Drug Monograph

Drug/Drug Class:	**Dupixent® (dupilumab) solution for injection/ Monoclonal Antibody Immunomodulators**
Prepared for:	MO HealthNet
Prepared by:	Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Dupixent® is available in a single dose pre-filled syringe that contains 300 mg dupilumab per 2 ml. Manufacturer: Regeneron Pharmaceuticals, Inc., Tarrytown, NY 10591
Summary of Findings:	In 2 different phase 3 clinical trials, Dupixent® monotherapy improved the signs and symptoms associated with moderate to severe atopic dermatitis when compared with placebo. The proportion of patients achieving an IGA score of 0 or 1 and at least a 2-point reduction from baseline was 38% and 36% for Dupixent® given every other week compared to 10% and 8% for placebo. Also, 51% and 44% of patients receiving Dupixent® achieved an EASI of at least 75% compared to 15% and 12% for placebo. Finally, 51% and 44% of patients receiving Dupixent® had an improvement of at least 3 out of 4 points in peak pruritus scores vs. 17% and 13% for placebo. Outcomes with weekly dosing were similar to every other week dosing.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☒ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☐ Appropriate Indications ☒ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction [2]

Atopic dermatitis is a very common, chronic disease that affects the skin. Atopic refers to a group of diseases in which there is often an inherited tendency to develop other allergic conditions, such as asthma and hay fever. Dermatitis means inflammation of the skin. In atopic dermatitis, the skin becomes extremely itchy. Scratching leads to redness, swelling, cracking, weeping, and scaling.

Atopic dermatitis occurs equally in males and females and affects an estimated 30 percent of people in the U.S. Although it may occur at any age, it most often begins in infancy and childhood.

Dosage Form(s) [1]

Dupixent® is available in a single dose pre-filled syringe that contains 300 mg dupilumab per 2 ml.

Manufacturer [1]

Regeneron Pharmaceuticals, Inc., Tarrytown, NY 10591

Indication(s) [1]

Dupixent® is indicated for the treatment of moderate to severe atopic dermatitis, with or without topical corticosteroids, in adult patients whose disease is not adequately controlled with topical prescription therapies or who are unable to receive topical prescription therapies.

Clinical Efficacy [1,2] (mechanism of action/pharmacology, comparative efficacy)

Dupixent® is a human monoclonal IgG4 antibody that inhibits interleukin-4 and interleukin-13 cytokine induced responses, including release of proinflammatory cytokines, chemokines, and IgE.

Pharmacokinetics:

	Dupixent®
Volume of Distribution	4.8 L
Metabolism	Catabolized into small peptides and amino acids

SOLO 1 AND SOLO 2 TRIALS

Dupixent® monotherapy improved the signs and symptoms associated with moderate to severe atopic dermatitis compared with placebo.

STUDY DESIGN	Two identical randomized, double-blind, multicenter, placebo controlled, phase 3 clinical trials (SOLO 1, N=671; SOLO 2, N=708)
INCLUSION CRITERIA	Adult patients with moderate to severe atopic dermatitis inadequately controlled with topical treatment or for whom topical treatment was inadvisable.
EXCLUSION CRITERIA	Not specified.
TREATMENT REGIMEN	Patients were randomized to receive Dupixent® 600 mg subcutaneously as a loading dose followed by 300 mg every week or every other week for 16 weeks or placebo.
RESULTS	Dupixent® every other week compared with placebo significantly increased the proportion of patients achieving an IGA score of 0 or 1 and at least a 2-point reduction from baseline (SOLO 1, 38% vs 10%; SOLO 2, 36% vs 8%). Dupixent® was also associated with a significantly greater proportion of patients who achieved an EASI of at least 75% (SOLO 1, 51% vs 15%; SOLO 2, 44% vs 12%) and an improvement of at least 3 out of 4 points in peak pruritus scores (SOLO 1, 47% vs 17%; SOLO 2, 51% vs 13%). Outcomes with weekly dosing were similar to every other week dosing.
SAFETY	Adverse events were similar between groups.

Contraindications [(1)]

- Known hypersensitivity to dupilumab or any of its excipients

Warnings and Precautions [(1)]

- Hypersensitivity reactions have been reported, including generalized urticarial, serum sickness, or serum sickness-like reactions; discontinue if occur
- Conjunctivitis and keratitis have been reported.
- Patient with comorbid asthma should not adjust or discontinue asthma treatment without consultation with a physician.

Adverse Effects [1]

Most common, ≥ 1%	Dupixent® (dupilumab) (n=529)	Placebo (n=517)
Injection site reactions	10%	5%
Conjunctivitis	10%	2%
Oral herpes	4%	2%
Other herpes simplex infection	2%	1%
Eye pruritus	1%	<1%

Drug Interactions [1]

- CYP450 substrates with narrow therapeutic indices: Warfarin, cyclosporine
- Live vaccines

Dosage and Administration [1]

The FDA recommended dose is an initial dose of 600 mg subcutaneously, divided in 2 different injection sites, followed by 300 mg every other week.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST/ DOSE*	COST/ MONTH*
Dupilumab	Dupixent	Sanofi-Aventis	300 mg prefilled syringes	300 mg every other week	$718.65	$1,437.30

* Maximum Allowable Cost

Conclusion

Dupixent® is the first biologic agent approved for the treatment of moderate to severe atopic dermatitis that is not adequately controlled with topical prescription therapies or when topical therapies are inadvisable. Dupixent® received breathrough therapy designation and priority review by the US Food and Drug Administration. Dupixent® is a monoclonal antibody that inhibits both interleukin-4 and interleukin-13 signaling. It is administered subcutaneously every other week and may be used with or without topical corticosteroids. In phase 3 clinical trials, Dupixent® monotherapy significantly improved signs and symptoms of atopic dermatitis, including pruritus, compared to placebo. Injection site reactions, conjunctivitis, and oral herpes infections are the most common adverse events.

Recommendation

This drug is being considered for inclusion in the state specific Preferred Drug List.

References

1) Product Information: Dupixent™, dupilumab injection. Sanofi-Aventis US, LLC, Bridgewater, NJ, 03/2017
2) Atopic Dermatitis. Retrieved 8/16.2017 from https://www.niams.nih.gov/health_info/atopic_dermatitis/default.asp

Prepared by: Luke Boehmer PharmD
Date: August 16, 2017

