Report Dupixent®- Dupilumab

Product & Mechanism of action

Active principle: Dupilumab

Brand Name: Dupixent®

Originator/ licensee: Sanofi-Aventis Groupe

Classification: NI

ATC code: D11AH05
Orphan Status:
Eu: No
Us: No
Mechanism of action: Dupilumab is a mAB that inhibits IL-4 and IL-13 signaling. IL-4 and IL-13 are major drivers of human type 2 inflammatory disease, and blocking the IL-4/IL-13 pathway in pts decreases many of the mediators of type 2 inflammation [1].

Authorized indications Licensing status

Authorized Indication:
EMA: Dupixent is indicated for the treatment of severe AD in children aged 6 months to 11 years, who are candidates for systemic therapy [2].

FDA: Dupixent is indicated for the treatment of pediatric pts aged 6 months and older with moderate-to-severe AD, whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable [3].

Route of administration: SC

Licensing status:
EU CHMP P.O. date: 26/01/2023
FDA M.A. date: 28/09/2022

EU Speed Approval Pathway: No
FDA Speed Approval Pathway: No

ABBREVIATIONS:
AE: Adverse event
AD: Atopic Dermatitis
BW: Bodyweight
CHMP: Committee for Medicinal Products for Human Use
CI_{95} = Confidence Interval of 95%
DG: Dupilumab group
EP: End-Point
IL: Interleukin
IGA: Investigator's Global Assessment
LPTCS: low-potency topical corticosteroids
M.A.: Marketing authorization
mAB: Monoclonal antibody
PG: Placebo group
PN: Prurigo Nodularis
P.O.: Positive opinion
Pts: Patients
sc: Subcutaneous
TCS: Topical corticosteroids
TEAE:sTreatment emergent adverse event
WI-NRS: Worst Itch Numeric Rating Scale

Essential therapeutic features

Summary of clinical EFFICACY: NCT03346434 is a randomised, double-blind, placebo-controlled, parallel-group, phase 3 trial aimed to assess the efficacy and safety of Dupilumab for severe AD in children aged 6 months to 5 years. Eligibility criteria included pts aged 6 months to <6 years at screening, with moderate to severe AD (IGA score= 3 - 4) and inadequate response to TCS before screening.
Pts assessed for eligibility were randomly assigned (1:1) to receive either Dupilumab (N=83; 200 mg for 5 kg≤BW<15 kg pts or 300 mg for 15 kg≤BW<30 kg pts) or placebo (N=79) every four weeks. From day 14 to the end of the treatment period, pts received a once-daily regimen of LPTCS. Once the pt reached an IGA score≤ 2, LPTCS use was tapered to three times/week and, at an IGA score=0, LPTCS use was stopped.
The primary EP was the proportion of pts with an IGA score= 0 - 1 at the end of the treatment period. A total of 82 (99%) pts in the DG and 75 (95%) pts in the PG completed the study treatment: 23 (28%) pts in the DG and three (4%) pts in the PG had IGA= 0 or 1, with a significant difference between groups of 24% [CI_{95} (13, 34); p<0.0001] [4].

Summary of clinical SAFETY: One pt in the PG was excluded from the safety analysis set because did not receive the study treatment. Safety data from NCT03346434 trial are summarized in the table below:

	Dupilumab Group (N=83)	Placebo Group (N=78)
Pts with≥1 TEAE	53 (64%)	58 (74%)
Pts with TEAEs leading to treatment discontinuation	1 (1%)	1 (1%)
Pts with≥1 serious TEAE	0	4 (5%)
Death	0	0
Pts with≥1 TEAE related to study drug	9 (11%)	5 (6%)

The most common TEAE reported in >3% of pts were: nasopharyngitis (8% and 9% of pts in the DG and PG respectively); upper respiratory tract infection (6% and 8% of pts in the DG and PG, respectively); exacerbation of atopic dermatitis (13% and 32% of pts in the DG and PG, respectively); asthma (4% and 6% of pts in the DG and PG, respectively); gastrointestinal disorders (10% and 8% of pts in the DG and PG, respectively); lymphadenopathy (4% and 8% of pts in the DG and PG, respectively) and pyrexia (1% and 9% of pts in the DG and PG, respectively).
Serious TEAE occurred only in the PG (e.g. atopic dermatitis, infected dermatitis, hypersensitivity, staphylococcal bacteraemia and staphylococcal cellulitis).

Ongoing studies:
For the same indication: Yes
For other indications: Yes

Discontinued studies (for the same indication): No

References:
1.https://www.ema.europa.eu/en/documents/product-information/dupixent-epar-product-information_en.pdf
2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/dupixent-7
3.https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761055s044lbl.pdf
4.Paller AS et AL. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022 Sep 17; doi: 10.1016/S0140-6736(22)01539-2. PMID: 36116481.
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NHS impact

Cost of therapy: The ex-factory price for apre-filled pen/syringe of Dupixent® (300 mg-200 mg) is 608,00€ [6].

Epidemiology: Limited data are available on the epidemiology of AD in children aged 6 months to 11 years. In Italy the prevalence of AD is assessed at 10% - 12% [7].
According to the literature AD occurs in the 15,6% of 6 months Europeanchildren [8].

POSSIBLE PLACE IN THERAPY: Treatment of AD includes a range of therapies such as emollients, bandages, phototherapy and topical and oral corticosteroids.
Topical tacrolimus is recommended as second-line treatment in adults and children aged >2 years with AD that is uncontrolled with topical corticosteroids.
Dupilumab offers an additional option to pts with severe AD uncontrolled with currently available therapies [9].

OTHER INDICATIONS IN DEVELOPMENT: Chronic Spontaneous Urticaria, Chronic Cold Urticaria, Allergic Bronchopulmonary Aspergillosis, Eosinophilic Esophagitis Allergic Fungal Rhinosinusitis, Chronic Obstructive Pulmonary Disease, Chronicrhinosinusitis Without Nasalpolyps, Cold Urticaria, Netherton Syndrome [10].

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: -

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATIOS: Yes.Difamilast andLebrikizumab arealready authorized in the European Union for other indications and they are under investigation for the treatment of AD in infants [10].

*Service reorganization: No
*Possible off label use: Yes