Report tralokinumab - Adtralza®

Product & Mechanism of action

Substance: tralokinumab

Brand Name: Adtralza

Originator/licensee: LEO Pharma A/S

Classification: NI

ATC code: D11

Orphan Status:
Eu: No
Us:

Mechanism of action:
Patients with AD produce high levels of IL-13, which can cause inflammation of the skin leading to the symptoms of this disease such as redness, swelling and itching. Tralokinumab is a monoclonal antibody designed to neutralise IL-13. By neutralising IL-13, tralokinumab prevents IL-13 from working and thereby reduces the inflammation and patient's symptoms [1].

Authorized indications Licensing status

Authorized Indication:
EMA: Tralokinumab is indicated for the treatment of moderate-to-severe atopic dermatitis in adult and adolescent pts 12 years and older who are candidates for systemic therapy.

Route of administration: sc

Licensing status
EU CHMP P.O. date: 15/09/2022
FDA M.A. date: /

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

ABBREVIATIONS:
AD: Atopic Dermatitis
AE: adverse event
CHMP: Committee for Medicinal Products for Human Use
EASI: Eczema Area and Severity Index score
IGA: Investigator Global Assessment
M.A.: Marketing Authorization
Pbo: placebo
P.O.: positive opinion
Q2W: Every to two weeks
Q4W: every 4 weeks
SAE: serious adverse event
TCS: topical corticosteroids

Essential therapeutic features

Summary of clinical EFFICACY:
(ECZTRA 6) NCT03526861 was a phase III, randomized, double-blind, placebo-controlled, multicentre trial to evaluate the efficacy, safety and tolerability of tralokinumab monotherapy in adolescent subjects (age 12 to < 18 years) with moderate-to-severe AD who are candidates for systemic therapy.
Co-primary endpoints were IGA score 0/1 and ≥ 75% improvement of EASI (EASI-75) at week 16.
Adolescent pts (n=195) were randomized 1:1:1 to sc tralokinumab 150mg (n=98) or 300mg (n=97) Q2W, or pbo (n=94) for an initial treatment period of 16 weeks.*
At week 16, significantly greater proportions of pts receiving tralokinumab achieved the primary endpoints of IGA and EASI-75 without use of rescue compared to those receiving pbo [2-3].
*Pts achieving primary endpoints without rescue treatment were re-randomized to tralokinumab Q2W or Q4W, at their same initial dosage for 36 weeks of maintenance treatment. Patients not achieving primary endpoints at week 16, those receiving rescue treatment from week 2 to week 16, and those meeting other specific criteria were transferred to open-label treatment of tralokinumab 300 mg Q2W plus optional mild-to-moderate strength TCS.

	tralokinumab 150mg	tralokinumab 300mg	pbo
% of pts who achieved clear or almost-clear skin as measured by IGA	28.6% (p<0.001)	17.5% (p=0.002)	4.3%
% of pts who achieved 75% or greater disease improvement from baseline measured by EASI	28.6% (p<0.001)	27.8% (p=0.001)	6.4%

Summary of clinical SAFETY:
Through week 16, percentages of AEs, SAEs, AEs leading to discontinuation, and conjunctivitis events were similar between the tralokinumab (150mg/300mg) and pbo treatment groups. The majority of AEs in all treatment groups were mild or moderate in severity and subjects recovered from most of the AEs [2-3].

	AEs n(%)	SAEs	AEs of special interest			
			Conjunctivitis	Eczema herpeticum	Skin infections requiring systemic treatment	Injection site reactions
Pbo	58 (61.7)	5 (5.3)	2 (2.1)	1 (1.1)	2 (2.1)	1 (1.1)
Tralokinumab 150 mg	66 (67.3)	3 (3.1)	4 (4.1)	1 (1.0)	5 (5.1)	9 (9.2)
Tralokinumab 300mg	63 (64.9)	1 (1.0)	3 (3.1)	0	2 (2.1)	7 (7.2)

Ongoing studies:
- ***For the same indication:*** Yes
- ***For other indications:*** No [4].

Discontinued studies (for the same indication): No [4].

NHS impact

Cost of therapy:
In italy, Adtralza 4 2x2 pre-filled syringe 150mg 1ml costs 1.155,20 € (ex factory price) [5].

Epidemiology:
AD is one of the most common inflammatory disorders, affecting up to 20% of children and 10% of adults in high-income countries [6].

POSSIBLE PLACE IN THERAPY
A typical MSAD treatment pathway involves emollients and topical corticosteroids (1st-line), topical calcineurin inhibitors (2nd-line), phototherapy (3rd-line, for adults only) and systemic immunosuppressant therapies (4th-line). Dupilumab (for pts ≥12 years of age) is recommended for the treatment of MSAD in pts that have not responded to at least one systemic therapy (5th-line) [7].

OTHER INDICATIONS IN DEVELOPMENT:
No

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

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION
Dupilumab [8].

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

References:
[1]. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/adtralza-0
[2]. https://jofskin.org/index.php/skin/article/view/1546/pdf
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[4]. https://adisinsight.springer.com/drugs/800019573
[5]. https://gallery.farmadati.it/Home.aspx
[6]. Langan S.M., Irvine A.D., et al.: Atopic dermatitis. Lancet 2020; 396: 345–60.
[7]. https://www.ema.europa.eu/en/documents/product-information/adtralza-epar-product-information_en.pdf
[8]. https://clinicaltrials.gov/