RXADVANCE
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If LClinical Policy Title:	dupilumab
Policy Number:	RxA.594
Drug(s) Applied:	Dupixent®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

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

Limitation of use: Dupixent® is not indicated for the relief of acute bronchospasm or status asthmaticus.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
dupilumab (Dupixent®)	Moderate-to-severe atopic dermatitis	Adults: Initial dose of 600 mg SC followed by 300 mg SC every other week Pediatric Patients (6 to 17 Years of Age): • Body weight 15 ≤ 30 kg: Initial dose of 600 mg SC followed by 300 mg SC every 4 week. • Body weight 30 ≤ 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.	600 mg initially, then 300 mg every other week

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
	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 every other week

Dosage Forms

- Pre-filled syringe with needle shield for injection: 200 mg/1.14 mL, 300 mg/2 mL
- Single-dose pre-filled pen: 300 mg/2 mL

Clinical Policy

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

I. Initial Approval Criteria

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

1. Diagnosis of atopic dermatitis;
2. Prescribed by or in consultation with a dermatologist or allergist;
3. Age 6 years of age or older;
4. Failure of two of the following (a, b, or c), unless contraindicated or clinically significant adverse effects are experienced:
   a. One formulary medium to very high potency topical corticosteroids, each used for ≥ 2 weeks;
   b. One non-steroidal topical therapy*: topical calcineurin inhibitor (e.g., tacrolimus 0.03% ointment and pimecrolimus 1% cream) or Eucrisa®, each used for ≥ 4 weeks;
      * These agents may require prior authorization
   c. One or more of the following systemic agents: corticosteroids, azathioprine, methotrexate, mycophenolate mofetil, or cyclosporine
5. 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

Commercial: 6 months

Medicaid: 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 a/an allergist, immunologist, or pulmonologist;
3. Age 12 years of age or older;
4. Member has experienced ≥ 2 exacerbations within the last 12 months, requiring any of the following despite adherent use of controller therapy (i.e., moderate 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 concomitantly with an ICS plus either a LABA or LTRA (if LABA contraindication/intolerance);
6. Dupixent will not be used concomitantly 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
Commercial: 6 months
Medicaid: 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 of age or older;
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. Member has failed maintenance therapy with at least two intranasal corticosteroids, each used for ≥ 8 weeks, unless contraindicated or clinically significant adverse effects are experienced (see Appendix B for examples);
6. Dupixent is prescribed concomitantly with an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced (see Appendix B for examples);
7. Dose does not exceed 300 mg every other week.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by, including but not limited to, reduction in itching and scratching;
3. If request is for a dose increase, new dose does not exceed 300 mg given every other week.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Asthma (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Demonstrated adherence to asthma controller therapy that includes an ICS plus either a LABA or LTRA (if LABA contraindication/intolerance);
3. Member is responding positively to therapy (see Appendix D);
4. If request is for a dose increase, new dose does not exceed 300 mg given every other week.

Approval Duration
Commercial: 6 months
Medicaid: 12 months

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Demonstrated adherence to an intranasal corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
3. Member is responding positively to therapy *(*see Appendix D);
4. If request is for a dose increase, new dose does not exceed 300 mg given every other week.

Approval Duration
Commercial: 6 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

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

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ATOPIC DERMATITIS		
Very High Potency Topical Corticosteroids		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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% 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®,Maxiflor®, Psorcon E®) cream		
fluocinonide acetonide 0.05% (Lidex®) cream, ointment, gel, solution		
triamcinolone acetonide 0.5% (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% cream, ointment, lotion		
triamcinolone acetonide 0.025%, 0.1% (Kenalog®) cream, ointment		
Low Potency Topical Corticosteroids		
alclometasone 0.05% cream, ointment	Apply topically to the affected varies area(s) BID	varies
desonide 0.05% (Desowen®) cream, ointment, lotion		
fluocinolone acetonide 0.01% (Synalar®) solution		
hydrocortisone 2.5% cream, ointment		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 once daily	Weight-based
methotrexate	7.5-25 mg/wk PO once weekly	25 mg/week
mycophenolate mofetil	1-1.5 PO BID	3 g/day
Systemic corticosteroids (e.g. prednisone, prednisolone, triamcinolone)	PO, IM, or parenteral; dose varies	varies
ASTHMA		
ICS (medium – high dose)		
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
flunisolide	> 320 mcg/day 80 mcg per actuation 2-4 actuations BID	2 actuations BID
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 once daily	1 actuation once daily
Asmanex® (mometasone)	>220 mcg/day HFA: 100 mcg, 200 mcg per actuation Twisthaler: 110 mcg, 220 mcg per actuation 1-2 actuations once daily to BID	2 inhalations BID
LABA		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 once daily	1 actuation once daily
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
Combination products (ICS + LABA)		
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 once daily	10 mg per day
zafirlukast (Accolate®)	10 to 20 mg PO BID	40 mg per day
zileuton ER	1200 mg PO BID	2400 mg per day
Zyflo® (zileuton)	600 mg PO QID	2400 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	128 mcg IN once daily or 200 mcg IN BID	1-2 inhalations/nostril/ day
flunisolide	2 sprays IN BID	2 sprays/nostril TID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
fluticasone propionate	1-2 sprays IN BID	2 sprays/nostril BID
mometasone (Nasonex®)	2 sprays IN BID	2 sprays/nostril BID
Omnaris®, Zetonna® (ciclesonide)	Omnaris: 2 sprays IN once daily Zetonna: 1 spray IN once daily	Omnaris: 2 sprays/ nostril/day Zetonna: 2 sprays/nostril/day
triamcinolone (Nasacort®)	2 sprays IN once daily	2 sprays/ nostril/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.

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 for the treatment of atopic dermatitis.
- 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.
- Positive response to therapy for asthma may include reduction in exacerbations or corticosteroid dose, improvement in forced expiratory volume over one second since baseline, or reduction in the use of rescue therapy.
- Lab results for blood eosinophil counts can be converted into cells/mcL using the following unit conversion calculator: https://www.fasenrahcp.com/m/fasenra-eosinophilcalculator.html
- Positive response to therapy for CRSwNP may include reduced nasal polyp size, reduced need for systemic corticosteroids, improved sense of smell, or improved quality of life.
- The Dupixent pre-filled pen is only for use in adults and adolescents aged 12 years and older.

References

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	02/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title was updated as "dupilumab." 2. Lines of business policy applies to all lines of business. 3. Dosing regimen for atopic dermatitis was updated. 4. Dosage form updated. 5. Initial approval criteria I.A.3 was updated to 6 years of age or older. 6. Initial and continued approval criteria was updated to add Medicaid approval duration. 7. Continued therapy criteria II.A.1, II.B.1 & II.C.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance." 8. Appendix B was updated: removed brand Maxiflor, Psorcon E, Florone E, Lidex E, Aristocort, Elocon, Aclovate, Hytone, Qvar,	10/09/2020	12/07/2020

Aerospan, Flovent, Rhinocort Aqua, Rhinocort, Flonase, Zyflo CR as they all were discontinued. 9. Verbiage for Appendix B was updated. 10. Appendix D was updated. 11. References were reviewed and updated.		