dose inhaled corticosteroid (ICS) and a minimum of one and up to two additional controller medications. Subjects were randomized to receive either 200 mg (N=631) or 300 mg (N=633) DUPIXENT Q2W (or matching placebo for either 200 mg [N=317] or 300 mg [N=321] Q2W) following an initial dose of 400 mg, 600 mg or placebo respectively. The primary endpoints were the annualized rate of severe exacerbation events during the 52-week placebo controlled period and change from baseline in pre-bronchodilator FEV1 at Week 12 in the overall population (unrestricted by minimum baseline blood eosinophils count). Additional secondary endpoints included annualized severe exacerbation rates and FEV1 in patients with different baseline levels of blood eosinophils as well as responder rates in the ACQ-5 and AQLQ(S) scores.

AS Trial 3 was a 24-week oral corticosteroid-reduction study in 210 subjects with asthma who required daily oral corticosteroids in addition to regular use of high dose inhaled corticosteroids plus an additional controller. After optimizing the OCS dose during the screening period, subjects received 300 mg DUPIXENT (N=103) or placebo (N=107) once Q2W for 24 weeks following an initial dose of 600 mg or placebo. Subjects continued to receive their existing asthma medicine during the study; however their OCS dose was reduced every 4 weeks during the OCS reduction phase (Week 4-20), as long as asthma control was maintained. The primary endpoint was the percent reduction of oral corticosteroid dose at Weeks 20 to 24 compared with the baseline dose, while maintaining asthma control in the overall population (unrestricted by minimum baseline blood eosinophils count). Additional secondary endpoints included the annualized rate of severe exacerbation events during treatment period and responder rate in the ACQ-5 and AQLQ(S) scores.

AS Trials 1 and 2 evaluated the frequency of severe asthma exacerbations defined as deterioration of asthma requiring the use of systemic corticosteroids for at least 3 days or hospitalization or emergency room visit due to asthma that required systemic corticosteroids. In the primary analysis population (subjects with baseline blood eosinophil count of ≥300 cells/mcL in AS Trial 1 and the overall population in AS Trial 2), subjects receiving either DUPIXENT 200 mg or 300 mg Q2W had significant reductions in the rate of asthma exacerbations compared to placebo. In the overall population in AS Trial 2, the rate of severe exacerbations was 0.46 and 0.52 for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo rates of 0.87 and 0.97. The rate ratio of severe exacerbations compared to placebo was 0.52 (95% CI: 0.41, 0.66) and 0.54 (95% CI: 0.43, 0.68) for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively.

Prespecified subgroup analyses of AS Trials 1 and 2 demonstrated that there were greater reductions in severe exacerbations in subjects with higher baseline blood eosinophil levels. In AS Trial 2, reductions in exacerbations were significant in the subgroup of subjects with baseline blood eosinophils ≥ 150 cells/mcL. In subjects with baseline blood eosinophil count < 150 cells/mcL, similar severe exacerbation rates were observed between DUPIXENT and placebo.
Significant increases in pre-bronchodilator FEV1 were observed at Week 12 for AS Trials 1 and 2 in the primary analysis populations (subjects with baseline blood eosinophil count of ≥ 300 cells/mcL in AS Trial 1 and the overall population in AS Trial 2). In the overall population in AS Trial 2, the FEV1 LS mean change from baseline was 0.32 L (21%) and 0.34 L (23%) for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo means of 0.18 L (12%) and 0.21 L (14%). The mean treatment difference versus placebo was 0.14 L (95% CI: 0.08, 0.19) and 0.13 L (95% CI: 0.08, 0.18) for DUPIXENT 200 mg Q2W and 300 mg Q2W, respectively. Subgroup analysis of AS Trials 1 and 2 demonstrated greater improvement in subjects with higher baseline blood eosinophils.

REFERENCES
8. Study of Dupilumab (REGN668/SAR231893) Monotherapy Administered to Adult Patients With Moderate-to-Severe Atopic Dermatitis (SOLO 1). NCT02277743. ClinicalTrials.gov.

Interleukin-4 (IL-4) Inhibitor Prior Authorization with Quantity Limit

TARGET AGENT
Dupixent® (dupilumab)

QUANTITY LIMIT TARGET AGENT- RECOMMENDED LIMIT

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
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<tbody>
<tr>
<td>Dupixent (dupilumab)</td>
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<tr>
<td>200 mg/1.14 mL pre-filled syringe</td>
<td>4460352000E530</td>
<td>M, N, O, or Y</td>
<td>2 syringes (2.28 mL)/28 days</td>
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<td>9027302000E520</td>
<td>M, N, O, or Y</td>
<td>2 syringes (4 mL)/28 days</td>
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PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Initial Evaluation

Target 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)
   OR
   B. The prescriber states the patient is currently being treated with 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:
         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 12 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 at least 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 a diagnosis of moderate to severe asthma AND ALL of the following:
   i. The patient is 12 years of age and over
   AND
   ii. ONE of the following:
      a. The patient has eosinophilic type asthma AND the patient has a baseline blood eosinophilic count of 150 cells/microliter or higher OR
      b. There is documentation the patient has oral corticosteroid dependent type asthma
   AND
   iii. The patient has baseline Forced Expiratory Volume (FEV1) that is less than 80% of predicted
   AND
   iv. The patient has ONE of the following:
      a. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months OR
      b. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months OR
      c. Controlled asthma that worsens when the doses of inhaled or systemic corticosteroids are tapered
   AND
   v. ONE of the following:
      a. The patient is NOT currently being treated with the requested agent AND is currently treated with a maximally tolerated inhaled corticosteroid within the past 90 days OR
      b. The patient is currently being treated with the requested agent AND is currently treated with an inhaled corticosteroid that is dosed as needed to control symptoms OR
      c. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to inhaled corticosteroids
   AND
vi. ONE of the following:
   a. The patient is currently treated with ONE of the following within the past 90 days:
      A. A long-acting beta-2 agonist (LABA) OR
      B. A leukotriene receptor antagonist (LRTA) OR
      C. Long-acting muscarinic antagonist (LAMA) OR
      D. Theophylline
      OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LRTA), long-acting muscarinic antagonist (LAMA), AND theophylline
      OR
   E. 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., atopic dermatitis - dermatologist, allergist, immunologist; asthma - allergist, immunologist, pulmonologist)
      AND
3. The patient will NOT receive the requested agent in combination with another biologic agent for the requested indication [e.g., Xolair, IL-5 inhibitor (Cinqair, Fasenra, Nucala)]
      AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent
      AND
5. ONE of the following:
      A. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
      B. ALL of the following:
         i. The requested quantity (dose) is greater than the program quantity limit
            AND
         ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
            AND
         iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

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. ONE of the following:
   A. The patient has a diagnosis of moderate-to-severe atopic dermatitis AND BOTH of the following:
      i. The patient has a reduction or stabilization from baseline in at least ONE of the following:
1. Affected body surface area
   OR
2. Flares
   OR
3. Pruritus, erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification

   AND
   ii. The patient will continue the use of topical emollients and good skin care practices along with the requested agent

   OR

B. The patient has a diagnosis of moderate to severe asthma AND BOTH of the following:
   i. The patient has had clinical response or disease stabilization with the requested agent as defined by ONE of the following:
      1. Increase in percent predicted Forced Expiratory Volume (FEV$_1$) from baseline
      OR
      2. Decrease in the dose of inhaled corticosteroids required to control the patient’s asthma
      OR
      3. Decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma
      OR
      4. Decrease in number of hospitalizations, need for mechanical ventilation, or visits to urgent care or emergency room due to exacerbations of asthma

   AND
   ii. ONE of the following:
      1. The patient is currently treated and is compliant with standard therapy (e.g. inhaled corticosteroids, long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LRTA), long-acting muscarinic antagonist (LAMA), theophylline) within the past 90 days
      OR
      2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL standard therapies

   OR

C. The patient has another FDA approved indication for the requested agent AND has received clinical benefit and/or disease stability with the requested agent

   AND

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. atopic dermatitis - dermatologist, allergist, immunologist; asthma - allergist, immunologist, pulmonologist)

   AND

4. The patient will NOT receive the requested agent in combination with another biologic agent for the requested indication [e.g., Xolair, IL-5 inhibitor (Cinqair, Fasenra, Nucala)]

   AND

5. The patient does NOT have an FDA labeled contraindication to the requested agent

   AND

6. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
   OR
   B. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication

AND

iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

**Length of Approval:** 12 months
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT
OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm
   
   **OR**

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   **OR**
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
   **OR**

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

**Length of Approval:** As per program specific criteria