North East London
Barts Health NHS Trust
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Barking, Havering and Redbridge University Hospitals NHS Trust

High-Cost Drugs Treatment Pathway for Atopic Dermatitis (Adults)

North East London

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Date	**Version**	**Comment/Changes**
November 2023	1.0	New document
January 2025	1.1	Addition of lebrikizumab to atopic dermatitis pathway
Sept 2025	1.2	Addition of nemolizumab to atopic dermatitis pathway

Contents

Definition

Moderate to Severe Atopic Dermatitis (AD) is defined by an Eczema Area and Severity Index (EASI) of 16 or more.

The disease may have a significant impact on physical, psychological or social wellbeing; and is either extensive, or localised but associated with significant functional impairment and/or high levels of distress. A Dermatology Life Quality Index (DLQI) should also be taken to assess quality of life.

Scope

This document outlines the advanced therapies treatment pathway for adult patients in North East London diagnosed with AD using four modes of action.
The present document should be used in conjunction with the National Institute for Health and Care Excellence (NICE) guidance and the published NICE Technology Appraisal (TA) guidance for each individual high cost drug (HCD). The pathway is intended to be adopted by all acute provider Trusts within North East London.

NICE Guidance and Technology Appraisals

Table 1: NICE Technology Appraisals for AD

NICE Technology Appraisal Number	Title
TA534	Overview | Dupilumab for treating moderate to severe atopic dermatitis | Guidance | NICE
TA681	Overview | Baricitinib for treating moderate to severe atopic dermatitis | Guidance | NICE
TA814	Overview | Abrocitinib, tralokinumab or upadacitinib for treating moderate to severe atopic dermatitis | Guidance | NICE
TA986	Overview | Lebrikizumab for treating moderate to severe atopic dermatitis in people 12 years and over | Guidance | NICE
TA1077	Overview | Nemolizumab for treating moderate to severe atopic dermatitis in people 12 years and over | Guidance | NICE

At the time of publication, this treatment pathway considers the above NICE TAs

Principles

This document is based on current NICE TAs available for the management of AD.
The pathway is subject to change as new evidence, NICE TAs and/or local agreements are released or updated that will impact on the information outlined in this document. This includes changes in drug costs that may impact on cost-effectiveness and drug choice in the treatment pathway.

It is expected that drugs presenting best value are selected where clinically appropriate. For further prescribing information including contraindications and cautions, please refer to the relevant drug monograph in the latest version of the BNF (British National Formulary)[1] or the respective drug's Summary of Product Characteristics[2-7].

Key steps prior to initiating HCD treatment for moderate to severe AD

The use of non-targeted systemic immunosuppressants should be maximised prior to commencing targeted therapies.

If only a partial response is observed, ensure the dose of the systemic treatment is appropriately optimized:

- Allow an 8 to 12-week interval following a dose change before assessment of response.
- If no longer tolerating treatment with oral methotrexate, consider a switch to subcutaneous methotrexate where clinically appropriate (e.g. gastrointestinal adverse effects with oral methotrexate, poor medication-adherence or concerns regarding absorption of oral formulation).

Eligibility criteria

Baricitinib is licensed for the treatment of moderate to severe AD in adults only. Abrocitinib, dupilumab, lebrikizumab, nemolizumab, tralokinumab and upadacitinib are licensed for the treatment of moderate to severe AD in adults and young people 12 years and over. Dupilumab is also licensed for the treatment of severe AD in children 6 months to 11 years. The present pathway is for patients aged 18 years of age and over or those seen in an adult's clinic. Paediatric services are commissioned by NHS England.

Dupilumab, baricitinib, abrocitinib, nemolizumab, tralokinumab, and upadacitinib are recommended as options for treating moderate to severe AD if:

- the disease has not responded to at least 1 other systemic therapy, such as, ciclosporin, methotrexate, azathioprine or mycophenolate mofetil OR
- these treatments are contraindicated OR
- these treatments are not tolerated.

Lebrikizumb is recommended as an option for treating moderate to severe AD if:

- the patients body weight is ≥40kg and
- the disease has not responded to at least 1 systemic immunosuppressant or these treatments are not suitable, and
- dupilumab or tralokinumab would otherwise be offered

Assessing response

Treatment response

NICE defines an adequate response (at 16 weeks following treatment) as:

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

Failure to achieve these clinical scores is considered inadequate response.

Validated clinical assessment tools for disease severity

Physicians global assessment (PGA)
Eczema Assessment and Severity Index (EASI)

Dermatology Life Quality Index (DLQI)
Patient Orientated Eczema Measure (POEM)
The investigator's global assessment (IGA)

It should be noted that NICE only use EASI and DLQI in each TA for eligibility and continuation criteria.

Lines of therapy

NICE do not state a definitive maximum number of lines of therapy in their guidance. Therefore, taking into consideration the presence of multiple drugs recommended by NICE, the number of lines of therapy has been based on the number of different mechanisms of action of the recommended drugs (Table 2).

The ICB has recognised and adopted the recommendation set out by the Regional Medicines Optimisation Committee (RMOC)[9] which recommends switching to a high-cost drug with a new mechanism of action.
The present pathway has categorised the recommended targeted therapies drugs for the treatment of AD into four separate groups based on their pharmacological properties or mode of actions (Table 2). Therefore, the targeted treatment of AD has been limited to a maximum of four lines of therapy.

Patients should exit the current pathway when the maximum lines of therapy have been exceeded and return to standard care.

If the responsible clinician deems the patient could still benefit from further HCD treatment, funding will need to be requested via an Individual Funding Request (IFR) to the patient's ICB.
Taken from the NEL IFR policy "*In order to support an IFR on the basis of failure to respond to standard care, the IFR Panel would normally need to be satisfied that the patient's inability to respond to, or be provided with, the usual treatment was a genuinely exceptional circumstance, which lies outside the natural history of the condition and is not characteristic of the relevant group of patients with the condition*".

The NICE committee considered that cost-effectiveness analyses for sequences should ideally be considered in decision making. But it acknowledged that there is no clinical data on sequential effectiveness and the clinical rationale for using various sequences of treatments would be personalised to each person. Therefore, the committee concluded that analysis of treatment sequences would be uncertain.
It is expected that this pathway will impart a cost pressure which is why a maximum of four lines of therapy has been chosen. However, in the context of initiatives to utilise best value-value medicines, there is opportunity to formalise cost-effective prescribing through the pathway.

Table 2: Pharmacological properties of the targeted therapies for AD in adults

Modes of inhibition/Action			
IL-4 receptor inhibitor	**IL-13 receptor inhibitor**	**IL-31 inhibitor**	**JAK inhibitor**
Dupilumab [2]	Tralokinumab [3]	Nemolizumab [5]	Baricitinib [6]
	Lebrikizumab [4]		Upadacitinib [7]
			Abrocitinib [8]

Definition of treatment failure

Primary Failure
The patient's atopic dermatitis does not demonstrate a response to therapy as outlined in the NICE TA.

Secondary Failure
The patient's atopic dermatitis initially achieves a response to therapy which is subsequently not sustained, resulting in failure to maintain a response as outlined in the NICE TA.

Adverse Reaction
If the patient has an adverse event before the initial response assessment period it will not count as a line of therapy. If the adverse reaction occurs after the initial response assessment period, the patient must have shown a response to therapy with that biologic for it not to count as a line of therapy.

JAK inhibitors: Safety concerns

The Medicines Healthcare and Regulatory Agency (MHRA) released the following safety alert with regards to the use of Janus kinase (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

Following the review by the European Medicines Agency (EMA) in 2022, the MHRA concluded that there was an increased incidence of malignancy, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE) and mortality across all JAK inhibitors used for chronic inflammatory disorders. The MHRA provides information to clinicians on patient risk factors for when these medicines should be avoided unless there is no suitable alterative.

Dosing options

JAK inhibitors

Abrocitinib, Baricitinib and Upadacitinib all have 2 daily dose options (low or high treatment doses). The choice of dose the patient would receive would depend on individual patient presentation. JAK inhibitors should be used with caution in those with risk factors for VTE, MACE and malignancy, and where possible the lower dose where possible should be used.

Table 3: JAK inhibitors and their recommended dosing schedule for adults according to their licence

Drug	Recommended dosing schedule as per licence
Abrocitinib	The recommended Abrocitinib maintenance dose is **100mg** or **200mg** orally once daily based on individual presentation, see the SPC for specific dosing information. The **lowest effective dose** should be used whenever possible, whilst considering the patient's risk factors.
Baricitinib	The recommended Baricitinib maintenance dose is **4mg** orally once daily**.** A dose of **2mg** once daily may be considered for certain patient groups, see the SPC for further information.

Upadacitinib	The recommended Upadacitinib maintenance dose is **15mg** or **30mg** orally once daily based on individual presentation, see the SPC for specific dosing information. The **lowest effective dose** should be used whenever possible, whilst considering the patient's risk factors.

Lebrikizumab
The recommended initiation dose of Lebrikizumab is 500mg (two 250mg injections) at both week 0 and week 2, followed by 250mg 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.

Nemolizumab
An initial dose of 60mg (2x30mg injections), followed by 30mg at week 4, 8, 12, and 16. Response should be assessed after 16 weeks and patients achieving a clinical response should be given a maintenance dose of 30mg every 8 weeks.

Tralokinumab
The recommended Tralokinumab maintenance dose is 300mg subcutaneous injection every other week.
There is an alternative dosing schedule for tralokinumab. After 16 weeks of treatment, for patients who achieved clear or almost clear skin, every fourth week dosing may be considered. This may be useful for patients who have achieved clear skin but are not tolerating every other week dosing.

NICE TA814 recommends both treatment schedules but recognises the less frequent dosing may not be used as often in clinical practice.

Treatment choices in special populations

Treatment choice in pregnancy and breastfeeding
Advise women of childbearing potential, who are starting targeted therapy for AD, to use effective contraception and to discuss conception plans with the consultant supervising their care. There are no known interactions between targeted therapies and contraceptive methods.
Breast-feeding: There is a limited amount of data from the use of targeted therapies in pregnant and breastfeeding women. Overall, it is unknown whether targeted therapies are excreted in human milk or absorbed systemically after ingestion. Consult the Summary of Product Characteristics for further information.

Surgery
If a patient is due to have an elective surgery, they should be advised to contact their dermatology team for advice on when or if to stop therapy prior to surgery. Targeted therapy can be resumed after the operation if there is no evidence of infection and wound healing is satisfactory.

Use of vaccinations

- Vaccination requirements should be reviewed and brought up to date prior to initiation of targeted therapies with reference to Department of Health Guidance
- In general, targeted therapies can be started **4 weeks** after administration of a live or live attenuated vaccine.
- Dupilumab treatment should be stopped for at least **12 months** before giving live vaccines, unless otherwise directed by a specialist (expert opinion suggests that 12 months may not be necessary for all targeted therapies). Refer to the SPC and the Department of Health Green Book (Immunisation against infectious disease, Chapter 6) for further information [10]
- Inactivated vaccines are safe to be administered concurrently with targeted therapies. However, where possible, inactivated vaccines should be administered **2 weeks** before starting therapy to ensure optimal immune responses.
- Patients should be advised to receive the Pneumococcal Polysaccharide Vaccine (PPV), annual 'inactivated' influenza vaccine and COVID-19 vaccine while on targeted therapy. The GP should be asked to ensure the patient is flagged as being on immunosuppression and requiring vaccination according to Department of Health Guidance.
- Refer to BAD immunisation document for further information.

Targeted therapies and associated risk of infection recommendations

- The risks and benefits of treatment with targeted therapies should be carefully considered prior to initiating therapy in patients with active, chronic or recurrent infections.
- Patients with pre-existing infections should be treated before initiating treatment with targeted therapies.
- Patients on targeted therapies should be monitored for signs and symptoms of infection throughout treatment.
- If an infection develops, the patient should be monitored carefully, and therapy should be discontinued if the patient is not responding to standard therapy. Treatment should not be resumed until the infection resolves.

Dupilumab and associated ocular events

Conjunctivitis, allergic conjunctivitis, eye pruritus, blepharitis, dry eye and keratitis related events have been reported with dupilumab, predominantly in AD patients. Some patients reported visual disturbances (e.g. blurred vision) associated with conjunctivitis or keratitis.

Patients treated with dupilumab who develop conjunctivitis or dry eye that does not resolve following standard treatment or signs and symptoms suggestive of keratitis should undergo ophthalmological examination, as appropriate.

Funding

Trusts are required to obtain ICB funding for the use of HCDs in the management of AD via Blueteq prior to starting therapy and for continuation of therapy as described on the Blueteq forms.

With a view to support data-driven care, commissioners will be extracting outcome data from Blueteq. Blueteq must therefore be used for the management of **all funding requests**. This includes recording treatment switches and cessation because of clinical review and/or remission and drug switching for patients who are confirmed or planning for pregnancy.
Where Blueteq is not currently in use by the Trust, an alternative mechanism for requesting funding and monitoring (e.g clinical audit) will be agreed with commissioners.

Patients transferred from out of area or from overseas

For patients who have already commenced on their treatment for atopic dermatitis:

- If the current treatment is covered by a NICE TA, then the patient can continue their treatment as per the TA.
- If the treatment is not covered by a NICE TA, or this pathway, then an application to IFR must be submitted to continue the funding for therapy.

It is the responsibility of the specialist Dermatologist to ensure the patient's GP is informed that the patient is receiving treatment with a HCD targeted therapy. It will then be the responsibility of the GP to update a person's medical record with this HCD targeted therapy.

Clinical Trials

The ICB will not automatically fund a patient's drug treatment commenced as part of a non-commercial or commercially sponsored clinical trial, nor upon the ending of an expanded access/compassionate use scheme, nor upon withdrawal of compassionate funding by a commercial company. The patient must meet NICE criteria for a drug to be continued and for funding by the ICB. Outside of these arrangements, the Provider must seek prior approval by the ICB before starting treatment.

References

1. BNF (British National Formulary) | NICE
2. Dupilumab (Dupixent) 300 mg solution for injection in pre-filled pen - Summary of Product Characteristics (SmPC) - (emc)
3. Tralokinumab (Adtralza) 150 mg solution for injection in pre-filled syringe - Summary of Product Characteristics (SmPC) - (emc)
4. Lebrikizumab (Ebglyss) 250 mg solution for injection in pre-filled pen - Summary of Product Characteristics (SmPC) - (emc)
5. Nemluvio 30 mg powder and solvent for solution for injection in pre-filled pen - Summary of Product Characteristics (SmPC) - (emc) | 100635
6. Baricitinib Lilly 4 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc)
7. Upadacitinib (RINVOQ) 15 mg prolonged-release tablets - Summary of Product Characteristics (SmPC) - (emc)
8. Abrocitinib (Cibinqo) 100 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc)
9. Regional Medicines Optimisation Committee (RMOC) Advisory Statement: Sequential Use of Biologic Medicines. Available from: https://nras.org.uk/wp-content/uploads/sites/2/2021/04/Sequential-use-of-biologic-medicines-RMOC-v-2.0-1.pdf
10. Department of Health Immunisation against Infectious disease – The Green Book https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the- green-book#the-green-book
11. British Association of Dermatologists guidelines for the safe and effective prescribing of methotrexate for skin disease 2016. https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.14816
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13. British Association of Dermatologists' guidelines for the safe and effective prescribing of azathioprine 2011. https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1365-2133.2011.10575.x
14. British Association of Dermatologists Patient Information Leaflet: Mycophenolate mofetil Updated May 2020. www.bad.org.uk/shared/get-file.ashx?id=108&itemtype=document

References checked: 30/07/2025

Atopic Dermatitis Pathway

Atopic Dermatitis unresponsive/contraindicated/intolerant to at least 1 systemic immunosuppressant (methotrexate, ciclosporin, azathioprine or mycophenolate mofetil)

Factors to consider when choosing appropriate drug:

- Different efficacy and safety profiles of each drug
- Co-morbidities and potential impact of each drug option (benefit or harm), including drug specific contra-indications
- The persons view`s and stated preference on administration route or frequency – discuss with patient
- Other relevant factors e.g., conception plans, adherence (increased or decreased frequency should be discussed), travel

After consideration of all factors choose the most clinically suitable, best value drug

†Please see Dosing information section for further information *if dupilumab or tralokinumab not suitable

If treatment fails, consider an alternative drug with a different mode of action.

***Adequate response:**
At least a 50% reduction in the EASI score AND At least a 4-point reduction in the DLQI score from baseline.

Moderate to severe atopic dermatitis defined by an EASI of ≥16 AND DLQI of ≥6

1st line: Abrocitinib†, Baricitinib†, Dupilumab, Lebrikizumab†*, Nemolizumab , Tralokinumab†, Upadacitinib†

Patient has demonstrated a response* in the first 16 weeks of treatment?

No

Yes

Has the patient suffered an ADR?

Yes

No

Continue treatment, monitor and review

Yes

Patient continues to have an adequate response to treatment as defined by NICE*

No

2nd line: Abrocitinib, Baricitinib, Dupilumab, Lebrikizumab, Nemolizumab, Tralokinumab, Upadacitinib

Patient has demonstrated a response* in the first 16 weeks of treatment?

No

Yes

Has the patient suffered an ADR?

Yes

No

Continue treatment, monitor and review

Yes

Patient continues to have an adequate response to treatment as defined by NICE*

No

3rd line: Abrocitinib, Baricitinib, Dupilumab, Lebrikizumab, Nemolizumab, Tralokinumab, Upadacitinib

Patient has demonstrated a response* in the first 16 weeks of treatment?

No

Yes

Has the patient suffered an ADR?

Yes

No

Continue treatment, monitor and review

Yes

Patient continues to have an adequate response to treatment as defined by NICE*

No

4th line: Abrocitinib, Baricitinib, Dupilumab, Lebrikizumab, Nemolizumab, Tralokinumab, Upadacitinib

Patient has demonstrated a response* in the first 16 weeks of treatment?

No

Yes

Has the patient suffered an ADR?

Yes

No

Continue treatment, monitor and review

Yes

Patient continues to have an adequate response to treatment as defined by NICE*

No

**If an adequate response* is not achieved after 4 lines of therapy:
Return to standard therapy or, if appropriate, apply for funding via IFR**

Appendix 1. Drug factors to consider (including modes of action)

The table below provides an approximate drug cost for each targeted therapy based upon first year of therapy, with the loading dose schedule taken into consideration. The cost will vary depending upon commercial arrangements and access to short-term free of charge supplies, which has not been taken into consideration for this guidance.

Mode of Action	Drug Name	Indication	TA (other indications)	Reviewed within	Drug cost*
JAK inhibitor	Upadacitinib 15mg (oral)	The disease has not responded to at least 1 systemic immunosuppressant, or these are not suitable	TA829 – Ankylosing Spondylitis TA665 – Severe Rheumatoid arthritis TA744 – Moderate Rheumatoid arthritis TA768 – Psoriatic arthritis TA856 – Ulcerative colitis TA905 – Crohn's disease TA861 – Non-radiographic axial Spondyloarthritis	16 weeks	££
	Upadacitinib 30mg (oral)				£££
	Baricitinib (oral)	The disease has not responded to at least one systemic immunosuppressant, such as ciclosporin, methotrexate, azathioprine, and mycophenolate mofetil, or these are not suitable.	TA466 – Moderate to Severe Rheumatoid Arthritis	16 weeks	££
	Abrocitinib 100mg (oral)	The disease has not responded to at least 1 systemic immunosuppressant, or these are not suitable		16 weeks	£
	Abrocitinib 200mg (oral)				
IL-13 receptor inhibitor	Lebrikizumab (subcutaneous injection)	• The disease has not responded to at least 1 systemic immunosuppressant, or these are not suitable • Dupilumab or tralokinumab would otherwise be offered		16 weeks	£££
	Tralokinumab (subcutaneous injection)	The disease has not responded to at least 1 systemic immunosuppressant, or these are not suitable		16 weeks	£ 4-week dosing

Mode of Action	Drug Name	Indication	TA (other indications)	Reviewed within	Drug cost*
					£££ 2-week dosing
IL-4 receptor inhibitor	Dupilumab (subcutaneous injection)	The disease has not responded to at least one 1 other systemic therapy, such as ciclosporin, methotrexate, azathioprine, and mycophenolate mofetil, or these are contraindicated or not tolerated	TA751 – Severe asthma with type 2 inflammation	16 weeks	**£££**
IL-31 receptor inhibitor	Nemolizumab (subcutaneous injection)	• The disease has not responded to at least 1 systemic immunosuppressant, or these are not suitable • A biological medicine would otherwise be offered		16 weeks	**£££**

**Prices are correct as of August 2025 and may be subject to change.*