BRAND NAME: DUPIXENT

PROPER NAME: Dupilumab

MANUFACTURER: Regeneron Pharmaceuticals, Inc.

INDICATION: DUPIXENT is an interleukin-4 receptor alpha antagonist indicated for the treatment of adult patients 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.

DESCRIPTION: Dupilumab, an interleukin-4 receptor alpha antagonist, is a human monoclonal antibody of the IgG4 subclass that binds to the IL-4Rα subunit and inhibits IL-4 and IL-13 signaling. Dupilumab has an approximate molecular weight of 147 kDa.

BLA NO: 761055

REGULATORY MILESTONES:

- 05/26/2010 - Pre-IND Meeting
- 05/21/2014 - End-of-Phase 2 Meeting
- 08/04/2014 - Guidance Meeting
- 12/16/2015 - Pre-BLA meeting
- 11/18/2014 - Breakthrough Therapy designation granted
- 11/18/2015 - Rolling review was granted
- 07/29/2016 - Priority review was granted following BLA submission

US Approval	March 28, 2017

EU Approval	September 27, 2017
Health Canada Approval	September 27, 2019
Japanese Ministry of Health, Labor and Welfare (MHLW) Approval	January 22, 2018
TGA	January 22, 2018

ADVISORY COMMITTEE:

No advisory committee meeting was held for this application. Although dupilumab is a new molecular entity and first-in class, the application itself did not present novel issues, not previously discussed, which merited advisory committee input. A related topic, the timing of pediatric development of systemic products for treatment of patients with moderate to severe atopic dermatitis not adequately controlled with optimized topical therapy, was presented to the Dermatology and Ophthalmology Drug Advisory Committee (DODAC) on 9 March 2015. At that meeting, preliminary safety, and efficacy data for dupilumab, gleaned from published literature, was presented to DODAC as an example of a relevant product under development. The committee was not asked to comment on the efficacy and safety of dupilumab per se, but rather to address issues related to pediatric development of products for the specified indication.

MANUFACTURING:

PARAMETER	DATA	REFERENCE
Manufacturer	Regeneron Pharmaceuticals, Inc.	
Indication	DUPIXENT is an interleukin-4 receptor alpha antagonist indicated for the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. It can be used with or without topical corticosteroids.	1
Cell Substrate	Recombinant human IgG4 monoclonal antibody	3

Manufacturing platform	The manufacture of dupilumab AS represents a standard manufacturing process for the manufacture of monoclonal antibodies. It is achieved in three main parts, the upstream process, which produces the antibody, the downstream process, which purifies the antibody and the formulation of the active substance (formulated active substance- FAS). Dupilumab is produced by a cell culture process with recombinant Chinese hamster ovary (CHO) cells that have been engineered to constitutively express dupilumab heavy and light chains. Dupilumab protein is expressed by the cells and is secreted into the culture medium. The recombinant protein product is harvested and purified leveraging standard chromatographic and membrane-based techniques and includes several steps ensuring adventitious agent safety. At the conclusion of purification, the AS is sterile-filtered and dispensed for long-term storage until needed for formulation.	3
Dose in vial/final container	300 mg/2 mL solution in a single-dose pre-filled syringe	1
Dose to patient	600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week.	1

1. Package insert - DUPIXENT
2. EPAR full - DUPIXENT
3. EPAR quality - Dupixent: EPAR - Public assessment report
4. FDA Review - DUPIXENT Injection

CLINICAL TRIALS:

NCT	TRIAL PHASE	NO OF PATIENTS ENROLLED	TITLE	COUNTRIES
Controlled Studies to Support Efficacy and Safety				
NCT02277743	3	671	Study of Dupilumab Monotherapy Administered to Adult Patients with Moderate-	United States, Bulgaria, Canada, Denmark, Estonia, Japan, Spain, Finland, Germany, Singapore

			to-Severe Atopic Dermatitis	
NCT02277769	3	708	Study of Dupilumab (REGN668/SAR231893) Monotherapy Administered to Adult Patients with Moderate-to-Severe Atopic Dermatitis	United States, Canada, Italy, France, Germany, Hong Kong, Korea, Republic of, Lithuania, Poland, Sweden, United Kingdom
NCT02260986	3	740	Study to Assess the Efficacy and Long-term Safety of Dupilumab (REGN668/SAR231893) in Adult Participants with Moderate-to-Severe Atopic Dermatitis	United States, Canada, Italy, Australia, Czechia, Hungary, Japan, Korea, Republic of, Netherlands, New Zealand, Poland, Spain, Romania, United Kingdom
Dose-Ranging Study; Supports Safety				
NCT01859988	2	380	Study of Dupilumab Administered to Adult Patients with Moderate-to-Severe Atopic Dermatitis	United States, Canada, Czechia, Germany, Japan, Hungary, Poland
PD and PK PD Studies; Support Safety				
NCT01979016	2	54	Study to Determine the Safety and Effectiveness of Dupilumab for Treatment of Atopic Dermatitis (AD)	United States, Canada
NCT02210780	2	194	Study of Dupilumab and Immune Responses in Adults with Atopic Dermatitis (AD)	United States
NCT01548404	2	109	Study of Dupilumab in Adult Patients with Extrinsic Moderate-to-Severe Atopic Dermatitis	Czechia, France, Germany, Hungary, Poland
Uncontrolled Clinical Study				
NCT01949311	3	2678	Open-label Study of Dupilumab in Patients with Atopic Dermatitis	United States, Austria, Italy, Australia, Belgium, France, Bulgaria, Canada, China, Czechia, Japan, Denmark,

				Estonia, Finland, Germany, Hungary, Ireland, Lithuania, Korea, Republic of, New Zealand, Poland, Spain, Slovakia, Romania, Russian Federation, Singapore, Netherlands, United Kingdom

POST APPROVAL CHANGES

DATE	TYPE OF CHANGE	DESCRIPTION	LINK