Clinical Policy: Dupilumab (Dupixent)

Reference Number: ERX.SPA.49
Effective Date: 06.01.17
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

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.

FDA Approved Indication(s)
Dupixent is indicated:

- For the treatment of patients aged 6 years 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 in patients with moderate-to-severe asthma aged 12 years and older with 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)

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Dupixent is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Atopic Dermatitis (must meet all)**:**

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 years;
4. Failure of one of the following systemic agents used for ≥ 3 months, unless clinically significant adverse effects are experienced or all are contraindicated: azathioprine, methotrexate, mycophenolate mofetil, cyclosporine;
5. Dupixent is not prescribed concurrently with Cinqair®, Fasenra®, Nucala®, or Xolair®;
6. Dose does not exceed the following:
   a. Initial (one-time) dose:
      i. Age ≥ 18 years, weight ≥ 60 kg, or age 6-17 years and weight 15 to < 30 kg: 600 mg;
      ii. Age 6-17 years and weight 30 to < 60 kg: 400 mg;
   b. Maintenance dose:
      i. Age ≥ 18 years or weight ≥ 60 kg: 300 mg every other week;
      ii. Age 6-17 years and weight 30 to < 60 kg: 200 mg every other week;
      iii. Age 6-17 years and weight 15 to < 30 kg: 300 mg every 4 weeks.

Approval duration: 6 months

B. Asthma (must meet all)**:**
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 ≥ 12 years;
4. Member has experienced ≥ 2 exacerbations within the last 12 months, requiring any of the following 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 visit or hospital admission;
   c. Intubation;
5. Dupixent is prescribed concurrently with an ICS plus either a LABA or LTRA;
6. Dupixent is not prescribed concurrently with Cinqair, Fasenra, Nucala, or Xolair;
7. Dose does not exceed the following (a or b):
   a. Initial (one-time) dose: 600 mg;
   b. Maintenance dose: 300 mg every other week.

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 three 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 Cinqair, Fasenra, Nucala, or Xolair;
8. Dose does not exceed 300 mg every other week.

Approval duration: 6 months

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Atopic Dermatitis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 Cinqair, Fasenra, Nucala, or Xolair;
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.

Approval duration: 12 months

B. Asthma (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus either a LABA or LTRA;
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 Cinqair, Fasenra, Nucala, or Xolair;
5. If request is for a dose increase, new dose does not exceed 300 mg every other week.

Approval duration: 12 months

C. Chronic Rhinosinusitis with Nasal Polyposis (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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 Cinqair, Fasenra, Nucala, or Xolair;
5. If request is for a dose increase, new dose does not exceed 300 mg every other week.

Approval duration: 12 months

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CRSwNP: chronic rhinosinusitis with nasal polyposis
FDA: Food and Drug Administration
GINA: Global Initiative for Asthma
ICS: inhaled corticosteroid
LABA: long-acting beta$_2$ agonist
LTRA: leukotriene modifier

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ATOPIC DERMATITIS		
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		
diflorasone diacetate 0.05% (Maxiflor®, Psorcon E®) cream, ointment		
halobetasol propionate 0.05% (Ultravate®) cream, ointment		
High Potency Topical Corticosteroids		
augmented betamethasone 0.05% (Diprolene® AF) cream, ointment, gel, lotion	Apply topically to the affected area(s) BID	Varies
diflorasone 0.05% (Florone®, Florone E®, Maxiflor®,Psorcon E®) cream		
fluocinonide acetonide 0.05% (Lidex®, Lidex E®) cream, ointment, gel, solution		
triamcinolone acetonide 0.5% (Aristocort®, Kenalog®) cream, ointment		
Medium Potency Topical Corticosteroids		
desoximetasone 0.05% (Topicort®) cream, ointment, gel	Apply topically to the affected area(s) BID	Varies
fluocinolone acetonide 0.025% (Synalar®) cream, ointment		
mometasone 0.1% (Elocon®) cream, ointment, lotion		
triamcinolone acetonide 0.025%, 0.1% (Aristocort®, Kenalog®) cream, ointment		
Low Potency Topical Corticosteroids		
alclometasone 0.05% (Aclovate®) cream, ointment	Apply topically to the affected area(s) BID	Varies
desonide 0.05% (Desowen®) cream, ointment, lotion		
fluocinolone acetonide 0.01% (Synalar®) solution		
hydrocortisone 2.5% (Hytone®) 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 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/week PO once weekly	25 mg/week
mycophenolate mofetil	1-1.5 gm PO BID	3 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ASTHMA		
ICS (medium – high dose)		
Qvar® (beclomethasone)	> 200 mcg/day 40 mcg, 80 mcg per actuation 1-4 actuations BID	4 actuations BID
budesonide (Pulmicort®)	> 400 mcg/day 90 mcg, 180 mcg per actuation 2-4 actuations BID	2 actuations BID
Alvesco® (ciclesonide)	> 160 mcg/day 80 mcg, 160 mcg per actuation 1-2 actuations BID	2 actuations BID
Aerospan® (flunisolide)	> 320 mcg/day 80 mcg per actuation 2-4 actuations BID	2 actuations BID
Flovent® (fluticasone propionate)	> 250 mcg/day 44-250 mcg per actuation 2-4 actuations BID	2 actuations BID
Arnuity Ellipta® (fluticasone furoate)	200 mcg/day 100 mcg, 200 mcg per actuation 1 actuation QD	1 actuation QD
Asmanex® (mometasone)	>220 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	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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
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

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

- 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.
- 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 2019 Global Initiative for Asthma (GINA) guidelines for difficult-to-treat and severe asthma recommend Dupixent be considered as adjunct therapy for patients 12 years of age and older with exacerbations or poor symptom control despite taking at least high dose ICS/LABA and who

have allergic or eosinophilic biomarkers or need maintenance oral corticosteroids. Per 2020 GINA guidelines, Dupixent may also be considered if the patient is uncontrolled on Step 4 treatment (medium dose ICS/LABA).

- 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/m/fasenra-eosinophil-calculator.html

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 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	See regimen
Moderate-to-severe asthma	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	300 mg every other week
CRSwNP	300 mg SC every other week	300 mg SC every other week

VI. Product Availability*

- Pre-filled syringes with needle shield for injection: 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 only for use in adults and adolescents aged 12 years and older. In adolescents 12 years of age and older, it is recommended that Dupixent be given by or under the supervision of an adult. Dupixent pre-filled syringe should be given by a caregiver in children 6-11 years of age.*

VII. References

1. Dupixent Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; June 2021. Available at: www.dupixent.com. Accessed June 22, 2021.
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7. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2020. Available at: www.ginasthma.org. Published 2020. Accessed October 23, 2020.
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9. 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.
10. 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.
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12. 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 June 16, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.17	05.17
4Q17 Annual Review – no clinical changes	09.26.17	11.17
1Q18 annual review: Removed “moderate-to-severe” from diagnosis as it’s not objectively defined while trial of other systemic therapies are required.	11.15.17	02.18
1Q 2019 annual review: criteria added for new FDA indication: moderate to-severe asthma; references reviewed and updated.	12.04.18	02.19
Updated atopic dermatitis indication with new FDA-approved age extension to patients 12 years of age and older; references reviewed and updated.	03.21.19	
Modified step through requirement for atopic dermatitis from total 3 agents (2 topical and 1 systemic) to 1 (systemic) per CVSC.	04.03.19	
Increased initial approval duration of AD from 16 weeks to 6 months; clarified positive response to therapy examples.	04.04.19	05.19
Criteria added for new FDA indication: CRSwNP; added allergists as potential prescribers for atopic dermatitis; references reviewed and updated.	08.06.19	11.19
1Q 2020 annual review: added requirement that Dupixent is not prescribed concurrently with other biologic therapies for asthma to all other indications and on re-authorization; references reviewed and updated.	11.07.19	02.20
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 reviewed and updated.	10.26.20	02.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
For nasal polyps, revised requirement from 2 intranasal steroids to 3 intranasal steroids including 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

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.