Pharmacy Management Drug Policy

SUBJECT: Interleukin Antagonists for Asthma and Other Conditions: Nucala (mepolizumab), Cinqair (reslizumab), Fasenra (benralizumab), Dupixent (dupilumab), Adbry (tralokinumab-ldrm), Ebglyss (lebrikizumab) & Nemluvio (nemolizumab)
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If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Asthma

Asthma is a heterogeneous syndrome that might be better described as a constellation of phenotypes, each with distinct cellular and molecular mechanisms, rather than as a singular disease. One of these phenotypes is eosinophilic asthma. Chronic airway inflammation results in symptoms that include wheezing, shortness of breath, chest tightness, and cough.

Development of eosinophilic inflammation is dependent on the biological activity of Interleukin-5 (IL-5), an inflammatory cytokine. IL-5 is responsible for growth, differentiation, recruitment, activation, and survival of eosinophils. Nucala (mepolizumab), Cinqair (reslizumab), and Fasenra (benralizumab), IL-5 antagonist monoclonal antibodies, antagonize the IL-5/eosinophil inflammatory pathway. Nucala and Cinqair do so by binding to IL-5, and Fasenra through direct binding to the IL-5 surface receptors on eosinophils.

Dupixent (dupilumab) is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes. These actions decrease interleukin signaling which reduces production and survival of eosinophils, thereby reducing inflammation. However, the mechanism of Dupixent action in asthma has not been definitively established.

Atopic Dermatitis

Atopic dermatitis is a chronic inflammatory disease of the skin. Symptoms vary in severity and the disease often follows a relapsing course. Clinical findings include pruritus (most common) erythema, dry skin, edema, erosions/excoriations, oozing/crusting, and lichenification. Pathogenesis involves a complex combination of genetic and environmental factors. Numerous cytokines are involved; however, IL-13 is found to be locally overexpressed in patients with atopic dermatitis, compromising skin integrity.

Adbry (tralokinumab-ldrm) and Ebglyss (lebrikizumab) are human IgG4 monoclonal antibodies that specifically bind to human interleukin13 (IL-13) and inhibits its interaction with the IL-13 receptor

complex. Adbry and Ebglyss inhibits IL-13-induced responses including the release of proinflammatory cytokines, chemokines and IgE.

Dupixent (dupilumab) is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes. This limits the release of proinflammatory cytokines, chemokines, nitric oxide, and IgE.

Nemolizumab is a humanized IgG2 monoclonal antibody that blocks the α subunit of the IL-31 receptor, modulates the neuroimmune response, and alleviates itching by directly blocking signaling.

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

CRSwNP is a subtype of chronic rhinosinusitis (CRS). It is a heterogeneous chronic inflammatory disease of the nasal lining and sinuses, resulting in the development of noncancerous soft tissue growth (polyps) in the sino-nasal cavity. Symptoms include loss of smell, nasal congestion, and nasal drainage. Most patients with CRSwNP show evidence of type 2 inflammation. Nasal polyp tissue is characterized by local eosinophil inflammation in a large majority of patients with this condition. Despite optimized treatment, nasal polyps have a high rate of recurrence.

Dupixent (dupilumab) is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes. This limits inflammation driven by IL-4 and IL-13, including actions by eosinophils, mast cells, histamine, and leukotrienes.

Nucala (mepolizumab) is an IL-5 antagonist (IgG1 kappa), inhibiting the bioactivity of IL-5 by blocking its binding to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface. IL-5 is the major cytokine responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils. Nucala reduces the production and survival of eosinophils. However, the exact mechanism in CRSwNP is unknown.

Chronic Obstructive Pulmonary Disease (COPD)

COPD is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum productions and/or exacerbation) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.

Dupixent (dupilumab) is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes. This limits inflammation driven by IL-4 and IL-13, including actions by elevated eosinophils which is a hallmark presentation of type 2 inflammation of COPD.

Eosinophilic Esophagitis (EoE)

EoE is a chronic, progressive, allergic inflammatory disease of the esophagus characterized by esophageal dysfunction and eosinophilic infiltration. It occurs when high levels of eosinophils accumulate in the esophageal tissue. Persistent inflammation can result in esophageal remodeling, fibrosis, and stricture formation. Symptoms vary by age. Children often have non-specific symptoms such as feeding difficulty, nausea and vomiting, abdominal pain, heartburn, and failure to thrive. Adolescents/Adults typically present with dysphagia and food impaction. Regarding pathogenesis, IL-

13 is overexpressed in the esophageal mucosa of patients with EoE and plays a role in eosinophil recruitment, remodeling, and fibrosis. IL-4 leads to signaling and recruitment of eosinophils into tissue, and IL-5 appears to be involved in the maturation and release of eosinophils.

Dupixent (dupilumab) is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes. Inhibition of IL-4 and IL-13 induced responses limits inflammation caused by multiple cell types and inflammatory mediators.

Eosinophilic Granulomatosis with Polyangiitis (EGPA)

EGPA is a systemic small- and medium-vessel necrotizing vasculitis, characterized by extravascular granulomas, eosinophilia, and tissue infiltration by eosinophils. It occurs in people with adult-onset asthma, allergic rhinitis, nasal polyposis, or a combination. Nucala (mepolizumab), by inhibiting IL-5 signaling, reduces the production and survival of eosinophils and is thought, therefore, to reduce inflammation. However, the mechanism of Nucala action in asthma and EGPA has not been definitively established.

Prurigo Nodularis (PN)

PN is a rare, chronic inflammatory skin condition primarily affecting older adults. The disease is characterized by a self-perpetuating itch-scratch cycle with symmetrically distributed, multiple, firm, pruritic nodules. The nodules are typically dome-shaped and often found on areas of the skin that are amenable to scratching, such as the extensor surfaces of the arms and legs and on the trunk (sparing the face, palms, soles, and difficult to reach areas). The absence of PN lesions on the upper mid-back is called the 'butterfly sign.' Nodules can be flesh-colored, erythematous, or brown/black, and range in number (a few to hundreds) and size (millimeters to several centimeters). The exact pathogenesis of PN is unclear but it is mediated by neural and immune mechanisms, including type 2 cytokines such as interleukin (IL) 4, IL-5, and IL-13 and IL-31.

Dupixent (dupilumab) is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes. Inhibition of IL-4 and IL-13 induced responses limits inflammation caused by multiple cell types and inflammatory mediators.

Nemolizumab is a humanized IgG2 monoclonal antibody that blocks the α subunit of the IL-31 receptor, modulates the neuroimmune response, and alleviates itching by directly blocking signaling.

Hypereosinophilic Syndrome (HES)

The Hypereosinophilic syndromes (HES) are a group of rare disorders marked by the sustained overproduction of eosinophils, in which eosinophilic infiltration and mediator release cause damage to multiple organs. Treatment is based on patient presentation, lab findings, and mutational analysis. Nucala (mepolizumab) by inhibiting IL-5 signaling, reduces the production and survival of eosinophils; however, the mechanism of action in HES has not been definitively established.

Adbry (tralokinumab-ldrm) indicated for the treatment of moderate-to-severe atopic dermatitis in patients 12 years and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Cinqair (reslizumab) is indicated for add-on maintenance treatment of patients with severe asthma aged ≥18 years who have an eosinophilic phenotype.

Dupixent (dupilimumab) is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.

Dupixent (dupilimumab) is indicated for the treatment of patients 6 months 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.

Dupixent (dupilimumab) is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

Dupixent (dupilimumab) is indicated for the treatment of adult and pediatric patients aged 1 years and older, weighing at least 15 kg, with eosinophilic esophagitis (EoE).

Dupixent (dupilimumab) is indicated for the treatment of adult patients with prurigo nodularis.

Fasenra (benralizumab) is indicated for add-on maintenance treatment of patients with severe asthma aged ≥ 6 years who have an eosinophilic phenotype.

Nucala (mepolizumab) is indicated for add-on maintenance treatment of patients with severe asthma aged ≥ 6 years who have an eosinophilic phenotype.
Nucala (mepolizumab) is indicated for add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP).

Nucala (mepolizumab) is indicated for the treatment of adult patients with Eosinophilic granulomatosis with polyangiitis (EGPA, also known as Churg-Strauss Syndrome [CSS]).

Nucala (mepolizumab) is indicated for the treatment of adult and pediatric patients aged 12 years and older with Hypereosinophilic syndrome (HES) for ≥ 6 months without an identifiable non-hematologic secondary cause.

POLICY:

Moderate to Severe Asthma

Based upon our criteria and review of the peer-reviewed literature, treatment with **Nucala, Cinqair, Fasenra, or Dupixent** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment that reduces the risk of asthma exacerbations in patients with moderate to severe eosinophilic or oral-corticosteroid dependent (Dupixent only) asthma. Therefore, it is considered **medically appropriate** if **all** the following criteria are met:

1. Patient must be at least 6 years of age for Fasenra, at least 6 years old for Dupixent, at least 18 years of age for Cinqair, and at least 6 years old for Nucala **AND**
2. Patient must be followed by, and drug ordered by an Allergist/Immunologist or Pulmonologist **AND**
3. Patient must have moderate to severe persistent asthma **AND**
4. Patient must be a non-smoker. Non-smoker is defined as someone who has not smoked in the preceding 6 months **AND**

5. Patient must have well-documented use of high-dose inhaled corticosteroids (ICS) (see **Tables 1-3** in policy guidelines section) for **at least 3 months**, be compliant with existing therapy, and have followed GINA guidelines for asthma treatment including an adequate trial of a high-dose inhaled steroid in combination with a long-acting beta agonist
   a. Compliance will be assessed based on pharmacy refill history. If the patient does not have pharmacy benefits through this health plan, a recent pharmacy profile will be requested. Progress notes documenting usage of sample medication may also be requested.
   b. If there is a contraindication to use of a long-acting beta agonist, then an alternative controller drug may be used in combination with a high-dose inhaled steroid such as a leukotriene inhibitor or long-acting muscarinic antagonist.
   c. Patient must have documentation of inadequate control despite optimal therapy (above) for a period of at least 3 months **AND**

6. Must be used in combination with existing asthma therapy (as defined above)
   a. Monotherapy will not be authorized as these agents are only FDA approved as an add-on maintenance treatment **AND**

7. Requests for Cinqair (medical benefit only), Fasenra (office-administered, medical benefit), and Nucala (office administered, medical benefit), will require documentation of an inability to self-inject. This requirement does not apply to Fasenra and Nucala requests for individuals 6-11 years of age.

   ****This applies to New Start AND Recertification requests (including new to plan) for all lines of business, except Medicare. Does NOT apply to Medicare B (Medicare Advantage) ****
   a. Fasenra—For pediatric patients 12 to less than 18 years of age, documentation must also include the inability of a caregiver to administer the medication. This requirement does not apply to Fasenra requests for individuals 6-11 years of age.
   b. Nucala – For pediatric patients 12 to less than 18 years of age, documentation must also include the inability of a caregiver to administer the medication. This requirement does not apply to Nucala requests for individuals 6-11 years of age.
      i. Nucala ages 6-11 years old – The FDA-approved dose is 40mg every 4 weeks. For those that meet for coverage under the medical benefit, the use of Nucala 40mg/0.4ml prefilled syringes is required to eliminate vial waste **AND**

8. For Nucala: Patient must have a peripheral blood eosinophil count of at least 150 cells per microliter within the **preceding 6 weeks** before Nucala request **OR** at least 300 cells per microliter at any time within the **preceding year AND**
   For Cinqair: Patient must have a peripheral blood eosinophil count of at least 400 cells per microliter within **the preceding 6 weeks AND**
   For Fasenra: Patient must have a peripheral blood eosinophil count of at least 150 cells per microliter within the **preceding 6 weeks AND**
   For Dupixent: Patient must have a peripheral blood eosinophil count of at least 150 cells per microliter within the **preceding 6 weeks.** *If the patient is oral corticosteroid dependent, then eosinophil count is not required**.** OCS-dependence (reliance on daily, maintenance oral prednisone, methylprednisolone, etc.) must be supported by clinical progress notes and/or pharmacy claims **AND**

*****See links to eosinophil calculators in policy guidelines section below*****

9. Patient must have experienced **2 or more** asthma exacerbations within the **preceding 12 months** that required medical intervention (defined as non-routine doctor visits, urgent care visits, emergency room visits, hospital admissions, or documented need for acute systemic steroids) despite existing therapy as outlined in criterion #5

10. Initial approval will be for 6 months. Subsequent recertifications after the initial 6-month approval will require an objective assessment of response from the provider (reductions in hospitalizations, ER visits, and rescue medication use) as well as compliance history with the inhaled corticosteroid and controller medication. Recertification will not be granted if the patient starts or re-starts smoking. See recertification statement and approval time-period table in policy guidelines section of this policy.

Chronic Obstructive Pulmonary Disease (COPD)

Based upon our criteria and review of the peer-reviewed literature, treatment with **Dupixent** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for Chronic Obstructive Pulmonary Disease (COPD). Therefore, it is considered **medically appropriate** if **all** the following criteria are met:

1. Must be requested by or in consultation with a Pulmonologist **AND**
2. Must be 18 years of age or older **AND**
3. Must have confirmed diagnosis of COPD by spirometry documenting FEV1/FVC ratio < 0.7 post bronchodilation **AND**
    a. Must have moderate to severe disease
        i. Moderate to severe disease defined as GOLD 2 (moderate) or GOLD 3 (severe) airflow obstruction as demonstrated by FEV1 < 70% predicted **AND**
    b. Must be symptomatic (grade ≥ 2 on mMRC dyspnea scale) **AND**
4. Must have minimum blood eosinophil count of 300 cells per microliter within the last 4 weeks
5. Must have [**a or b] + c** in the previous year despite receiving maintenance triple therapy consisting of a long-acting muscarinic antagonist (LAMA), long-acting beta agonist (LABA), and inhaled corticosteroid (ICS) or LAMA–LABA alone if ICS agents were contraindicated.
    a. Two moderate exacerbations. A moderate exacerbation is defined as in need of treatment with systemic corticosteroids and/or antibiotics was required
    b. One severe exacerbation, defined as an exacerbation resulted in hospitalization or observation for over 24 hours in an emergency department or urgent care facility
    c. Symptoms of chronic bronchitis (chronic productive cough) for 3 months, in the absence of other known causes of chronic cough
6. Must have been using **a or b** for at least 3 months in the past year:
    a. Triple Therapy consisting of a long-acting muscarinic antagonist (LAMA), long-acting beta agonist (LABA), and inhaled corticosteroid (ICS) **OR**
    b. LAMA–LABA alone *if* ICS agents were contraindicated.
7. Must continue concomitant use of 6a or 6b with Dupixent
8. Initial approval will be for 6 months. Reauthorization for 2 years at a time will require documentation of the following:
    a. Patient has experienced a decrease in symptoms while on therapy
    b. Patient is continuing to use concomitant triple maintenance therapy

Eosinophilic Granulomatosis with Polyangiitis (EGPA)

Based upon our criteria and review of the peer-reviewed literature, treatment with **Nucala** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for adult patients with eosinophilic granulomatosis with polyangiitis (EGPA, also known as Churg-Strauss Syndrome [CSS]). Therefore, it is considered **medically appropriate** if **all** the following criteria are met:

1. Patient must be at least 18 years of age **AND**

2. Patient must be followed by, and drug ordered by an Allergist/Immunologist, Rheumatologist, Pulmonologist, Neurologist, or appropriate specialist based on the organ/tissue involvement **AND**

3. Patient must have a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA)
   a. There must be a history or presence of asthma **AND**
   b. There must be a history or presence of blood eosinophil level of at least 10% or an absolute eosinophil count of more than 1000 cells per microliter (See links to eosinophil calculators in policy guidelines section below) **AND**
   c. There must be history of **two or more** of the following clinical findings: histopathological evidence of eosinophilic vasculitis via biopsy, motor deficit or nerve conduction abnormality, pulmonary infiltrates, sino-nasal abnormality, cardiomyopathy, glomerulonephritis, alveolar hemorrhage, palpable purpura, or positive test for antineutrophil cytoplasmic antibody (ANCA) **AND**

4. Provider must attest that the patient has 'Active*, Non-Severe* disease.' This criterion is based upon the most recent clinical guidelines published by the ACR/Vasculitis Foundation (2021). Current guidelines do not support use for 'Active, *Severe* disease.'
   a. *Non-severe* disease is defined as vasculitis without life- or organ-threatening manifestations. Examples of symptoms in patients with non-severe disease include rhinosinusitis, asthma, mild systemic symptoms, uncomplicated cutaneous disease, mild inflammatory arthritis
      - Remission induction: Nucala + corticosteroids is recommended over other traditional treatments (such as corticosteroids +/- methotrexate, azathioprine, or mycophenolate mofetil)
      - Relapsed disease: For patients receiving maintenance therapy with only low dose corticosteroids or methotrexate, azathioprine, or mycophenolate mofetil, Nucala 'add-on' to these treatments is recommended over other interventions
   b. *Severe* EGPA is defined as vasculitis with life-or organ-threatening manifestations (within 3 months), such as alveolar hemorrhage, glomerulonephritis, central nervous system vasculitis, mononeuritis multiplex, cardiac involvement, mesenteric ischemia, or limb/digit ischemia
      - Remission induction: Cyclophosphamide or rituximab is recommended over Nucala
      - Remission maintenance: Methotrexate, azathioprine, or mycophenolate mofetil are recommended over Nucala **AND**

5. Nucala will not be approved for granulomatosis with polyangiitis (also known as GPA or Wegener's granulomatosis) or microscopic polyangiitis **AND**

6. Requests for Nucala (office-administered, medical benefit) will require documentation of an inability to self-inject. ****This applies to New Start AND Recertification requests (including new to plan) for all lines of business, except Medicare. Does NOT apply to Medicare B (Medicare Advantage)****

7. Initial approval will be for 6 months. Recertification will be for 2 years and require documentation of attainment and maintenance of remission. Remission defined as absence of clinical signs/symptoms attributed to EGPA while maintained on an oral corticosteroid dose no greater than 7.5 mg per day prednisone or equivalent. Given the heterogenous nature of this disease that may have multi-organ involvement, consideration may be given on recertification when there is additional subjective evidence or statement of medical necessity from provider showing clear improvement in symptoms attributed to the use of Nucala which warrants continued use (such as reduced rate of relapse, corticosteroid dose reduction, and reduced eosinophil level).

Hypereosinophilic Syndrome (HES)

Based upon our assessment and review of the peer-reviewed literature, treatment with **Nucala** has been medically proven to be an effective and therefore, **medically appropriate** for Hypereosinophilic Syndrome (HES) if **ALL** the following criteria are met:

1. Patient must be at least 12 years old **AND**
2. Must have a diagnosis of Hypereosinophilic Syndrome (HES) for ≥ 6 months, without an identifiable non-hematologic secondary cause. Please note, this excludes patients with non-hematologic secondary HES (such as drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy, FIP1L1-PDGFRα kinase-positive HES, and eosinophilia of unknown clinical significance (unexplained HE, but without apparent complications/clinical manifestations related to organ/tissue infiltration)) **AND**
3. Patient must be followed by an Allergist/Immunologist, or an appropriate specialist based on the involved organ/tissue (ex. Pulmonologist for lung involvement) **AND**
4. Must have a blood eosinophil count of ≥ 1000 cells/microL within the last 6 weeks **AND**
5. Must have experienced ≥ 2 HES flares within the past 12 months (HES flare defined as HES-related worsening of clinical symptoms or blood eosinophil counts requiring escalation in therapy (ex. increased doses or addition of other drugs). Note: Background HES therapy includes, but is not limited to, chronic or episodic oral corticosteroids (ex. prednisone), immunosuppressive (ex. interferon alfa, methotrexate, cyclosporine, azathioprine), and/or cytotoxic therapy (ex. hydroxyurea, imatinib, cyclophosphamide) **AND**
6. Requests for Nucala (office-administered, medical benefit) will require documentation of an inability to self-inject. ****This applies to New Start AND Recertification requests (including new to plan) for all lines of business, except Medicare. Does NOT apply to Medicare B (Medicare Advantage)****
    a. For pediatric patients < 18 years of age, documentation must also include the inability of a caregiver to administer the medication **AND**
7. Initial approval will be for 6 months. Recertification will be for 2 years and require documentation of a decrease in the frequency/severity of HES flares compared to baseline. Given the heterogeneous nature of the disease and variability in affected organs, consideration may be given on recertification when there is additional subjective evidence or statement of medical necessity from provider showing clear improvement in symptoms attributed to the use of Nucala which warrants continued use of the drug (such as an improvement of symptoms, a reduction of background HES therapy, and/or a significant reduction in eosinophil count).

Atopic Dermatitis

Based upon our criteria and review of the peer-reviewed literature, treatment with **Dupixent, Adbry, Ebglyss and Nemluvio** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for moderate-severe atopic dermatitis. Therefore, they are considered **medically appropriate** if **all** the following criteria are met:

1. Must be prescribed by or in consultation with an Allergist/Immunologist, or Dermatologist **AND**
2. For **Dupixent**: must be ≥ 6 months of age. For **Adbry, Ebglyss and Nemluvio**, must be ≥ 12 years of age. **AND**

3. Must have a diagnosis of moderate to severe atopic dermatitis
    a. Must involve at least 10% body surface area
        i. Consideration will be given to those who have less than 10% body surface area involvement but have severe disease of the hands, feet, or other sensitive areas **OR** severe itch that has been unresponsive to topical therapies **AND**
    b. Must have evidence of functional impact on everyday activities **AND**

4. Must have had a trial and failure or contraindication to:
    a. Medium to higher potency prescription topical corticosteroid therapy (see **Table 4** in policy guidelines section)
        i. Adequate trial is defined as ≥ 28 days or for the maximum duration recommended by the product prescribing information (i.e., 14 days for super-potent topical corticosteroids), whichever is shorter **AND**
    b. Tacrolimus or pimecrolimus (Does not apply for children **less than** 2 years of age)
        i. Adequate trial is defined as ≥ 6 weeks based on prescribing information **AND**
    c. Treatment with at least one of the above therapies must have occurred within the previous 6 months.

5. Adbry, Ebglyss and Nemluvio will require documentation of serious side effects or drug failure with Dupixent **AND** Rinvoq

6. Dupixent, Adbry, Ebglyss and Nemluvio will not be approved in combination in combination with another monoclonal antibody or Janus Kinase Inhibitor (such as Opzelura, Cibinqo or Rinvoq) as the efficacy and safety of these combinations uses have not been established. **AND**

7. **Dupixent:** Initial and subsequent approval duration is 2 years. Upon recertification, documentation of ongoing benefit in terms of disease improvement or stability is required.

8. **Adbry Adults**: Initial approval will be for 6 months. Recertification will be as follows:
    a. **Weight < 100kg:** A recent assessment of disease status will be required. Provider attestation of disease status will be accepted.
        i. For patients that achieve 'Clear' (IGA 0) or 'Almost Clear' (IGA 1) skin, a trial of an extended dosing interval of 300mg every 4 weeks will be required based on drug labeling. If the patient fails the extended interval trial (i.e., loss of disease control or worsening symptoms), they will not be required to re-attempt on subsequent recertifications.
        ii. If documentation is provided that the patient is not 'Clear' (IGA 0) or 'Almost Clear' (IGA 1) but has had an improvement in disease while on the medication compared to baseline, a dosing frequency of 300mg every 2 weeks can be continued. Approval duration is 2 years
        iii. If documentation indicates that the patient has not experienced any clinical improvement compared to baseline, further treatment will not be authorized.
    b. **Weight ≥ 100kg:** Documentation of ongoing benefit in terms of disease improvement or stability is required. Approval duration is 2 years.

9. **Adbry 12-17 years old:** Initial and subsequent approval duration is 2 years. There will be no dose evaluation until the patient turns 18 years old. After 18 years old, dosing will be evaluated per Adbry adult dosing above. Upon recertification, documentation of ongoing benefit in terms of disease improvement or stability is required.

10. **Ebglyss**:
    a. Initial therapy is approved for 16 weeks: Ebglyss 500 mg (two 250 mg injections) at Week 0 and Week 2, followed by 250 mg every two weeks until Week 16
        i. If patient did not achieve 'Clear' (IGA 0) or 'Almost Clear' (IGA 1) skin, an extended 6 months of 250mg every two weeks following the initial therapy can be considered for one time only
    b. If patient achieved "Clear" (IGA 0) or "Almost Clear" (IGA 1) skin after the initial therapy: Maintenance therapy: Ebglyss 250mg once every four weeks after initial therapy can be approved for 2 years at a time.
    c. Upon recertification documentation of ongoing benefit in terms of disease improvement or stability is required.
    d. QL: 1 pen (2mL) per 28 days

11. **Nemluvio:**
    a. Initial therapy is approved for 16 weeks: The initial dose is Nemluvio 60 mg (two 30 mg injections), followed by 30 mg given every 4 weeks
        i. For patients that achieve 'Clear' (IGA 0) or 'Almost Clear' (IGA 1) skin after 16 weeks of treatment, a dosing frequency of 30mg *every 8 weeks* is recommended and will be approved. Approval duration is 2 years
            a) Use Nemluvio with topical corticosteroids and/or topical calcineurin inhibitors. When the disease has sufficiently improved, discontinue use of topical therapies.
        ii. If documentation is provided that the patient is not 'Clear' (IGA 0) or 'Almost Clear' (IGA 1) after the initial therapy of 16 weeks but has had an improvement in disease while on the medication compared to baseline, a dosing frequency of 30mg *every 4 weeks* can be continued and approved. Approval duration is 2 years
    b. If documentation indicates that the patient has not experienced any clinical improvement compared to baseline, further treatment will not be authorized.
    c. Quantity is limited to 1mL per 28 days.
    d. Subcutaneous Nemluvio will be approved as pharmacy benefit for self-injection

Chronic Rhinosinusitis with Nasal Polyps

Based upon our criteria and review of the peer-reviewed literature, treatment with **Nucala or Dupixent** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for chronic rhinosinusitis with nasal polyps. Therefore, it is considered **medically appropriate** if **all** the following criteria are met:

1. Must be followed by and drug ordered by an Allergist/Immunologist, or Otolaryngologist **AND**

2. Must have a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP)
    a. Chronic is defined as having lasted for at least 12 weeks **AND**
    b. Must currently have nasal polyposis, confirmed by evidence (such as direct examination, nasal endoscopy, imaging studies (such as a sinus CT scan))

3. Must be ≥ 12 years of age for Dupixent OR ≥ 18 years of age for Nucala **AND**

4. Step therapy applies – Step therapy (a **AND** b) applies to New Starts for all lines of business, **including** Medicare Part B:
    a. Must have documented inadequate response despite at least 3 months of compliant use of

mometasone nasal spray at a dose of 2 sprays in each nostril twice daily (compliance will be verified through pharmacy claims history. Note: each inhaler =17g = 120 sprays, therefore claims should reflect **34g/30 days** for the required dosing) **AND**

b. Must have documented inadequate response despite at least 3 months of compliant use of Xhance nasal spray at a dose of 2 sprays in each nostril twice daily (compliance will be verified through pharmacy claims history. Note: each inhaler =16ml = 120 sprays, therefore claims should reflect **32ml/30 days** for the required dosing) **AND**

5. Must have had either:
   a. Prior nasal surgery **OR**
   b. Prior treatment with a course of systemic corticosteroids

6. Must be used in combination with an intranasal corticosteroid
   a. Dupixent or Nucala as monotherapy for this indication will not be authorized as both agents are only FDA approved as an add-on maintenance treatment

7. Requests for Nucala (office-administered, medical benefit) will require documentation of an inability to self-inject. ****This applies to New Start AND Recertification requests (including new to plan) for all lines of business, except Medicare. Does NOT apply to Medicare B (Medicare Advantage) ****

8. Initial approval will be granted for 6 months. All recertifications will be for 2 years and will require documentation of continued use of an intranasal corticosteroid and clinical benefit from Dupixent or Nucala use (e.g., reduced nasal polyp size, improved nasal congestion, reduced sinus opacification, decreased sino-nasal symptoms, improved sense of smell)

Prurigo Nodularis

Based upon our criteria and review of the peer-reviewed literature, treatment with **Dupixent** and **Nemluvio** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for prurigo nodularis. Therefore, it is considered **medically appropriate** if **all** the following criteria are met:

1. Must be prescribed by or in consultation with an Allergist, Immunologist, Dermatologist or HIV specialist **AND**

2. Must be ≥ 18 years of age **AND**

3. Must have a diagnosis of Prurigo Nodularis (PN) for at least 3 months
   a. Provider must attest that patient currently has at least 20 PN nodules **AND**
4. **Dupixent**: Must have had a trial and failure or contraindication to medium to super-potent prescription topical corticosteroid therapy (see **Table 4** in policy guidelines section)
      i. Adequate trial is defined as ≥ 28 days or for the maximum duration recommended by the product prescribing information (i.e., 14 days for super-potent topical corticosteroids), whichever is shorter **AND**
      ii. Trial must have occurred within the previous 6 months **AND**
   a. Approved dosing: an initial dosage of 600mg (two 300mg SC injections) once, followed by maintenance dosage of 300mg SC every 2 weeks

5. **Nemluvio**: Must have tried at least **TWO** of the following topical treatments without treatment success: Medium to super-potent topical corticosteroid therapy (see **Table 4** in policy guidelines section), pimecrolimus, tacrolimus, or calcipotriol.
      i. Adequate trial is defined as ≥ 28 days or for the maximum duration recommended by the product prescribing information (i.e., 14 days for super-potent topical

corticosteroids), whichever is shorter AND
ii. Trial must have occurred within the previous 6 months **AND**

a. Must have tried and failed **Dupixent**, or provide documentation why Dupixent cannot be used **AND**
b. Approved dosing:
   i. Adult Patients Weighing < 90kg: an initial dosage of 60 mg (two 30mg SC injections), followed by 30 mg SC injection given every 4 weeks
   ii. Adult Patients Weighing ≥ 90kg: an initial dose of 60 mg (two 30 mg SC injections), followed by 60 mg SC injection given every 4 weeks
   iii. Quantity is limited to 1mL per 28 days.
c. Subcutaneous Nemluvio will be approved as pharmacy benefit for self-injection

6. Initial approval will be for 6 months. All recertifications will be for 2 years and require documentation of an improvement in symptoms compared to baseline (such as decreased itch, decreased size/number of nodules).
7. Combination use of Nemluvio with Dupixent, Rinvoq, Otezla, Cibingo, Opzulura or other biologics will not be approved as the efficacy and safety with these concurrent uses have not been established.

Eosinophilic Esophagitis

Based upon our criteria and review of the peer-reviewed literature, treatment with **Dupixent** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for eosinophilic esophagitis. Therefore, it is considered **medically appropriate** if **all** the following criteria are met:

1. Must be at least 1 years of age **AND** weigh ≥ 15kg **AND**
2. Must be prescribed by a Gastroenterologist or Allergist/Immunologist **AND**
3. Must have a diagnosis of Eosinophilic Esophagitis with **both** the following:
   a. An upper endoscopy with an esophageal biopsy showing ≥ 15 eosinophils per high-power field (eos/hpf) (or 60 eosinophils per mm^2) **AND**
   b. The provider must attest other causes of symptoms/esophageal eosinophilia have been ruled out (including, but not limited to: GERD, hypereosinophilic syndrome, eosinophilic granulomatosis with polyangiitis) **AND**
4. The provider must attest that a dietary management strategy (such as an empiric elimination diet, a targeted allergen elimination diet, or an elemental diet) has been discussed and implemented, when appropriate **AND**
5. Must have had serious side effects or drug failure with a high-dose Proton Pump Inhibitor (such as pantoprazole, omeprazole, etc.) for at least 8 weeks **AND**
6. Must have had serious side effects or drug failure with a topical steroid treatment (such as swallowed fluticasone or budesonide) for at least 8 weeks **AND**
7. See Policy Guidelines for appropriate dosing based on patient's weight.
8. Initial approval will be for 6 months. Recertification will be for 2 years and require documentation of histologic remission as defined as < 15 eos/hpf on repeat endoscopy/biopsy (Testing required at 6 months and then ever 2 years thereafter)

POLICY GUIDELINES:

1. Prior authorization is contract dependent.
2. Cinqair is administered by a healthcare professional and is covered under the medical benefit.
3. Fasenra prefilled syringe is administered by a healthcare professional and is covered under the medical benefit. Fasenra autoinjector (Fasenra PEN) is self-administered and is covered under the pharmacy benefit.
   a. If an authorization is added under one benefit, it will be terminated under the other. For example: if the member was approved under the medical benefit and now is requesting coverage under the pharmacy benefit, the authorization on the medical benefit will be terminated when the pharmacy authorization is approved.
4. Dupixent prefilled syringes and pens are self-administered and are covered under the pharmacy benefit.
5. Adbry prefilled syringes are self-administered and are covered under the pharmacy benefit.
6. Nucalavial for injection is administered by a healthcare professional and is covered under the medical benefit. Nucala prefilled autoinjector (100mg/ml) and prefilled syringes (100mg/ml and 40mg/0.4ml) can be healthcare professional or self-administered and may be covered under the medical (healthcare professional) or pharmacy benefit (self-administered)
   a. If an authorization is added under one benefit, it will be terminated under the other. For example: if the member was approved under the medical benefit and now is requesting coverage under the pharmacy benefit, the authorization on the medical benefit will be terminated when the pharmacy authorization is approved.
7. Dosing will be approved in line with FDA approved dosing as follows:
   a. Nucala has indication-dependent dosing as follows:
      - Eosinophilic asthma:
        i. Adults, adolescents, and children 12 years and older: 100 mg subcutaneously once every 4 weeks
        ii. Patients aged 6 to 11 years: 40 mg subcutaneously once every 4 weeks.
      - EGPA or HES:
        i. 300mg subcutaneously once every 4 weeks (as 3 separate 100-mg injections into the upper arm, thigh, or abdomen)
      - CRSwNP
        i. 100 mg subcutaneously once every 4 weeks
   b. Cinqair dosing for adults 18 years of age and older: 3 mg/kg intravenously once every 4 weeks.
   c. Fasenra dosing for adults, adolescents, and children 6 years and older who weigh at least 35 kg: 30 mg subcutaneously once every 4 weeks for the first 3 doses, then 30 mg subcutaneously once every 8 weeks thereafter (into the upper arm, thigh, or abdomen).
   Fasenra dosing for adolescent who are 6-11 years old and are LESS than 35 kg: 10 mg subcutaneously once every 4 weeks for the first 3 doses, then 10 mg subcutaneously once every 8 weeks thereafter (into the upper arm, thigh, or abdomen).
   Another loading dose will not be granted for patients who have received a loading dose under the pharmacy or medical benefit and request to switch to the other benefit for continued therapy.
   d. Adbry dosing for adults 18 years of age and older: 600mg (given as four 150mg injections) as a loading dose, then 300mg (given as two 150mg injections) every other week. A dosage of 300 mg every 4 weeks may be considered for patients below 100 kg who achieve clear or almost clear skin after 16 weeks of treatment.
   e. Dupixent is self-administered with indication-dependent dosing as follows:
      - Atopic dermatitis:
        i. Adults-Initial dosage: 600 mg subcutaneously (given as two 300 mg injections)
        Maintenance dosage: 300 mg subcutaneously given once every other week

ii. Pediatric patients (6 months - 17 years):

Dosage in Pediatric Patients 6 Months to 5 Years of Age (2.3):

Body Weight	Initial and Subsequent Dosage
5 to less than 15 kg	200 mg (one 200 mg injection) every 4 weeks (Q4W)
15 to less than 30 kg	300 mg (one 300 mg injection) every 4 weeks (Q4W)

Dosage in Pediatric Patients 6 Years to 17 Years of Age (2.3):

Body Weight	Initial Loading Dose	Subsequent Dosage[a]
15 to less than 30 kg	600 mg (two 300 mg injections)	300 mg Q4W
30 to less than 60 kg	400 mg (two 200 mg injections)	200 mg Q2W
60 kg or more	600 mg (two 300 mg injections)	300 mg Q2W

[a] Q2W – every other week; Q4W – every 4 weeks

- Eosinophilic or Oral-corticosteroid dependent Asthma:

Table 2: Dosage of DUPIXENT for Subcutaneous Administration in Adults and Adolescents 12 Years and Older with Asthma

Initial Loading Dose	Subsequent Dose
400 mg (two 200 mg injections)	200 mg every 2 weeks (Q2W)
or	
600 mg (two 300 mg injections)	300 mg every 2 weeks (Q2W)
Dosage for patients with oral corticosteroid-dependent asthma or with co-morbid moderate-to-severe atopic dermatitis or adults with co-morbid chronic rhinosinusitis with nasal polyposis	
600 mg (two 300 mg injections)	300 mg every 2 weeks (Q2W)

Dosage in Pediatric Patients (6 to 11 Years of Age)

The recommended dosage of DUPIXENT for patients 6 to 11 years of age is specified in Table 3.

Table 3: Dosage of DUPIXENT for Subcutaneous Administration in Pediatric Patients 6 to 11 Years of Age with Asthma

Body Weight	Initial[a] and Subsequent Doses
15 to less than 30 kg	100 mg every other week (Q2W) or 300 mg every four weeks (Q4W)
≥30 kg	200 mg every other week (Q2W)

[a] For pediatric patients (6 to 11 years old) with asthma, no initial loading dose is recommended.

For pediatric patients (6 to 11 years old) with asthma and co-morbid moderate-to-severe atopic dermatitis, follow the recommended dosage as per Table 1 which includes an initial loading dose *[see Dosage and Administration (2.1)]*.

- Chronic rhinosinusitis with nasal polyps:
  i. 300 mg subcutaneously given once every other week
- Prurigo Nodularis:
  i. Initial dosage: 600 mg subcutaneously (given as two 300 mg injections)
  Maintenance dosage: 300 mg subcutaneously given once every other week
- Eosinophilic Esophagitis:

Table 5: Dosage of DUPIXENT in Adult and Pediatric Patients 1 Year of Age and Older with Eosinophilic Esophagitis

Body Weight	Recommended Dosage
15 to less than 30 kg	200 mg every other week (Q2W)
30 to less than 40 kg	300 mg every other week (Q2W)
40 kg or more	300 mg every week (QW)

8. Cinqair will only be authorized when administered by a healthcare professional in the prescriber's office or within a supervised medical treatment facility. Because of the risk of anaphylaxis, patients should be closely observed for an appropriate period of time after administration and health care providers administering Cinqair should be prepared to manage anaphylaxis which can be life-threatening. Patients should also be informed of the signs and symptoms of anaphylaxis and instructed to seek immediate medical care should symptoms occur.
9. Request for concurrent use of Adbry, Nucala, Cinqair, Fasenra and Dupixent with other inflammatory agents such as Xolair or Tezspire will be evaluated for safety and efficacy and subject to off-label review.
10. Adbry, Nucala, Cinqair, Fasenra, and Dupixent will not be authorized in the following circumstances:
    a. Adbry is only approved for subcutaneous injection. Nucala is only approved for subcutaneous injection. Cinqair is only approved for intravenous infusion. Fasenra is only approved for subcutaneous injection. Dupixent is only approved for subcutaneous injection. Administration in any manner other than which drug is FDA-approved will not be authorized.
    b. Relief of acute bronchospasm or status asthmaticus
    c. Any non-FDA approved dosing regimen
    d. Fasenra will not be approved for chronic rhinosinusitis with nasal polyps or eosinophilic esophagitis.
11. If Adbry, Nucala, Cinqair, Fasenra, or Dupixent therapy is initiated with samples and the member does not meet policy criteria for coverage (as outlined above) before the start of therapy, coverage will not be granted upon completion of samples.
12. Safety of concurrent use of Adbry, Nucala, Cinqair, Fasenra, and Dupixent with other monoclonal antibodies used to treat inflammation (TNF-inhibitors, interleukin antagonists, etc.) has not been established.
13. For contacts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
    a. The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    b. The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    c. The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    d. The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
    e. The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
    f. The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.
14. For members with Medicare Part B, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at

https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.

15. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
    Unless otherwise stated above within the individual drug criteria, approval time periods are listed in the table below.
    a. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

Line of Business	Initial approval	Continued approval
Commercial, Exchange, and SafetyNet (Medicaid, HARP, CHP, Essential Plan)	All sites of service – 2 years	All sites of service – 2 years
Medicare	All sites of service – 2 years	All sites of service – 2 years

16. The following websites have eosinophil calculators for converting reported units:
    a. http://gsknucala.com/
    b. https://www.fasenrahcp.com/m/fasenra-eosinophil-calculator.html
    c. https://www.omnicalculator.com/health/eosinophil-count
    d. https://www.merckmanuals.com/medical-calculators/AbsEoCount.htm
17. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
18. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.

Table 1

Estimated comparative daily doses for inhaled glucocorticoids in adolescents ≥12 years and adults

Drug	Low dose (total daily dose)	Medium dose (total daily dose)	High dose (total daily dose)*
Beclomethasone HFA (Qvar RediHaler product available in United States) Administer as 2 divided doses	80 to 160 mcg	>160 to 320 mcg	>320 to 640 mcg
40 mcg per actuation	2 or 4 inhalations	¶	¶
80 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Beclomethasone HFAΔ (Qvar product available in Canada, Europe, and elsewhere) Administer as 2 divided doses	100 to 200 mcg	>200 to 400 mcg	>400 to 800 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
100 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Budesonide DPI (Pulmicort Flexhaler product available in United States) Administer as 2 divided doses	180 to 360 mcg	>360 to 720 mcg	>720 to 1440 mcg
90 mcg per actuation	2 or 4 inhalations	¶	¶
180 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Budesonide DPIΔ (Pulmicort Turbuhaler or Turbohaler product available in Canada, Europe, and elsewhere) Administer low doses (ie, ≤400 mcg/day) once daily; administer higher doses (ie, >400 mcg/day) as 2 to 4 divided doses	200 to 400 mcg	>400 to 800 mcg	>800 to 2400 mcg
100 mcg per actuation	2 to 4 inhalations	¶	¶
200 mcg per actuation	1 to 2 inhalations	3 to 4 inhalations	¶
400 mcg per actuation	1 inhalation	2 inhalations	3 to 6 inhalations
Ciclesonide HFA (Alvesco product available in United States, Europe, and elsewhere) United States: Administer as 2 divided doses Australia, Europe, and elsewhere: Administer lower doses (ie, 160 to 320 mcg/day) once daily; administer 640 mcg dose as 2 divided doses	160 mcg	320 mcg	640 mcg
80 mcg per actuation	2 inhalations	4 inhalations	¶
160 mcg per actuation	◇	2 inhalations	4 inhalations
Ciclesonide HFAΔ (Alvesco product available in Canada) Administer lower doses (eg, 100 to 400 mcg) once daily; administer 800 mcg dose as 2 divided doses	100 to 200 mcg	>200 to 400 mcg	>400 to 800 mcg
100 mcg per actuation	1 to 2 inhalations	3 to 4 inhalations	¶
200 mcg per acutation	1 inhalation	2 inhalations	3 to 4 inhalations

Fluticasone propionate HFA (Flovent HFA product available in United States) Administer as 2 divided doses	176 to 220 mcg	>220 to 440 mcg	>440 to 1760 mcg
44 mcg per actuation	4 inhalations	¶	¶
110 mcg per actuation	2 inhalations	4 inhalations	¶
220 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
Fluticasone propionate HFAΔ (Flovent HFA product available in Canada; Flixotide Evohaler product available in Europe and elsewhere) Administer as 2 divided doses	100 to 250 mcg	>250 to 500 mcg	>500 to 2000 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
125 mcg per actuation	2 inhalations	4 inhalations	¶
250 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
Fluticasone propionate DPI (Flovent Diskus product available in United States and Canada; Flixotide Accuhaler product available in Europe and elsewhere) Administer as 2 divided doses	100 to 250 mcg	>250 to 500 mcg	>500 to 2000 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
100 mcg per actuation	2 inhalations	4 inhalations	¶
250 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
500 mcg per actuation (strength not available in United States)	◇	◇	2 or 4 inhalations
Fluticasone propionate DPI (Armonair Digihaler product available in United States; Aermony Respiclick product available in Canada) Administer as 2 divided doses	110 mcg	226 mcg	464 mcg
55 mcg per actuation	2 inhalations	¶	¶
113 mcg per actuation	◇	2 inhalations	¶
232 mcg per actuation	◇	◇	2 inhalations
Fluticasone furoate DPI (Arnuity Ellipta product available in United States, Canada, Australia, and elsewhere, but not available in Europe or UK) Administer once daily **NOTE:** Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only once daily.	50 mcg (by use of pediatric DPI, which is off-label in adolescents and adults)	100 mcg	200 mcg
50 mcg per actuation	1 inhalation	¶	¶
100 mcg per actuation	◇	1 inhalation	2 inhalations
200 mcg per actuation	◇	◇	1 inhalation
Mometasone DPI (Asmanex Twisthaler product available in United States) May administer lower doses (ie, 220 to 440 mcg/day) once daily; administer 880 mcg dose as 2 divided doses	220 mcg	>220 to 440 mcg	>440 to 880 mcg
110 mcg per actuation	2 inhalations	¶	¶
220 mcg per actuation	1 inhalation	2 inhalations	4 inhalations

Mometasone DPI (Asmanex Twisthaler product available in United States) May administer lower doses (ie, 220 to 440 mcg/day) once daily; administer 880 mcg dose as 2 divided doses	220 mcg	>220 to 440 mcg	>440 to 880 mcg
110 mcg per actuation	2 inhalations	¶	¶
220 mcg per actuation	1 inhalation	2 inhalations	4 inhalations
Mometasone HFA (Asmanex HFA product available in United States) Administer as 2 divided doses	200 mcg	>200 to 400 mcg	>400 to 800 mcg
100 mcg per actuation	2 inhalations	4 inhalations	¶
200 mcg per actuation	◇	2 inhalations	4 inhalations
Mometasone DPIΔ (Asmanex Twisthaler product available in Canada, Europe, and elsewhere) May administer lower doses (ie, 200 to 400 mcg/day) once daily; administer 800 mcg dose as 2 divided doses	200 mcg	>200 to 400 mcg	>400 to 800 mcg
200 mcg per actuation	1 inhalation	2 inhalations	¶
400 mcg per actuation	◇	1 inhalation	2 inhalations

- **The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy.** The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effects.
- Suggested total daily doses for low, medium, and high dose inhaled glucocorticoid regimens are based on daily doses recommended by Global Initiative for Asthma (GINA), National Asthma Education and Prevention Program (NAEPP), and/or product labeling[1-5]. This is not a table of equivalence.
- Depending on the specific product, total daily doses are administered once or divided and given twice daily. Refer to local product information or a clinical drug reference (eg Lexicomp).
- Some doses are outside the approved product information recommendations.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant metered dose inhaler.

* Evidence for additional improvement with dose increases >1000 mcg/day is limited.

¶ Select alternate preparation with higher mcg/actuation to improve convenience.

Δ Products shaded in light gray color are not available in the United States but are available widely elsewhere.

◇ Select preparation with fewer mcg/actuation.

Table 2

Usual doses of combined inhaled glucocorticoids and bronchodilators

Medication	Low dose	Medium dose	High dose
ICS-SABA combination			
Budesonide-albuterol HFA (Brand name: Airsupra)*			
NOTE: Not used for maintenance therapy.			
Acute symptom relief: Budesonide-albuterol (80 mcg/90 mcg) 2 inhalations as needed (usual maximum: 12 inhalations/day).			
ICS-LABA combinations			
Beclomethasone [beclometasone]-formoterol DPI or HFA (Not available in United States or Canada, but available elsewhere [sample brand names: Formodual, Fostair, Foster])¶Δ			
100 mcg/6 mcg	1 inhalation twice a day	2 inhalations twice a day	
200 mcg/6 mcg			2 inhalations twice a day
Budesonide-formoterol HFA (Brand name: Symbicort)¶			
80 mcg/4.5 mcg	2 inhalations twice a day		
160 mcg/4.5 mcg		2 inhalations twice a day	
Fluticasone furoate-vilanterol DPI (Brand name: Breo Ellipta)Δ			
NOTE: Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only **once** daily.			
50 mcg/25 mcg◇	1 inhalation once daily		
100 mcg/25 mcg		1 inhalation once daily	
200 mcg/25 mcg			1 inhalation once daily
Fluticasone propionate-formoterol MDI (Not available in United States or Canada, but available elsewhere [sample brand name: Flutiform])			
50 mcg/5 mcg	2 inhalations twice daily		
125 mcg/5 mcg		2 inhalations twice daily	
250 mcg/10 mcg			2 inhalations twice daily
Fluticasone propionate-salmeterol DPI (Brand names: Advair Diskus, Wixela Inhub)Δ			
100 mcg/50 mcg	1 inhalation twice a day		
250 mcg/50 mcg		1 inhalation twice a day	
500 mcg/50 mcg			1 inhalation twice a day
Fluticasone propionate-salmeterol HFA (Brand name: Advair HFA)			
45 mcg/21 mcg	2 inhalations twice a day		
115 mcg/21 mcg		2 inhalations twice a day	
230 mcg/21 mcg			2 inhalations twice a day
Fluticasone propionate-salmeterol DPI (Brand names: AirDuo RespiClick, AirDuo Digihaler)Δ§			
55 mcg/14 mcg	1 inhalation twice a day		
113 mcg/14 mcg	1 inhalation twice a day	1 inhalation twice a day	
232 mcg/14 mcg			1 inhalation twice a day
Mometasone-formoterol HFA (Brand name: Dulera)			
100 mcg/5 mcg		2 inhalations twice a day	
200 mcg/5 mcg			2 inhalations twice a day
Mometasone-indacaterol DPI (Brand name: Atectura Breezhaler; available in Canada)Δ			
80 mcg/150 mcg	1 inhalation (capsule) once a day		
160 mcg/150 mcg		1 inhalation (capsule) once a day	
320 mcg/150 mcg			1 inhalation (capsule) once a day
ICS-LAMA-LABA combinations¥			
Fluticasone furoate-umeclidinium-vilanterol DPI (Brand name: Trelegy Ellipta)Δ			
100 mcg/62.5 mcg/25 mcg		1 inhalation once daily	
200 mcg/62.5 mcg/25 mcg			1 inhalation once daily
Mometasone-glycopyrrolate (glycopyrronium)-indacaterol DPI (Brand name: Enerzair Breezhaler; available in Canada)*Δ			
160 mcg/50 mcg/150 mcg			1 inhalation (capsule) once a day

Do not exceed the maximum number of inhalations/puffs per day listed in the table due to the risk of toxicity from an excess dose of long-acting beta-agonist (ie, salmeterol, formoterol, or vilanterol). Brand names and dose per puff or per inhalation of commercially available fixed dose combinations are according to United States prescribing information, unless otherwise noted. Consult local product information before use.

ICS: inhaled glucocorticoid (inhaled corticosteroid); SABA: short-acting beta-agonist; LABA: long-acting beta-agonist; LAMA: long-acting muscarinic antagonist; HFA: metered dose inhaler with hydrofluoroalkane propellant; DPI: dry powder inhaler; SMI: soft mist inhaler.

* Not approved for use in patients <18 years old.

¶ When using ICS-formoterol as reliever, use one to two inhalations as needed. Maximum daily dose of maintenance and rescue is 12 inhalations.

Δ DPI contains lactose which may have small amounts of milk protein.

◇ Fluticasone furoate-vilanterol 50 mcg/25 mcg DPI is approved for use in patients 5 to 11 years old; use in adolescents and adults is off-label.

§ In AirDuo inhalers, the daily dose of salmeterol is approximately one-fourth of the dose in Advair, and the daily dose of fluticasone is approximately one-half that of the comparable low-, medium-, and high-dose strengths of Advair.

¥ Alternatively, tiotropium SMI (Brand name: Spiriva Respimat) can be used with an ICS or ICS-LABA inhaler. The dose in asthma is two inhalations (1.25 mcg/inhalation) once daily.

Reference: Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. https://ginasthma.org/wp-content/uploads/2023/05/GINA-2023-Full-Report-2023-WMS.pdf. Updated 2023 (Accessed on June 13, 2023).

Table 3

Estimated comparative daily doses for inhaled glucocorticoids in children

Drug	Low daily dose		Medium daily dose		High daily dose	
	Child 0 to 4	Child 5 to 11	Child 0 to 4	Child 5 to 11	Child 0 to 4	Child 5 to 11
Beclomethasone HFA 40 or 80 mcg/puff	NA	40 mcg/puff - 1 to 2 puffs twice per day	NA	40 mcg/puff - 2 to 4 puffs twice per day 80 mcg/puff - 1 to 2 puffs twice per day	NA	80 mcg/puff - 3 to 4 puffs twice per day
Budesonide DPI* (breath activated) 90 or 180 mcg/inhalation	NA	90 mcg/inhalation - 1 to 2 inhalations twice per day	NA	180 mcg/inhalation - 1 to 2 inhalations twice per day	NA	180 mcg/inhalation - 3 to 4 inhalations twice per day
Budesonide nebulization suspension¶ 0.25 mg/2 mL, 0.5 mg/2 mL, or 1 mg/2 mL	0.25 to 0.5 mg once daily or as 2 divided doses	0.5 mg once daily or as 2 divided doses	0.75 to 1 mg once daily or as 2 or 3 divided doses	1 mg once daily or as 2 divided doses	1.25 to 2 mg once daily or as 2 divided doses	2 mg once daily or as 2 divided doses
Ciclesonide HFAΔ 80 or 160 mcg/puff	NA	80 mcg/puff - 1 to 2 puffs once daily	NA	80 mcg/puff - 3 to 4 puffs once daily	NA	80 mcg/puff - 5 to 6 puffs once daily or as 2 divided doses 160 mcg/puff - 3 puffs once daily or as 2 divided doses
Fluticasone HFA◇ 44, 110, or 220 mcg/puff	44 mcg/puff - 2 puffs twice per day◇	44 mcg/puff - 1 to 2 puffs twice per day	44 mcg/puff - 2 to 4 puffs twice per day 110 mcg/puff - 1 puff in AM and 2 puffs in PM	44 mcg/puff - 2 to 4 puffs twice per day 110 mcg/puff - 1 puff in AM and 2 puffs in PM	110 mcg/puff - 2 puffs twice per day 220 mcg/puff - 1 puff twice per day	110 mcg/puff - 2 puffs twice per day 220 mcg/puff - 1 puff twice per day
Fluticasone DPI (breath activated)§ 50, 100, or 250 mcg/inhalation	NA	50 mcg/inhalation - 1 to 2 inhalations twice per day	NA	50 mcg/inhalation - 3 to 4 inhalations twice per day 100 mcg/inhalation - 1 inhalation in AM and 2 inhalations in PM to 2 inhalations twice per day	NA	100 mcg/inhalation - 2 inhalations in AM and 3 inhalations in PM 250 mcg/inhalation - 1 inhalation twice per day
Mometasone aerosol DPI (breath activated)* 110 or 220 mcg/inhalation	NA	110 mcg/inhalation - 1 inhalation once daily	NA	110 mcg/inhalation - 2 to 3 inhalations once daily	NA	110 mcg/inhalation - 4 inhalations once daily or 2 inhalations twice per day 220 mcg/inhalation - 2 inhalations once daily or 1 inhalation twice per day
Mometasone HFA MDI 50, 100, or 200 mcg/puff	NA	50 mcg/puff - 1 puff once or twice per day	NA	50 mcg/puff - 2 to 3 puffs twice per day 100 mcg/puff - 1 puff twice per day	NA	100 mcg/puff - 2 puffs twice per day 200 mcg/puff - 1 inhalation twice per day

Some doses may be outside approved package labeling, especially in the high-dose range. Doses shown and strengths (ie, mcg per puff or inhalation) are based upon product descriptions approved in the United States, which may differ from how strengths are described for products available in other countries. Consult local product information before use.

HFA: hydrofluoroalkane; NA: not approved and no data available for this age group; DPI: dry-powder inhaler; AM: in morning; PM: in evening; US FDA: US Food and Drug Administration; MDI: metered-dose inhaler.

* Contains milk protein.

¶ Budesonide suspension is compatible with albuterol, ipratropium, and levalbuterol nebulizer solutions in the same nebulizer. Use only jet nebulizers as ultrasonic nebulizers are ineffective for suspensions.

Δ Ciclesonide is not approved by the US FDA for use in children under 12. It is approved for use in children 6 years of age and older in Canada, some European countries, and elsewhere.

◇ For fluticasone HFA, the low dose for children <4 years is higher than for children 5 to 11 years of age due to lower dose delivered with facemask and data on efficacy in young children.

§ Contains lactose.

Data from:

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Table 4

Comparison of representative topical corticosteroid preparations (classified according to the United States system)

Potency group*	Corticosteroid	Vehicle type/form	Brand names (United States)	Available strength(s), percent (except as noted)
Super-high potency (group 1)	Betamethasone dipropionate, augmented	Ointment (optimized)	Diprolene	0.05
		Gel, lotion	[Generic only]	0.05
	Clobetasol propionate	Cream, ointment	Temovate	0.05
		Gel, solution (scalp)	[Generic only]	0.05
		Cream	Tasoprol	0.05
		Cream (emollient base)	Temovate E¶	0.05
		Lotion, shampoo, spray aerosol	Clobex	0.05
		Foam aerosol	Olux, Olux-E, Tovet	0.05
		Lotion	Impeklo	0.05
		Ointment	Clobetavix	0.05
		Shampoo	Clodan	0.05
		Solution (scalp)	Cormax¶	0.05
	Diflucortolone valerate (not available in United States)	Ointment, oily cream	Nerisone Forte (United Kingdom, others)	0.3
	Fluocinonide	Cream	Vanos	0.1
	Flurandrenolide	Tape (roll)	Cordran	4 mcg/cm^2
High potency (group 2)	Amcinonide	Ointment	Cyclocort¶, Amcort¶	0.1
	Betamethasone dipropionate	Ointment	Diprosone¶	0.05
		Cream, augmented formulation (AF)	Diprolene AF	0.05
	Clobetasol propionate	Cream	Impoyz	0.025
	Desoximetasone	Cream, ointment, spray	Topicort	0.25
		Gel	Topicort	0.05
	Diflorasone diacetate	Ointment	ApexiCon¶, Florone¶	0.05
		Cream (emollient)	ApexiCon E	0.05
	Fluocinonide	Cream, gel, ointment, solution	Lidex¶	0.05
	Halcinonide	Cream, ointment, solution	Halog	0.1
	Halobetasol propionate	Lotion	Bryhali	0.01
High potency (group 3)	Amcinonide	Cream	Cyclocort¶, Amcort¶	0.1
		Lotion	Amcort¶	0.1
	Betamethasone dipropionate	Cream (hydrophilic emollient)	Diprosone¶	0.05
	Betamethasone valerate	Ointment	Valisone¶	0.1
		Foam	Luxiq	0.12
	Desoximetasone	Cream, ointment	Topicort, Topicort LP¶	0.05
	Diflorasone diacetate	Cream	Florone¶, Psorcon	0.05
	Diflucortolone valerate (not available in United States)	Cream, oily cream, ointment	Nerisone (United Kingdom, others)	0.1
	Fluocinonide	Cream (aqueous emollient)	Lidex-E¶	0.05
	Fluticasone propionate	Ointment	Cutivate¶	0.005
	Mometasone furoate	Ointment	Elocon¶	0.1
	Triamcinolone acetonide	Cream, ointment	Aristocort HP¶, Kenalog¶, Triderm	0.5

Medium potency (group 4)	Betamethasone dipropionate	Spray	Sernivo	0.05
	Clocortolone pivalate	Cream	Cloderm	0.1
	Fluocinolone acetonide	Ointment	Synalar	0.025
	Flurandrenolide	Ointment	Cordran	0.05
	Fluticasone propionate	Cream	Cutivate¶	0.05
	Hydrocortisone valerate	Ointment	Westcort¶	0.2
	Mometasone furoate	Cream, lotion, solution	Elocon¶	0.1
	Triamcinolone acetonide	Cream	Kenalog¶, Triderm	0.1
		Ointment	Kenalog¶	0.1
		Ointment	Trianex, Tritocin	0.05
		Aerosol spray	Kenalog	0.2 mg per 2 second spray
		Dental paste	Oralone	0.1
Lower-mid potency (group 5)	Betamethasone dipropionate	Lotion	Diprosone¶	0.05
	Betamethasone valerate	Cream	Beta-Val¶, Valisone¶	0.1
	Desonide	Ointment	DesOwen¶, Tridesilon¶	0.05
		Gel	Desonate, DesRx	0.05
	Fluocinolone acetonide	Cream	Synalar	0.025
	Flurandrenolide	Cream, lotion	Cordran, Nolix	0.05
	Fluticasone propionate	Lotion	Beser, Cutivate	0.05
	Hydrocortisone butyrate	Cream, lotion	Locoid, Locoid Lipocream	0.1
		Ointment, solution	[Generic only]	0.1
	Hydrocortisone probutate	Cream	Pandel	0.1
	Hydrocortisone valerate	Cream	Westcort¶	0.2
	Prednicarbate	Cream (emollient), ointment	Dermatop¶	0.1
	Triamcinolone acetonide	Lotion	Kenalog¶	0.1
		Ointment	Kenalog¶	0.025
Low potency (group 6)	Alclometasone dipropionate	Cream, ointment	Aclovate¶	0.05
	Betamethasone valerate	Lotion	Beta-Val¶, Valisone¶	0.1
	Desonide	Cream	DesOwen, Tridesilon	0.05
		Lotion	DesOwen¶, LoKara¶	0.05
		Foam	Verdeso	0.05
	Fluocinolone acetonide	Cream, solution	Synalar	0.01
		Shampoo	Capex	0.01
		Oil$^{\Delta}$	Derma-Smoothe/FS Body, Derma-Smoothe/FS Scalp	0.01
	Triamcinolone acetonide	Cream, lotion	Kenalog¶, Aristocort¶	0.025
Least potent (group 7)	Hydrocortisone (base, ≥2%)	Cream	Ala-Cort, Hytone¶, Nutracort¶	2.5
		Ointment	Hytone¶	2.5
		Lotion	Hytone¶, Ala Scalp, Scalacort DK	2
		Solution	Texacort	2.5
	Hydrocortisone (base, <2%)	Ointment	Cortaid¶, Cortizone 10, Hytone¶, Nutracort¶	1
		Cream	Ala-Cort, Cortaid¶, Cortizone 10, Hytone¶, KeriCort, Synacort¶	1
		Gel	Cortizone 10	1
		Lotion	Aquanil HC, Cortizone 10, Sarnol-HC	1
		Spray	Cortaid¶	1
		Solution	Cortaid¶, Noble¶, Scalp Relief, Scalpicin	1

* Listed by potency according to the United States classification system: group 1 is the most potent, group 7 is the least potent. Other countries use a different classification system with only 4 or 5 groups.

¶ Inactive United States brand name for specific product; brand may be available outside United States. This product may be available generically in the United States.

Δ 48% refined peanut oil.

Data from:

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UPDATES:

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6/19	Revision

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7/17	Revision
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