HTA202

Health technology assessment (HTA) and reimbursement decisions for the new anti-IL-13 monoclonal antibody lebrikizumab for patients with moderate-to-severe atopic dermatitis (AD) in Europe

Laia Solé-Feu[1], Bülent Akmaz[1], Jean Michel Joubert[2], Matthew Cressey[3], Maria del Barrio[1]

[1]Global Market Access, Pricing and Medical Affairs, Almirall S.A., Barcelona, Spain.

[2]Affaires Gouvernementales, Almirall SAS, Issy-les-Moulineaux, Paris, France.

[3]Value and Access, Almirall Ltd, London, UK.

Almirall, S.A. has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including atopic dermatitis, in Europe. Lilly has exclusive rights for the development and commercialization of lebrikizumab in the United States and the rest of the world outside of Europe.

BACKGROUND & OBJECTIVE

- Almirall applied for reimbursement to the national health technology assessment (HTA) bodies across Europe and the United Kingdom for lebrikizumab, an anti-interleukin-13 monoclonal antibody approved by the EMA and the MHRA for the treatment of moderate-to-severe atopic dermatitis (AD).
- This analysis illustrates the complexity of adapting the regulatory clinical package to local HTA requirements in three key European countries.

CONCLUSION

- Based on this targeted approach to meet local HTA agencies' requirements, lebrikizumab has been positively recommended for reimbursement in Germany, France, and the United Kingdom.
- The robustness of the clinical data presented, together with the PICO methodology delivered was reinforced from the G-BA/IQWiG, HAS and NICE outcomes.
- As a result, Almirall has been able to enable AD patients' access to lebrikizumab, covering an unmet need.

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HTA by European country	GERMANY (Gemeinsamer Bundesausschuss IQWiG)	FRANCE (HAS Haute Autorité de Santé)	ENGLAND (NICE National Institute for Health and Care Excellence)
Clinical evidence submitted	▪ The clinical evidence was aligned with the EMA regulatory clinical package including data from the three randomized, double-blind, placebo-controlled pivotal Phase 3 studies: – ADvocate 1 and ADvocate 2 (NCT04146363 and NCT04178967)[1,2] – ADhere (NCT04250337)[3] ▪ Data from the extension study ADjoin (NCT04392154) of the pivotal trials.	▪ Data from four randomized, double-blind, placebo-controlled Phase 3 studies: – ADvocate 1 and ADvocate 2[1,2] – ADhere[3] – ADvantage (NCT05149313) ▪ Data from the extension study ADjoin of the ADvocate 1 and 2, and ADhere trials.	▪ Data from four randomized, double-blind, placebo-controlled Phase 3 studies: – ADvocate 1 and ADvocate 2[1,2] – ADhere[3] – ADvantage ▪ Data from the extension study ADjoin of the ADvocate 1 and 2, and ADhere trials.
Target population for reimbursement	▪ EMA-approved target population: – Adults and adolescents aged 12 years and older with a body weight ≥40 kg with moderate-to-severe AD who are candidates for systemic therapy.	▪ Target subgroup of patients based on an additional efficacy/safety clinical trial of lebrikizumab (ADvantage): – Adults and adolescents aged 12 years and older with a body weight ≥40 kg with moderate-to-severe AD who are candidates for systemic treatment and who have failed, are not adequately controlled or non-eligible for cyclosporine.	▪ Subgroup of patients: – Adults and adolescents aged 12 years and older with a body weight ≥40 kg with moderate-to-severe AD who are candidates for systemic treatment and who have failed to ≥1 systemic immunosuppressant or are not suitable for these treatments.
Outcomes for decision making	▪ All clinical outcomes pre-defined by G-BA and available in the clinical study reports in the areas of mortality, morbidity, quality of life, and safety.	▪ Primary and secondary outcomes of Investigator's Global Assessment score of 0 or 1, ≥75% reduction in the Eczema Area and Severity Index (EASI 75), EASI 90, and ≥4-point reduction in the Pruritus Numeric Rating Scale.	▪ Composite outcome of EASI 50 plus ≥4-point reduction in the Dermatology Life Quality Index. ▪ EASI 75 was accepted as proxy due to unavailability of the combined outcome for all comparators.
Head-to-head / Indirect comparisons	▪ Therapy with dupilumab (possibly in combination with topical corticosteroids and/or topical calcineurin inhibitors) was determined by the G-BA as the appropriate comparator therapy. ▪ However, no head-to-head comparative data was available/delivered.	▪ In the absence of direct comparisons, matching-adjusted indirect comparisons versus biologics (dupilumab and tralokinumab) were carried out in the target population to demonstrate the added benefit of lebrikizumab.	▪ There were no clinical trials directly comparing lebrikizumab with its relevant comparators. ▪ Thus, a network meta-analysis to obtain response rate odds comparing lebrikizumab with biologics (dupilumab and tralokinumab) and JAK inhibitors (upadacitinib, abrocitinib, and baricitinib) was conducted.
Pharmacoeconomic model	▪ An annual cost comparison was done with the appropriate comparator (dupilumab) – To calculate the annual therapy costs, the required number of packs by potency was first determined based on consumption. – The pharmaceutical costs were then calculated based on the cost per pack, after deduction of the statutory discounts, using the number of packs by potency.	▪ No pharmacoeconomic model was evaluated.	▪ Cost-effectiveness model which consisted of a short-term (1 year) decision tree capturing treatment induction and a long-term Markov model (year 2 onwards) in a lifetime horizon. ▪ The model structure was aligned with previous NICE multiple technology appraisal (MTA) on upadacitinib, abrocitinib, and tralokinumab for treating AD.
Evaluation	▪ Lebrikizumab received a positive evaluation from G-BA/IQWiG based on the clinical results from the three pivotal trials, according to the EMA label. ▪ However, no added benefit was determined.	▪ HAS determined the SMR level (medical service) provided by lebrikizumab as "Important" in the population not adequately controlled or non-eligible for cyclosporine. ▪ The ASMR level was V (no added therapeutic benefit) as compared to standard of care (other biological treatments).	▪ Lebrikizumab demonstrated to be cost effective against its class (biologics). ▪ Cost-effectiveness estimates for lebrikizumab compared with current biological medicines (dupilumab or tralokinumab) were within the range that NICE considers a cost-effective use of NHS resources.

METHODS

- In the absence of the EU having an overarching and unified approach to HTA (EU HTA), Almirall prepared specific HTA dossiers by country: G-BA/IQWiG in Germany, HAS in France, and NICE in England.
- This bespoke approach was based on the regulatory clinical package of lebrikizumab, the PICO (Patient, Intervention or exposure, Comparator, Outcome) methodology, and the local HTA requirements.

References

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Abbreviations

AD=atopic dermatitis; ASMR=amélioration du service medical rendu; EASI=Eczema Area and Severity Index; EMA=European Medicines Agency; EU=European Union; G-BA=Gemeinsamer Bundesausschuss; HAS=Haute Autorité de Santé; HTA=health technology assessment; IQWiG=Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; JAK=Janus kinase; MAIC=matching-adjusted indirect comparison; MHRA=Medicines and Healthcare products Regulatory Agency; NHS=National Health Service; NICE=National Institute for Health and Care Excellence; PICO=Patient, Intervention, Comparator, Outcome; SMR=service médical rendu.

Disclosures

LS-F, **BA**, **JMJ**, **MC**, and **MdB** are employees of Almirall.

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