Surrey Heartlands Integrated Care System
Area Prescribing Committee (APC)

Integrated Care Partnership - Surrey Downs, Guildford & Waverley, North-West Surrey, and East Surrey Places & associated partner organisations.

NICE Technology Appraisals (TA) briefing paper for local implementation

NICE TA Guidance name and number	Lebrikizumab for treating moderate to severe atopic dermatitis in people 12 years and over [NICE TA 986] **Note that the service that would provide lebrikizumab for atopic dermatitis in adolescents (12 to 17 years) would be commissioned by NHS England**		
Available at	https://www.nice.org.uk/guidance/ta986		
Date of issue	10 July 2024	**Implementation deadline**	3 months [10 October 2024]

Medicine details[1]	
Name and brand name	Lebrikizumab (Ebglyss)
Manufacturer	Almirall
Mode of action	**Mechanism of action** Lebrikizumab is an immunoglobulin (IgG4) monoclonal antibody that binds with high affinity (<10 pM) to interleukin (IL)-13 and selectively inhibits IL-13 signalling through the IL-4 receptor alpha (IL-4Rα)/ IL-13 receptor alpha 1 (IL-13Rα 1) heterodimer, thereby inhibiting the downstream effects of IL-13. Inhibition of IL-13 signalling is expected to be of benefit in diseases in which IL-13 is a key contributor to the disease pathogenesis. Lebrikizumab does not prevent the binding of IL-13 to the IL-13 receptor alpha 2 (IL-13Rα 2 or decoy receptor), which allows the internalisation of IL-13 into the cell.
Licenced indication	Lebrikizumab (Ebglyss) is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years of age and older with a body weight of at least 40 kg who are candidates for systemic therapy.
Formulation	Solution for injection (pre-filled pens)
Dosage	Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of atopic dermatitis. **Posology** The recommended dose of lebrikizumab is 500 mg (two 250 mg injections) at both week 0 and week 2, followed by 250 mg administered subcutaneously every other week up to week 16.

	Consideration should be given to discontinuing treatment in patients who have shown no clinical response after 16 weeks of treatment. Some patients with initial partial response may further improve with continued treatment every other week up to week 24. Once clinical response is achieved, the recommended maintenance dose of lebrikizumab is 250 mg every fourth week. Lebrikizumab can be used with or without topical corticosteroids (TCS). Topical calcineurin inhibitors (TCI) may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.
Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	The pivotal clinical trials were ADvocate 1, ADvocate 2, ADhere and ADvantage. ADhere and Advantage were more relevant to clinical practice. These two clinical trials are combination trials which included treatment with topical corticosteroids. Please note that the license for lebrikizumab states that 'Lebrikizumab can be used with or without topical corticosteroids (TCS)'. The SmPC states that lebrikizumab is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older with a body weight of at least 40 kg who are candidates for systemic therapy. In the NICE application the company only asked for lebrikizumab to be considered for people who have had at least 1 systemic immunosuppressant treatment. Therefore, this NICE TA does not include everyone who it is licensed for. Surrey Heartlands does not commission continued treatment every other week up to week 24 in patients with initial partial response. *This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the licence following NICE publication will need to be considered by the Area Prescribing Committee and will not be routinely funded by local commissioners, as the incremental cost per QALY would not have been considered.*

NICE TA recommendations[2]

Recommendations

1. Recommendations

1.1. Lebrikizumab is recommended as an option for treating moderate to severe atopic dermatitis that is suitable for systemic treatment in people 12 years and over with a body weight of 40 kg or more, only if:

- the atopic dermatitis has not responded to at least 1 systemic immunosuppressant or these treatments are not suitable, and
- dupilumab or tralokinumab would otherwise be offered, and
- the company provides it according to the commercial arrangement.

1.2. Stop lebrikizumab after 16 weeks if the atopic dermatitis has not responded adequately. An adequate response is:

- at least a 50% reduction in the Eczema Area and Severity Index score (EASI 50) from when treatment started and
- at least a 4-point reduction in the Dermatology Life Quality Index (DLQI) from when treatment started.

1.3. Take into account how skin colour could affect the EASI score and make any clinical adjustments needed.

1.4. Take into account any physical, sensory or learning disabilities, or communication

difficulties that could affect the responses to the DLQI, and make any clinical adjustments needed.

1.5. If people with the condition and their healthcare professionals consider lebrikizumab to be 1 of a range of suitable treatments, after discussing the advantages and disadvantages of all the options, the least expensive should be used. Administration costs, dosage, price per dose and commercial arrangements should all be taken into account.

1.6. These recommendations are not intended to affect treatment with lebrikizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop. For young people, this decision should be made jointly by the healthcare professional, the young person, and their parents or carers.

Why the committee made these recommendations

Standard treatment for moderate to severe atopic dermatitis (eczema) includes topical emollients and corticosteroids (treatments applied to the skin). If these treatments are not effective, systemic immunosuppressant treatments such as ciclosporin and methotrexate can be added. If there is an inadequate response after at least 1 of these systemic treatments, or if these are unsuitable, a Janus kinase (JAK) inhibitor (abrocitinib, baricitinib or upadacitinib) or a biological medicine (dupilumab or tralokinumab) can be used.

For this evaluation, the company asked for lebrikizumab to be considered only for people who have had at least 1 systemic immunosuppressant treatment. This does not include everyone who it is licensed for.

Clinical trial evidence shows that lebrikizumab is more effective than placebo at improving the symptoms of atopic dermatitis. It has not been directly compared in a clinical trial with standard treatments. But indirect comparisons with JAK inhibitors and biological medicines suggest that it is broadly likely to work as well as these.

The cost-effectiveness estimates for lebrikizumab are within the range that NICE normally considers an acceptable use of NHS resources when compared with other biological medicines (dupilumab or tralokinumab), but not when compared with JAK inhibitors. So, lebrikizumab is only recommended when dupilumab or tralokinumab would otherwise be offered.

Decision making framework (DMF)

National guidance and priorities

The ICS has a legal obligation to commission this medicine in line with the NICE TA.

- This NICE TA has been assigned an implementation deadline of 3 months
- The implementation deadline is 10 October 2024

Clinical effectiveness

- Clinical trial evidence shows that lebrikizumab is more effective than placebo at improving the symptoms of atopic dermatitis. It has not been directly compared in a clinical trial with standard treatments. But indirect comparisons with JAK inhibitors and biological medicines suggest that it is broadly likely to work as well as these.

Patient safety

Points to be covered in this section will include:

- The product should be used within its product licence (although the NICE TA covers a more restricted cohort).
- ▼ This is a Black Triangle drug – this medicinal product is subject to reporting of all suspected adverse drug reactions to the MHRA. This will allow timely identification of new safety information.
- MHRA alerts for medicines within the pathway

- JAK inhibitors **https://www.gov.uk/drug-safety-update/janus-kinase-jak-inhibitors-new-measures-to-reduce-risks-of-major-cardiovascular-events-malignancy-venous-thromboembolism-serious-infections-and-increased-mortality .**
- Dupilumab the risk of ocular adverse reactions **https://www.gov.uk/drug-safety-update/dupilumab-dupixentv-risk-of-ocular-adverse-reactions-and-need-for-prompt-management**

- **The NICE committee in their assessment of lebrikizumab stated:**

…….The clinical and patient experts expressed concerns about the side effects of some current systemic treatments. They noted that there is an unmet need for additional biological medicines that are effective and have less side effects than some current systemic treatments. The committee concluded that there is an unmet need for additional effective treatments for atopic dermatitis that have better safety profiles.

Medicines Resource Unit comments:

- **Note that the NICE committee made no reference in the guidance that lebrikizumab had a better safety profile to the other treatments.**

Patient factors

Include practical aspects (not clinical outcomes) e.g.

- **www.medicines.org.uk** Lebrikizumab is produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology and may not be suitable for vegans or vegetarians.
- An additional treatment option would be valued by patients. There are 2 other modes of action already in the available pathway, this does not constitute a novel mode of action or a new line of treatment.
- It is recommended to rotate the injection site with each injection. Lebrikizumab should not be injected into skin that is tender, damaged or has bruises or scars.
- Prior to treatment it is recommended that patients are brought up to date with all age-appropriate immunisations according to current immunisation guidelines.
- This medicine is available under a homecare service (HealthNet Alcura and PolarSpeed) so can be delivered directly to the patient. When the patient is confident in self-administering, this may reduce the number of hospital appointments to those required for review and/or monitoring.
- Patients must adhere to the storage requirements
- Patients would need to be reviewed on a regular basis by the prescribing clinician to ensure concordance, monitor for adverse effects and efficacy.

Environmental impact

- Additional packaging will be generated and will be an environmental impact with regards to waste management.
- Lebrikizumab should be stored in a refrigerator and will likely be delivered to a patient's home in a refrigerated vehicle through homecare delivery. This will add additional carbon – increase air pollution).
- Discharge into wastewater (post metabolism unknown effect).
- Sharps waste requires safe collection and disposal.

Equality & diversity

The NICE committee noted the following potential equality issues:

- The EASI score might underestimate the severity of atopic dermatitis in people with brown or black skin, which could lead to undertreatment in people with brown or black skin.
- Physical, sensory or learning disabilities, or communication difficulties could affect responses to the DLQI.
- Race and disability are protected characterises under the Equality Act 2010. The committee took this into account in its decision making. It concluded that, when using the EASI score, healthcare professionals should take into account skin colour and how this could affect the EASI score, and make any clinical adjustments needed. It also concluded that, when using the DLQI, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's response to the DLQI, and make any clinical adjustments

needed.

Note 1: Drugs approved by NICE for adult conditions will be commissioned in children at specialised paediatric centres if the patient meets the NICE criteria and there is evidence to suggest that the drug is safe and clinically appropriate to use in children as per the NHS England Medicines for Children Policy (see https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/ and a Blueteq form is available.

Place in therapy relative to available treatments

- Refer to revised ICS pathways.
- Janus Kinase Inhibitors (abrocitinib, upadacitinib (15mg) and baricitinib) are the least costly medications within the atopic dermatitis pathway.
- Lebrikizumab will be offered as an alternative IL13 (alongside tralokinumab)

Medicines Resource Unit comments:

- **A precedent has been set in all the high cost immunomodulator pathways. Lebrikizumab is a monoclonal antibody that binds to Interleukin 13 and inhibits IL-13. Tralokinumab is also in the Atopic Dermatitis pathway and has the same mode of action.**
- There will continue to be 3 lines of treatment available within the Atopic Dermatitis pathway.

Stakeholder views

The paper was sent out for consultation and comments and responses are noted on the front sheet.

Cost-effectiveness

www.nice.org.uk
The company has a commercial arrangement. This makes lebrikizumab available to the NHS with a discount. Users can input the confidential price of lebrikizumab and amend other variables in the resource impact template.

The payment mechanism for the technology is determined by the responsible commissioner and depends on the technology being classified as high cost.

We expect the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £8,800 per 100,000 population, based on a population for England of 57.16 million people).

This is because the technology is a further treatment option and the overall cost of treatment will be similar for this patient group. However, across all of the treatment options included in the resource impact template, there may be a larger resource impact because of the expected increase in use of treatments rather than standard care.

Section 1: cost of the technology

The list price for lebrikizumab is £2,271.26 per 2-pack of 250 mg/2 ml solution for injection prefilled pens or syringes (excluding VAT; company submission, accessed April 2024).

License states (www.medicines.org.uk)
Posology
The recommended dose of lebrikizumab is 500 mg (two 250 mg injections) at both week 0 and week 2, followed by 250 mg administered subcutaneously every other week up to week 16.

Consideration should be given to discontinuing treatment in patients who have shown no clinical response after 16 weeks of treatment. Some patients with initial partial response may further improve with continued treatment every other week up to week 24.

Once clinical response is achieved, the recommended maintenance dose of lebrikizumab is

250 mg every fourth week.

Please note:

- **NICE does not recommend treatment every other week beyond 16 weeks if a patient does not meet continuation criteria.**

- **Treatment every other week to week 24 has not been taken into consideration in the NICE resource template.**

Annual cost per patient (or complete course if shorter)

Costs in secondary care 1st year & subsequent year (list price but commercial discount available)

Year 1		
Dose	**Week**	**List price cost:**
500mg	0 & 2	£4,542.52
250mg	4, 6, 8, 10, 12, 14 & 16	£7,949.41
Clinical response achieved: (in line with NICE)		
250mg	Every 4 weeks (9 doses)	£10,220.67
Total year 1 with induction		**£22,712.60**

Year 2 onwards		
250mg	Every 4 week (13 doses)	**£14,763.19**

Price relative to comparable medicines:
3 modes of action currently NICE approved for treatment of atopic dermatitis

- Janus Kinase Inhibitors – Abrocitinib, upadacitinib & baricitinib
- IL4/IL13 – Dupilumab
- IL13 – Tralokinumab & lebrikizumab

For maintenance treatment, the JAK inhibitors are more cost-effective than the IL inhibitors (except for upadacitinib 30mg).

The JAK inhibitors in order of cost-effectiveness are:

1. Abrocitinib
2. Upadacitinib 15mg
3. Baricitinib

- For maintenance treatment, the IL inhibitors in order of cost-effectiveness are:

1. Lebrikizumab
2. Tralokinumab

Please note that the cost of upadacitinib 30mg and dupilumab lies between that of lebrikizumab and tralokinumab at maintenance.

Cost effective order first 16 weeks of treatment (induction)	Cost effective order (including induction 1st year):	Cost effective order (for maintenance treatment from week 16 onward)

Note no induction for oral treatments		
1. Dupilumab. (subcutaneous injection) 10 doses in 1st 16 weeks	1. Abrocitinib (oral) -JAK	1. Abrocitinib (oral) -JAK
2. Tralokinumab (subcutaneous injection) 10 doses in 1st 16 weeks	2. Upadacitinib 15mg (oral) -JAK	2. Upadacitinib 15mg (oral) -JAK
3. Lebrikizumab (subcutaneous injection) 11 doses in 1st 16 weeks	3. Baricitinib (oral) -JAK	3. Baricitinib (oral) -JAK
	4. Dupilumab. (subcutaneous injection) 28 doses in 1st year	4. **Lebrikizumab (subcutaneous injection) -IL13** 13 doses per year (4 weekly dosing)
	5. Upadacitinib 30mg (oral)	5. Dupilumab. (subcutaneous injection) -1L4/1L13 26 doses per year (EOW dosing)
	6. Tralokinumab (subcutaneous injection) 28 doses in 1st year	6. Upadacitinib 30mg (oral) -JAK
EOW – Every Other Week	7. **Lebrikizumab (subcutaneous injection)** 20 doses in 1st year	7. Tralokinumab (subcutaneous injection) -IL13 26 doses per year (EOW dosing)

The Surrey Heartlands Director of Pharmacy and Medicines Optimisation has delegated authority to enable the Committee to be a decision-making committee providing the impact of any single decision does not exceed £100,000 within an individual Place per annum. Decisions with a cost impact of over £100,000 within an individual Place per annum require authorisation from Surrey Heartlands Health & Care Professionals Committee at their next meeting. Exception to this will be for any decision made in relation to a NICE Technology Appraisal (which are subject to requiring mandatory funding by commissioners) and other urgent items. The exceptions will be taken to the next Executive Meeting (which meets weekly) for authorisation.

Traffic light recommendation to APC

NHS Payment Scheme (NHSPS) excluded high-cost drug: see NHS England » 2023-25 NHS Payment Scheme
Yes

Recommended traffic light status and rationale:
RED

- Specialist ONLY drugs - treatment initiated and continued by specialist clinicians.
- Medicine excluded from national tariff
- Commercial arrangement – simple discount patient access scheme for lebrikizumab.

Implementation

NICE TA implementation must be within 3 months of publication.

Actions to implement:

Primary care

- This is a National Tariff excluded high-cost drug and is commissioned by ICSs for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving this medicine and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

Secondary care

- Providers are NHS hospital trusts.
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- The initiation, administration and on-going treatment is managed by secondary care.
- Specialists will be required to notify the high-cost drugs teams of initiation of treatment using the Blueteq® system.
- Dermatology teams will ensure patients response to treatment is regularly assessed and treatment switched to an alternative treatment as follows:

	Definition	Action
Primary Failure	Occurs when the response criteria (as defined within the NICE TA) is not fully met when response to treatment is assessed at the time interval defined within the NICE TA	Move to the NEXT treatment line/mode of action (if one is available)
Secondary Failure	Occurs when the response to treatment (as defined within the NICE TA) is no longer met	Move to the NEXT treatment line/mode of action (if one is available)
Primary intolerance/ adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side-effects of that treatment that occurs during the initial time period defined by the NICE TA	Use another option from the SAME treatment line
Secondary intolerance/ adverse effects	An occurrence that causes discontinuation of treatment, due to inability to tolerate side effects of that treatment that occurs after the initial time period defined by the NICE TA	Move to the NEXT treatment line OR discuss at Dermatology Clinical Network.
Conception	If conception plans or pregnancy indicate a change of drug is advisable, it is agreed that this does not constitute a change in line of treatment	Please update Blueteq accordingly

- Homecare arrangements will be managed by the trust.

ICS

Consider if non-drug related activity is required i.e., further commissioning needs, any saving on drug costs / non-drug activity anticipated.

- This technology is commissioned by integrated care systems.
- Pathway to be discussed by the dermatology clinical network members to discuss:
    - Mode of action
    - Place in therapy within the pathway

PAD and Joint Formulary

- PAD will need to be updated with decision from APC
- Addition of revised pathway to PAD – Consideration for Guideline Atopic Dermatitis profile page
- Removal of current (out of date) pathway from PAD

Proposed tick box forms

Blueteq® forms have been developed.

References:

1 Summary of Product Characteristics. emc. Available at: www.medicines.org.uk Accessed <30.08.2024>

2 NICE Technology Appraisal Guidance: . Available at: https://www.nice.org.uk/guidance/ta986 Accessed <29/08/2024>

4 NICE Resource Impact Template: . Available at: https://www.nice.org.uk/guidance/ta986/resources Accessed <24/07/2024>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Clare Johns	Lead Pharmacy Technician – MRU	20/08/2024	None
Supported by	Tejinder Bahra	Lead Pharmacist MRU	29/08/2024	None
Reviewed by	Dermatology Clinical Network members		30/08/2024	

Explanation of declaration of interest:
None.

Version control sheet:

Version	Date	Author	Status	Comment
1			Draft	Out for consultation
			Final	Out for clinical comment