Clinical Policy: Dupilumab (Dupixent)

Reference Number: CP.PHAR.336
Effective Date: 06.01.17
Last Review Date: 05.24
Line of Business: Commercial*, Medicaid*

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Dupilumab (Dupixent®) is an interleukin-4 receptor alpha antagonist.

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** **California Commercial Exchange Plans and NY CHIP Plans** should not be approved using these criteria; for **California Commercial Exchange Plans** refer to the HIM.PA.SP69 Dupilumab (Dupixent) criteria and for **NY CHIP Plans** refer to the NY.HIM.SP69 Dupilumab (Dupixent) criteria*

FDA Approved Indication(s)

Dupixent is indicated:

- For the treatment of adult and pediatric patients aged 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 can be used with or without topical corticosteroids.
- As an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma.
- As an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).
- For the treatment of adult and pediatric patients aged 1 year and older, weighing at least 15 kg, with eosinophilic esophagitis (EoE).
- For the treatment of adult patients with prurigo nodularis (PN).

Limitation(s) of use: Not for the relief of acute bronchospasm or status asthmaticus

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Dupixent is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Atopic Dermatitis – *FOR MEDICAID and California/Oregon COMMERCIAL ONLY* (must meet all)**:**
**Refer to HIM.PA.SP69 for California Commercial Exchange Plans; refer to NY.HIM.SP69 for NY CHIP Plans*

1. Diagnosis of atopic dermatitis affecting one of the following (a or b):
   a. At least 10% of the member's body surface area (BSA);
   b. Hands, feet, face, neck, scalp, genitals/groin, and/or intertriginous areas;
2. Prescribed by or in consultation with a dermatologist or allergist;
3. Age ≥ 6 months;
4. Failure of both of the following (a and b), unless contraindicated or clinically significant adverse effects are experienced:
   a. Two formulary medium to very high potency topical corticosteroids of different molecular identities, each used for ≥ 2 weeks;
   b. One non-steroidal topical therapy* used for ≥ 4 weeks: topical calcineurin inhibitor (e.g., tacrolimus 0.03% ointment, pimecrolimus 1% cream) or Eucrisa®;
      **These agents may require prior authorization*
5. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry™, Cinqair®, Fasenra®, Nucala®, Tezspire™, Xolair®) or a Janus kinase (JAK) inhibitor (e.g., Olumiant®, Rinvoq®, Cibinqo®, Opzelura™);
6. Dose does not exceed one of the following (a, b, or c):
   a. Age 6 months to 5 years and weight 5 to < 15 kg: 200 mg every 4 weeks;
   b. Age 6 months to 5 years and weight 15 to < 30 kg: 300 mg every 4 weeks;
   c. Age ≥ 6 years and the following:
      i. Initial (one-time) dose:
         1) Age ≥ 18 years, weight ≥ 60 kg, or age 6-17 years and weight 15 to < 30 kg: 600 mg;
         2) Age 6-17 years and weight 30 to < 60 kg: 400 mg;
      ii. Maintenance dose:
         1) Age ≥ 18 years or weight ≥ 60 kg: 300 mg every other week;
         2) Age 6-17 years and weight 30 to < 60 kg: 200 mg every other week;
         3) Age 6-17 years and weight 15 to < 30 kg: 300 mg every 4 weeks.

Approval duration: 6 months

B. Asthma – *FOR MEDICAID and California/Oregon COMMERCIAL ONLY** (must meet all)**:**
**Refer to HIM.PA.SP69 for California Commercial Exchange Plans; refer to NY.HIM.SP69 for NY CHIP Plans*

1. Diagnosis of asthma and one of the following (a or b):
   a. Absolute blood eosinophil count ≥ 150 cells/mcL within the past 3 months;
   b. Currently receiving maintenance treatment with systemic glucocorticoids and has received treatment for at least 4 weeks;
2. Prescribed by or in consultation with an allergist, immunologist, or pulmonologist;
3. Age ≥ 6 years;
4. Member has experienced ≥ 2 exacerbations within the last 12 months, requiring one of the following (a or b), despite adherent use of controller therapy (i.e., medium- to high-dose inhaled corticosteroid [ICS] plus either a long-acting $beta_2$ agonist [LABA] or leukotriene modifier [LTRA] if LABA contraindication/intolerance):
   a. Oral/systemic corticosteroid treatment (or increase in dose if already on oral corticosteroid);
   b. Urgent care/emergency room (ER) visit or hospital admission;

5. Dupixent is prescribed concurrently with an ICS plus either a LABA or LTRA;
6. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
7. Dose does not exceed the following:
   a. Initial (one-time) dose for age ≥ 12 years: 600 mg;
   b. Maintenance dose:
      i. Age ≥ 12 years: 300 mg every other week;
      ii. Age 6-11 years and weight ≥ 30 kg: 200 mg every other week;
      iii. Age 6-11 years and weight 15 to < 30 kg: 300 mg every 4 weeks.

Approval duration: 6 months

C. Chronic Rhinosinusitis with Nasal Polyposis (must meet all)**:**
1. Diagnosis of CRSwNP with documentation of all of the following (a, b, and c):
   a. Presence of nasal polyps;
   b. Disease is bilateral;
   c. Member has experienced signs and symptoms (e.g., nasal congestion/blockage/ obstruction, loss of smell, rhinorrhea) for ≥ 12 weeks;
2. Prescribed by or in consultation with an allergist, immunologist, or otolaryngologist;
3. Age ≥ 18 years;
4. Member has required the use of systemic corticosteroids for symptom control within the last 2 years, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B for examples)*;
5. Failure of maintenance therapy with at least two intranasal corticosteroids, one of which must be Xhance™, each used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B for examples)*;
6. Dupixent is prescribed concurrently with an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B for examples)*;
7. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
8. Dose does not exceed 300 mg every other week.

Approval duration: 6 months

D. Eosinophilic Esophagitis (must meet all)**:**
1. Diagnosis of EoE confirmed by ≥ 15 intraepithelial eosinophils per high-power field (eos/hpf) on endoscopic biopsy;
2. Prescribed by or in consultation with an allergist, immunologist, or gastroenterologist;
3. Age ≥ 1 year;
4. Weight ≥ 15 kg;
5. Member does not have hypereosinophilic syndrome or eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome);
6. Failure of one of the following (a or b), unless clinically significant adverse effects are experienced or both are contraindicated:
   a. Proton pump inhibitor *(see Appendix B for examples)*;

b. Corticosteroid *(see Appendix B for examples)*;
7. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
8. Dose does not exceed the following:
   a. Weight 15 to < 30 kg: 200 mg every other week;
   b. Weight 30 to < 40 kg: 300 mg every other week;
   c. Weight ≥ 40 kg: 300 mg every week.

Approval duration: 6 months

E. Prurigo Nodularis (must meet all)**:**
1. Diagnosis of PN with documentation of both of the following (a and b):
   a. Worst Itch-Numeric Rating Scale (WI-NRS) ≥ 7 on a scale of 0 ("no itch") to 10 ("worst imaginable itch");
   b. ≥ 20 nodular lesions total on both legs, and/or both arms and/or trunk;
2. Prescribed by or in consultation with a dermatologist;
3. Age ≥ 18 years;
4. Failure of a ≥ 2-week course of a medium to very high potency topical corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
5. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
6. Dose does not exceed the following:
   a. Initial (one-time) dose: 600 mg;
   b. Maintenance dose: 300 mg every other week.

Approval duration: 6 months

F. Immunotherapy-related Pruritus (off-label) (must meet all)**:**
1. Diagnosis of immune checkpoint inhibitor-related severe (G3) pruritus that is refractory (*see Appendix E*);
2. Member has an increased IgE level;
3. Prescribed by or in consultation with an oncologist;
4. Dupixent is not prescribed concurrently with Cinqair, Fasenra, Nucala, Xolair, or Tezspire;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

G. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Atopic Dermatitis – *FOR MEDICAID and California/Oregon COMMERCIAL ONLY ** (must meet all)**:**

**Refer to HIM.PA.SP69 for California Commercial Exchange Plans; refer to NY.HIM.SP69 for NY CHIP Plans*

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by, including but not limited to, reduction in itching and scratching;
3. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
4. If request is for a dose increase, new dose does not exceed:
   a. Age ≥ 18 years or weight ≥ 60 kg: 300 mg every other week;
   b. Age 6-17 years and weight 30 to < 60 kg: 200 mg every other week;
   c. Age 6-17 years and weight 15 to < 30 kg: 300 mg every 4 weeks;
   d. Age 6 months to 5 years and weight 5 to < 15 kg: 200 mg every 4 weeks;
   e. Age 6 months to 5 years and weight 15 to < 30 kg: 300 mg every 4 weeks.

Approval duration:
Medicaid – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Asthma – *FOR MEDICAID and California/Oregon COMMERCIAL ONLY ** (must meet all)**:**

**Refer to HIM.PA.SP69 for California Commercial Exchange Plans; refer to NY.HIM.SP69 for NY CHIP Plans*

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;

2. Demonstrated adherence to asthma controller therapy (an ICS plus either a LABA or LTRA) as evidenced by proportion of days covered (PDC) of 0.8 in the last 6 months (i.e., member has received asthma controller therapy for at least 5 of the last 6 months);
3. Member is responding positively to therapy (examples may include but are not limited to: reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline, reduction in the use of rescue therapy);
4. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
5. If request is for a dose increase, new dose does not exceed:
   a. Age ≥ 12 years: 300 mg every other week;
   b. Age 6-11 years and weight ≥ 30 kg: 200 mg every other week;
   c. Age 6-11 years and weight 15 to < 30 kg: 300 mg every 4 weeks.

Approval duration:
Medicaid – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Chronic Rhinosinusitis with Nasal Polyposis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Demonstrated adherence to an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
3. Member is responding positively to therapy (examples may include but are not limited to: reduced nasal polyp size, reduced need for systemic corticosteroids, improved sense of smell, improved quality of life);
4. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
5. If request is for a dose increase, new dose does not exceed 300 mg every other week.

Approval duration:
Medicaid – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

D. Eosinophilic Esophagitis (must meet all)**:**

1. Currently meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;

2. Member is responding positively to therapy (examples may include but are not limited to: reduced eos/hpf count, improvement in dysphagia symptoms);
3. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
4. If request is for a dose increase, new dose does not exceed the following:
   a. Weight 15 to < 30 kg: 200 mg every other week;
   b. Weight 30 to < 40 kg: 300 mg every other week;
   c. Weight ≥ 40 kg: 300 mg every week.

Approval duration:
Medicaid – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

E. Prurigo Nodularis (must meet all)**:**

1. Currently meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy (examples may include but are not limited to: improvement in itching or skin pain, reduction in number of nodules);
3. Dupixent is not prescribed concurrently with another biologic immunomodulator (e.g., Adbry, Cinqair, Fasenra, Nucala, Tezspire, Xolair) or a JAK inhibitor (e.g., Olumiant, Rinvoq, Cibinqo, Opzelura);
4. If request is for a dose increase, new dose does not exceed 300 mg every other week.

Approval duration:
Medicaid – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

F. Immunotherapy-related Pruritus (off-label) (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Dupixent for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

G. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Acute bronchospasm or status asthmaticus.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CRSwNP: chronic rhinosinusitis with nasal polyposis
EoE: eosinophilic esophagitis
eos/hpf: eosinophils per high-power field
FDA: Food and Drug Administration
GINA: Global Initiative for Asthma
ICS: inhaled corticosteroid
JAK: Janus kinase
LABA: long-acting beta$_2$ agonist
LTRA: leukotriene modifier
PDC: proportion of days covered
PN: prurigo nodularis
WI-NRS: Worst Itch-Numeric Rating Scale

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ATOPIC DERMATITIS, PN		
Very High Potency Topical Corticosteroids		
augmented betamethasone 0.05% (Diprolene® AF) cream, ointment, gel, lotion	Apply topically to the affected area(s) BID	Varies
clobetasol propionate 0.05% (Temovate®) cream, ointment, gel, solution		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
diflorasone diacetate 0.05% (Maxiflor®, Psorcon E®) cream, ointment		
fluocinonide 0.1% cream		
flurandrenolide 4 mcg/cm^2 tape		
halobetasol propionate 0.05% (Ultravate®) cream, ointment		
High Potency Topical Corticosteroids		
amcinonide 0.1% ointment, lotion	Apply topically to the affected area(s) BID	Varies
augmented betamethasone 0.05% (Diprolene® AF) cream, ointment, gel, lotion		
betamethasone valerate 0.1%, 0.12% (Luxiq®) ointment, foam		
clobetasol propionate 0.025% (Impoyz®) cream		
diflorasone 0.05% (Florone®, Florone E®, Maxiflor®,Psorcon E®) cream		
fluocinonide acetonide 0.05% (Lidex®, Lidex E®) cream, ointment, gel, solution		
fluticasone propionate 0.005% cream, ointment		
halcinonide 0.1% cream, ointment, solution (Halog®)		
halobetasol propionate 0.01% lotion (Bryhali®)		
mometasone furoate 0.1% ointment		
triamcinolone acetonide 0.5% (Aristocort®, Kenalog®) cream, ointment		
Medium Potency Topical Corticosteroids		
clocortolone pivalate 0.1% cream	Apply topically to the affected area(s) BID	Varies
desoximetasone 0.05%, 0.25% (Topicort ®) cream, ointment, gel, spray		
fluocinolone acetonide 0.025% (Synalar®) cream, ointment		
flurandrenolide 0.05% lotion, ointment (Cordran®)		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hydrocortisone valerate 0.2% cream		
mometasone 0.1% (Elocon®) cream, ointment, lotion		
triamcinolone acetonide 0.025%, 0.1% (Aristocort®, Kenalog®) cream, ointment		
Other Classes of Agents		
Protopic® (tacrolimus), Elidel® (pimecrolimus)	Children ≥ 2 years and adults: Apply a thin layer topically to affected skin BID. Treatment should be discontinued if resolution of disease occurs.	Varies
Eucrisa® (crisaborole)	Apply to the affected areas BID	Varies
cyclosporine	3-6 mg/kg/day PO BID	300 mg/day
azathioprine	1-3 mg/kg/day PO QD	Weight-based
methotrexate	7.5-25 mg/wk PO once weekly	25 mg/week
mycophenolate mofetil	1-1.5 g PO BID	3 g/day
ASTHMA		
ICS (medium – high dose)		
Qvar® (beclomethasone)	> 100 mcg/day 40 mcg, 80 mcg per actuation 1-4 actuations BID	4 actuations BID
budesonide (Pulmicort®)	> 200 mcg/day 90 mcg, 180 mcg per actuation 2-4 actuations BID	2 actuations BID
Alvesco® (ciclesonide)	> 80 mcg/day 80 mcg, 160 mcg per actuation 1-2 actuations BID	2 actuations BID
Flovent® (fluticasone propionate)	> 100 mcg/day 44-250 mcg per actuation 2-4 actuations BID	2 actuations BID
Arnuity Ellipta® (fluticasone furoate)	≥ 50 mcg/day 100 mcg, 200 mcg per actuation 1 actuation QD	1 actuation QD
Asmanex® (mometasone)	> 100 mcg/day HFA: 100 mcg, 200 mcg per actuation Twisthaler: 110 mcg, 220 mcg per actuation 1-2 actuations QD to BID	2 inhalations BID
LABA		
Serevent® (salmeterol)	50 mcg per dose	1 inhalation BID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	1 inhalation BID	
Combination Products (ICS + LABA)		
Dulera® (mometasone/ formoterol)	100/5 mcg, 200/5 mcg per actuation 2 actuations BID	4 actuations per day
Breo Ellipta® (fluticasone/vilanterol)	100/25 mcg, 200/25 mcg per actuation 1 actuation QD	1 actuation QD
Advair® (fluticasone/ salmeterol)	Diskus: 100/50 mcg, 250/50 mcg, 500/50 mcg per actuation HFA: 45/21 mcg, 115/21 mcg, 230/21 mcg per actuation 1 actuation BID	1 actuation BID
fluticasone/salmeterol (Airduo RespiClick®)	55/13 mcg, 113/14 mcg, 232/14 mcg per actuation 1 actuation BID	1 actuation BID
Symbicort® (budesonide/ formoterol)	80 mcg/4.5 mcg, 160 mcg/4.5 mcg per actuation 2 actuations BID	2 actuations BID
LTRA		
montelukast (Singulair®)	4 to 10 mg PO QD	10 mg per day
zafirlukast (Accolate®)	10 to 20 mg PO BID	40 mg per day
zileuton ER (Zyflo® CR)	1,200 mg PO BID	2,400 mg per day
Zyflo® (zileuton)	600 mg PO QID	2,400 mg per day
Oral Corticosteroids		
dexamethasone (Decadron®)	0.75 to 9 mg/day PO in 2 to 4 divided doses	Varies
methylprednisolone (Medrol®)	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisolone (Millipred®, Orapred ODT®)	40 to 80 mg PO in 1 to 2 divided doses	Varies
prednisone (Deltasone®)	40 to 80 mg PO in 1 to 2 divided doses	Varies
CRSwNP		
Intranasal Corticosteroids		
beclomethasone (Beconase AQ®, Qnasl®)	1-2 sprays IN BID	2 sprays/nostril BID
budesonide (Rhinocort® Aqua, Rhinocort®)	128 mcg IN QD or 200 mcg IN BID	1-2 inhalations/ nostril/day
flunisolide	2 sprays IN BID	2 sprays/nostril TID
fluticasone propionate (Flonase®)	1-2 sprays IN BID	2 sprays/nostril BID
mometasone (Nasonex®)	2 sprays IN BID	2 sprays/nostril BID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Omnaris®, Zetonna® (ciclesonide)	Omnaris: 2 sprays IN QD Zetonna: 1 spray IN QD	Omnaris: 2 sprays/ nostril/day Zetonna: 2 sprays/ nostril/day
triamcinolone (Nasacort®)	2 sprays IN QD	2 sprays/ nostril/day
Xhance™ (fluticasone propionate)	1 to 2 sprays (93 mcg/spray) to nostril IN BID	744 mcg/day
Oral Corticosteroids		
dexamethasone (Decadron®)	0.75 to 9 mg/day PO in 2 to 4 divided doses	Varies
methylprednisolone (Medrol®)	4 to 48 mg PO in 1 to 2 divided doses	Varies
prednisolone (Millipred®, Orapred ODT®)	5 to 60 mg PO in 1 to 2 divided doses	Varies
prednisone (Deltasone®)	5 to 60 mg PO in 1 to 2 divided doses	Varies
EoE		
Corticosteroids: examples – • Topical: o Budesonide administered as an oral viscous slurry of budesonide inhalation suspension [Pulmicort Respules®] with sucralose or similar carrier vehicle o Fluticasone propionate administered using a metered dose inhaler • Oral: o Prednisone	Varies	Varies
Proton pump inhibitors (e.g., omeprazole, esomeprazole, lansoprazole, rabeprazole, pantoprazole)	Varies	Varies
Immunotherapy-related pruritus		
H1 blockers: examples – diphenhydramine, chlorpheniramine, hydroxyzine, cetirizine, loratadine, fexofenadine	Varies	Varies
antihistamines, H2 blockers: examples – cimetidine, famotidine		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
corticosteroids: examples – methylprednisolone, prednisolone	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to Dupixent or any of its excipients
- Boxed warning(s): none reported

Appendix D: General Information

- Atopic dermatitis
  - The Phase III pivotal studies (SOLO 1 and SOLO 2) of Dupixent showed no significant difference in clinical outcomes between dosing of Dupixent every week and every other week for the treatment of atopic dermatitis.
- Asthma
  - During clinical trials (LIBERTY ASTHMA QUEST), among patients with a baseline blood eosinophil count of < 150 per cubic millimeter, the exacerbation rate was similar with dupilumab and with placebo: 0.47 (95% CI, 0.36 to 0.62) with lower-dose dupilumab and 0.51 (95% CI, 0.35 to 0.76) with matched placebo, and 0.74 (95% CI, 0.58 to 0.95) with higher-dose dupilumab and 0.64 (95% CI, 0.44 to 0.93) with matched placebo.
  - The Global Initiative for Asthma (GINA) guidelines for difficult-to-treat and severe asthma recommend Dupixent be considered as adjunct therapy for patients 6 years of age and older with exacerbations or poor symptom control despite taking at least high dose ICS/LABA and who have eosinophilic biomarkers or need maintenance oral corticosteroids.
  - Patients could potentially meet asthma criteria for both Xolair and Dupixent, though there is insufficient data to support the combination use of multiple asthma biologics. The combination has not been studied. Approximately 30% of patients in the Nucala MENSA study also were candidates for therapy with Xolair.
  - Lab results for blood eosinophil counts can be converted into cells/mcL using the following unit conversion calculator: https://www.fasenrahcp.com/eosinophil-calculator.
  - PDC is a measure of adherence. PDC is calculated as the sum of days covered in a time frame divided by the number of days in the time frame. To achieve a PDC of 0.8, a member must have received their asthma controller therapy for 144 days out of the last 180 days, or approximately 5 months of the last 6 months.

Appendix E: Immunotherapy-related Pruritus

- Immunotherapy refers to immune checkpoint inhibitors. Immune checkpoint inhibitors comprise a class of agents that target immune cell checkpoints, such as programmed cell death-1 (PD-1; e.g., Opdivo®, Keytruda®) and PD-1 ligand (PD-L1; e.g., Tecentriq®, Bavencio®, Imfinzi®), as well as cytotoxic T-lymphocyte–associated antigen 4 (e.g., Yervoy®, Imjudo®).

- NCCN grading of pruritus
  - G1: Mild or localized
  - G2: Moderate. Intense or widespread; intermittent; skin changes from scratching (e.g., edema, papulation, excoriations, lichenification, oozing/crusts); limiting instrumental ADLs
  - G3: Severe. Intense or widespread; constant; limiting self-care ADLs or sleep

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Moderate-to-severe atopic dermatitis	*Adults*: Initial dose of 600 mg SC followed by 300 mg SC every other week *Adolescents 6-17 years of age*: • Body weight 15 to < 30 kg: Initial dose of 600 mg SC followed by 300 mg SC every 4 weeks • Body weight 30 kg to < 60 kg: Initial dose of 400 mg SC followed by 200 mg SC every other week • Body weight ≥ 60 kg: Initial dose of 600 mg SC followed by 300 mg SC every other week *Pediatrics 6 months - 5 years of age*: • Body weight 5 to < 15 kg: 200 mg SC every 4 weeks • Body weight 15 to < 30 kg: 300 mg SC every 4 weeks	See regimen
Moderate-to-severe asthma	*Adults and adolescents (12 years and older)*: Initial dose of 400 mg SC followed by 200 mg SC every other week; or Initial dose of 600 mg SC followed by 300 mg SC every other week For patients requiring concomitant oral corticosteroids or with co-morbid moderate-to-severe atopic dermatitis for which Dupixent is indicated, start with an initial dose of 600 mg SC followed by 300 mg SC every other week *Adolescents 6-11 years of age*: • Body weight 15 to < 30 kg: Initial dose and subsequent dose of 300 mg every four weeks	See regimen

Indication	Dosing Regimen	Maximum Dose
	• Body weight ≥ 30 kg: Initial dose and subsequent dose of 200 mg SC every other week For pediatric patients (6 to 11 years old) with asthma and co-morbid moderate-to-severe atopic dermatitis, follow the recommended adolescent atopic dermatitis dosing, which includes an initial loading dose	
CRSwNP	300 mg SC every other week	300 mg every other week
EoE	*Adult and pediatric patients ≥ 1 year of age, weight ≥ 15 kg*: • Body weight 15 to < 30 kg: 200 mg SC every other week • Body weight 30 to < 40 kg: 300 mg SC every other week • Body weight ≥ 40 kg: 300 mg SC every week	300 mg/week
PN	Initial dose of 600 mg SC followed by 300 mg SC every other week	See regimen

VI. Product Availability*

- Pre-filled syringes with needle shield for injection: 100 mg/0.67 mL, 200 mg/1.14 mL, 300 mg/2 mL
- Pre-filled pen: 200 mg/1.14 mL, 300 mg/2 mL

**The pre-filled pen is for use in adult and pediatric patients aged 2 years and older, while the pre-filled syringe is for use in adult and pediatric patients aged 6 months and older. In pediatric patients 12 to 17 years of age, Dupixent should be administered under the supervision of an adult. In pediatric patients 6 months to less than 12 years of age, Dupixent should be administered by a caregiver.*

VII. References

1. Dupixent Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; January 2024. Available at: www.dupixent.com. Accessed February 12, 2024.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed November 7, 2023.

Atopic dermatitis

3. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. New England Journal of Medicine. 2016; 375: 2335-48.
4. Sidbury R, Alikhan A, Bercovitch L, et al. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. J Am Acad Dermatol. 2023;89(1):e1-e20.
5. Davis DMR, Drucker AM, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. Published online November 3, 2023.

6. Wollenberg A, Christen-Zäch S, Taieb A, et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. J Eur Acad Dermatol Venereol. 2020 Dec;34(12):2717-2744.
7. Leshem YA, Hajar T, Hanifin JM, et al. What the Eczema Area and Severity Index score tells us about the severity of atopic dermatitis: an interpretability study. British Journal of Dermatology 2015; 172(5):1353-1357.
8. Drucker AM, Ellis AG, Bohdanowicz M, et al. Systemic immunomodulatory treatments for patients with atopic dermatitis: A systematic review and network meta-analysis. JAMA Dermatol. 2020;156(6):659.
9. Boguniewicz M, Fonacier L, Guttman-Yassky E, et al. Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape. Ann Allergy Asthma Immunol. 2018;120(1):10-22.e2.
10. Ting S, Elsada A, Hayre J, Powell J. Dupilumab for treating moderate to severe atopic dermatitis: Technology appraisal guidance (TA534). National Institute for Health and Care Excellence (NICE); 1 August 2018. Available at: https://www.nice.org.uk/guidance/ta534. Accessed October 25, 2022.
11. Harper JI, Ahmed I, Barclay G, et al. Cyclosporin for severe childhood atopic dermatitis: short course versus continuous therapy. Br J Dermatol. 2000;142(1):52-58.

Asthma

12. National Asthma Education and Prevention Program: Expert panel report III: Guidelines for the diagnosis and management of asthma. Bethesda, MD: National Heart, Lung, and Blood Institute, 2007. (NIH publication no. 08-4051). Available at http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines. Accessed November 5, 2023.
13. National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group: 2020 Focused Updates to the Asthma Management Guidelines. Bethesda, MD: National Heart, Lung, and Blood Institute, 2020. Available at https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates. Accessed November 5, 2023.
14. Global Initiative for Asthma. Global strategy for asthma management and prevention (2023 update). Available from: www.ginasthma.org. Accessed November 5, 2023.
15. Global Initiative for Asthma. Difficult-to-treat and severe asthma in adolescent and adult patients – diagnosis and management, v4.0 August 2023. Available at: www.ginasthma.org. Accessed November 5, 2023.

CRSwNP

16. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngology–Head and Neck Surgery 2015, Vol. 152(2S) S1–S39.
17. Peters AT, Spector S, Hsu J, et al. Diagnosis and management of rhinosinusitis: a practice parameter update. Ann Allergy Asthma Immunol 2014. 113:347-85.
18. Fokkens WJ, Lund V, Bachert C, et al. EUFOREA consensus on biologics for CRSwNP with or without asthma. doi: 10.1111/all.13875.
19. Han JK, Bosson JV, Cho SH, et al. Multidisciplinary consensus on a stepwise treatment algorithm for management of chronic rhinosinusitis with nasal polyps. Int Forum Allergy Rhinol. 2021;1-10. Available at: https://onlinelibrary.wiley.com/doi/10.1002/alr.22851. Accessed October 25, 2022.

20. Rank MA, Chu DK, Bognanni A, et al. The Joint Task Force on practice parameters GRADE guidelines for the medical management of chronic rhinosinusitis with nasal polyposis. J Allergy Clin Immunol. 2023;151(2):386-398.

EoE

21. Dellon ES, Liacouras CA, Molina-Infante J et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: Proceedings of the AGREE conference. Gastroenterology. 2018; 155: 1022–1033.
22. Hiran I, Chan, ES, Rank MA, et al. AGA Institute and the Joint Task Force on Allergy-Immunology practice parameters clinical guidelines for the management of eosinophilic esophagitis. Gastroenterology. 2020; 158(6): 1776-1786.

PN

23. Elmariah S, Kim B, Berger T, et al. Practical approaches for diagnosis and management of prurigo nodularis: United States expert panel consensus. J Am Acad Dermatol. 2021; 84(3): 747-760.
24. Sanofi. Study of dupilumab for the treatment of patients with prurigo nodularis, inadequately controlled on topical prescription therapies or when those therapies are not advisable (LIBERTY-PN PRIME). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT04183335. Accessed November 7, 2023.
25. Sanofi. Study of dupilumab for the treatment of patients with prurigo nodularis, inadequately controlled on topical prescription therapies or when those therapies are not advisable (PRIME2). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT04202679. Accessed November 7, 2023.

Immunotherapy-related Pruritus

26. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 6, 2023.
27. National Comprehensive Cancer Network. Management of immunotherapy-related toxicities version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Accessed November 6, 2023.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399; J3590	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: added requirement that Dupixent is not prescribed concurrently with other biologic therapies for asthma to	11.07.19	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
all other indications and on re-authorization; references reviewed and updated.		
For CRSwNP revised redirection from two to three intranasal corticosteroids per SDC and prior clinical guidance.	01.15.20	
Atopic dermatitis: added requirement for at least 10% BSA involvement, unless hands, feet, face, neck, scalp, genitals/groin, and/or intertriginous areas are affected; modified age restriction from 12 years to 6 years and revised max dosing requirements per updated FDA labeling; removed corticosteroids as a systemic agent trial option per ADA guidelines; specified that systemic agents should be tried for at least 3 months; added new pre-filled pen formulation.	06.22.20	08.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.26.20	02.21
For nasal polyps, specified that one of the tried intranasal steroids must be Xhance and modified trial duration from 8 weeks to 4 weeks per 2021 consensus panel treatment algorithm; RT4: added newly approved 200 mg/1.14 mL pre-filled pen.	06.16.21	08.21
1Q 2022 annual review: RT4: expanded age to 6+ years old for asthma and added new 100 mg prefilled syringe formulation; for asthma continuation criteria, defined adherence as PDC of 0.8; added Legacy WellCare line of business (WCG.CP.PHAR.336 to retire); added "Acute bronchospasm or status asthmaticus" to section III as indications for which coverage is not authorized per PI; references reviewed and updated.	11.16.21	02.22
RT4: criteria added for new FDA indication of EoE and pediatric age expansion in AD; for AD redirection to oral immunosuppressants, added minimum age of 2 years; for all indications, added Tezspire as an agent with which Dupixent should not be used concurrently.	07.13.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.21.22	
For AD indication: clarified that topical corticosteroids requirement is for corticosteroids of different molecular identities and expanded examples of medium to very high potency topical corticosteroids in Appendix B; removed low potency topical corticosteroids from Appendix B.	11.04.22	
1Q 2023 annual review: RT4: criteria added for new FDA indication of PN; for all indications, modified list of agents for which concurrent use is not allowed to include non-asthma biologic immunomodulators and JAK inhibitors; for product	02.01.23	02.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
availability, updated age limits and recommendations for pre-filled pens vs syringes; references reviewed and updated.		
Per February SDC, for CRSwNP modified requirement from three intranasal steroids to require only two.	02.21.23	05.23
1Q 2024 annual review: for atopic dermatitis removed oral systemic therapy step criterion per updated guideline and competitor analysis; added off-label indication and criteria for immunotherapy-related pruritus per NCCN; references reviewed and updated. RT4: updated EoE indication to reflect pediatric extension to 1 year and older, weighing at least 15 kg.	02.12.24	02.24
Per March SDC, HIM line of business removed as separate criteria is required; for asthma and atopic dermatitis added reference to "Refer to HIM.PA.SP69 for California Exchange Plans and refer to NY.HIM.SP69 for NY CHIP Plans"; for Asthma initial approval criteria, added allowance for emergency room visit and removed intubation option.	03.26.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.