Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

NICE Technology Appraisals: Local implementation

NICE TA Guidance	Abrocitinib, tralokinumab or upadacitinib for treating moderate to severe atopic dermatitis (TA814)		
Available at	https://www.nice.org.uk/guidance/ta814		
Date of issue	03 August 2022	**Implementation deadline**	30 days (for abrocitinib), 90 days for the others

Medicine details	
Name, brand name	1. Abrocitinib (Cibinqo), Pfizer 2. Tralokinumab (Adtralza), Leo 3. Upadacitinib (Rinvoq), AbbVie
Manufacturer	As above
Licensed indication	1 Abrocitinib (Cibinqo) is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy. 2 Tralokinumab (Adtralza) is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients who are candidates for systemic therapy. 3 Upadacitinib (Rinvoq) is indicated for the treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.
Formulation	1 Each **film-coated tablet** contains either 50mg, 100mg or 200mg abrocitinib. 2 Each **pre-filled syringe** contains 150 mg of tralokinumab in 1 mL solution (150 mg/mL). This product is of biological origin (mouse myeloma cells). 3 Each **prolonged-release tablet** contains upadacitinib hemihydrate, equivalent to 15mg, 30 mg or 45mg of upadacitinib.
Usual dosage	1. The dosage schedule for abrocitinib is available in the summary of product characteristics for abrocitinib. 2.The dosage schedule for tralokinumab is available in the summary of product characteristics for tralokinumab. 3. The dosage schedule for upadacitinib is available in the summary of product characteristics for upadacitinib.
NICE, recommended dosage/schedule	As above

Disease and potential patient group	
Brief description of disease	Atopic eczema (atopic dermatitis) is the most common form of eczema, a condition that causes the skin to become itchy, dry and

	cracked. Atopic eczema is more common in children, often developing before their first birthday. But it may also develop for the first time in adults. It's usually a long-term (chronic) condition, although it can improve significantly, or even clear completely, in some children as they get older.
Potential patient numbers per 100,000	Information below taken from the NICE resource template. See Appendix 1 below Note that ICBs are not the commissioners for atopic dermatitis in children under the age of 18. The responsible commissioner for this cohort of patients is NHS England.

SUMMARY

NICE recommendation

1.1 NICE has recommended abrocitinib and upadacitinib as options for treating moderate to severe atopic dermatitis that is suitable for systemic treatment in adults and young people 12 years and over, only if:
• the disease has not responded to at least 1 systemic immunosuppressant, or these are not suitable.
• the companies provide abrocitinib and upadacitinib according to the commercial arrangement.

1.2 Tralokinumab is recommended as an option, for treating moderate to severe atopic dermatitis that is suitable for systemic treatment in adults, only if:
• the disease has not responded to at least 1 systemic immunosuppressant, or these are not suitable.
• the company provides tralokinumab according to the commercial arrangement.

1.3 Stop abrocitinib, upadacitinib or tralokinumab at 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.

1.4 Take into account how skin colour could affect the EASI score and make any appropriate adjustments.

1.5 Take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI and make any appropriate adjustments.

Why the committee made these recommendations

Standard treatment for moderate to severe atopic dermatitis (eczema) includes topical treatments such as emollients and corticosteroids. If these treatments are not effective, systemic immunosuppressants such as methotrexate and ciclosporin can be added. Dupilumab and baricitinib are used if systemic immunosuppressants are not effective.

The clinical trial evidence shows that abrocitinib, tralokinumab and upadacitinib all reduce symptoms of atopic dermatitis compared with placebo. Abrocitinib and upadacitinib were indirectly compared with ciclosporin, but the results are highly uncertain.

Abrocitinib, upadacitinib and tralokinumab were each directly or indirectly compared with

dupilumab and baricitinib for use after systemic immunosuppressants, but the results are uncertain.

Despite the uncertainty the most likely cost-effectiveness estimates are within the range that NICE normally considers an acceptable use of NHS resources. Therefore, abrocitinib, upadacitinib or tralokinumab are recommended as options for moderate to severe atopic dermatitis that has not responded to at least 1 systemic immunosuppressant.

Cost implications*

Cost of product:
The list price of abrocitinib is £893.76 for a 28-pack of 100 mg or 200 mg tablets (excluding VAT, BNF online, accessed March 2022). The company has a commercial arrangement. This makes abrocitinib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

The list price of tralokinumab is £1,070 for a 4-pack of 150 mg per 1 ml pre-filled syringes (excluding VAT, BNF online, accessed March 2022). The company has a commercial arrangement. This makes tralokinumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

The list price of upadacitinib is £805.56 for a 28-pack of 15 mg modified-release tablets or £1,611.12 for a 28-pack of 30 mg modified-release tablets (excluding VAT, BNF online, accessed March 2022). The company has a commercial arrangement. This makes upadacitinib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Annual cost per patient from information above (outside of commercial arrangement)

Abrocitinib (oral treatment)
£11,618.88 per year

Upadacitinib (oral treatment)
15mg - £10,472.28/ year
30mg – £20,944.56/ year
• A dose of 30 mg once daily may be appropriate for patients with high disease burden or for patients with an inadequate response to 15 mg once daily.

Tralokinumab
150mg per 1ml prefilled syringe - £14,980 first year cost

Subsequent years - £13,910

Induction 600mg (4 injections) followed by 2 injections (300mg) required for further doses, every other week

Has dose escalation been considered as part of the NICE costing template?
Note 30mg dose of upadacitinib is available for those patients with high disease burden or inadequate response to 15mg (separate discussion regarding implementation of dose escalation for this patient cohort – for discussion at the Dermatology Clinical Network)

Costing information/100,000 population and per CCG:
To be confirmed prior to APC discussion

Availability of PAS and details (if appropriate): No PAS available. There are simple discount patient access schemes for abrocitinib, tralokinumab and upadacitinib. NHS organisations can get details on the Commercial Access and Pricing (CAP) Portal.

Availability of homecare service (if appropriate): Yes, if provider arranges for contract

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status.*

Alternative treatments and cost per patient (per year / per month as appropriate)

Other NICE recommended products:
There are currently only NICE Clinical Guidelines for Atopic dermatitis in patients under 12 years old (does not apply to the cohort of patients applicable to this TA).

Currently there are NICE Technology Appraisals for the following drugs:

- Tacrolimus/pimecrolimus – topical immunosuppressant agents
- Baricitinib – an oral JAK inhibitor
- Dupilumab – a IL4/IL13 inhibitor, delivered by subcutaneous injection

Options not reviewed by NICE but used in standard practice:
Emollients – see Surrey PAD's dry skin guidelines
Topical corticosteroids such as betamethasone or mometasone
Non-biologic systemic therapies such as ciclosporin, methotrexate, azathioprine or mycophenolate.

Impact to patients

- Another treatment option will be welcomed by patients.
- Abrocitinib and upadacitinib are both oral agents, these may be preferred over the injectable products for those who cannot tolerate injections or have an ethical or religious objection to using biologic drugs.
- Abrocitinib and upadacitinib have identical mode of actions as baricitinib (already available to patients) but tralokinumab has a slightly different mode of action to those drugs available to patient with atopic dermatitis and patients would appreciate be able to access treatment with this drug.
- All 3 drugs should be made available under a homecare service so will be delivered directly to the patient.

Impact to primary care prescribers

- The technologies for adults are commissioned by integrated care systems and clinical commissioning groups, the technologies for adolescents are commissioned by NHS England. Providers are NHS hospitals trusts.
- Primary care prescribers should be aware that their patient is receiving one of these drugs 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.

Impact to secondary care

- The initiation, administration and on-going treatment is managed by secondary care.
- Homecare arrangements will be managed by the trust.
- Patients eligible for these treatments will already be known to the atopic dermatitis clinics, so there will be very low impact to clinic capacity from current levels.

Impact to Integrated Care Board

- The technology is commissioned by integrated care systems and clinical commissioning groups and they are required to comply with the recommendations of this NICE TA within 30 days of its date of publication (for abrocitinib) and 90 days for tralokinumab and upadacitinib.
- Providers are NHS hospital trusts.

Implementation

- NICE TA implementation must be within 30 days of publication (for abrocitinib) and 90

days for the other drugs.

- Blueteq forms to be developed
- Trusts to follow internal governance procedures to add these drugs to their formulary, so that prescribers can initiate use as per NICE TA.
- Trusts to ensure that these drugs are available to prescribe to patients via the homecare route as appropriate.
- Atopic Dermatitis high-cost drugs pathway to be discussed at Dermatology Network (attached pathway as example).
- Dose escalation of upadacitinib is to be discusses at Dermatology Network for further action.

Recommendation to APC

PbRe: Yes

Colour classification guidelines

Recommended traffic light status (see attached guidelines):

RED (due to its PBR status)

Additional comments:
None

Area Prescribing Committee - Decision-making criteria

1	National guidance and priorities	• NICE published this Technology Appraisal (TA813) on 3rd August 2022 with a 30-day implementation deadline (as opposed to the usual 90 days) for abrocitinib. The other 2 drugs are to be implemented within 90 days of publication. • Surrey Heartlands ICB is mandated to fund this treatment.
2	Clinical effectiveness	• Abrocitinib, tralokinumab and upadacitinib are to be used as per its licensed indication only, and as per the NICE guidance recommendations. NICE concluded that these drugs are at least as clinically effective as other drugs available. • Safety and efficacy in people under the age of 12 years has not been established for abrocitinib and upadacitinib. • Use of tralokinumab (within license) is restricted to adults only.
3	Patient safety	• Abrocitinib and upadacitinib are licensed for this indication in the UK. They are to be taken by mouth only. • Tralokinumab is licensed for this indication in the UK, it is an injectable drug; packaged and marketed with the intention that patients would self-inject. Risk of sharps injury would be mitigated by suitable patient training and waste management. • As with all systemic immunosuppressants, prescribers should be aware of patient risk of reduced immune response to infection, and this should be considered when triaging patient exhibiting symptoms. GP practice records should be maintained accordingly (this should be reiterated in the PAD narrative). • JAK inhibitors, such as abrocitinib and upadacitinib, are associated with raised incidence of VTE and PE episodes (tofacitinib, not offered in psoriatic arthritis, but a JAK inhibitor, is subject to MHRA alert October 2021), and also of raising blood-lipid levels. Prescribing clinicians are already aware of and monitor/counsel patients accordingly.
4	Patient factors	• Abrocitinib and upadacitinib constitute alternative options for those patients who have yet to try a JAK inhibitor • Tralokinumab (as a new class of drug) adds a further

		therapeutic line to the current treatment pathway. Patients will now have 3 lines of treatment available within the high-cost atopic dermatitis pathway. • Patient education materials, injection technique training and additional support is provided. • Alternative options / products are available to those patients who will not/cannot use injectable products.
5	Environmental impact	• Tralokinumab is only available as an injection. It is likely that the product would be delivered to the patient's home via a dedicated homecare service using a refrigerated van - this could be considered as an **additional carbon load** due to extra road traffic **(increased air pollution).** • **Medical sharps waste** would be collected and disposed of by the homecare company for incineration **(increased air pollution)** • **Packaging waste** from all 3 drugs would be additional to usual municipal waste recycling or landfill. • Discharge into the **wastewater** system (post-metabolism) from an individual patient is unlikely to have a significant impact short term, however the long-term impact to the water ecosystem is unknown.
6	Equality & diversity	• **Disabilities** – patients with physical or learning impairment may not be able to access tralokinumab treatment if they cannot to easily/safely use the pre-filled syringe that the drug is packaged in. Alternative drug / administration options are available for those patients who are not able to self-inject. • **Religion & beliefs** - Tralokinumab is produced using mouse myeloma cells, and therefore is considered a "biological" medicine. This NICE TA could be considered to have a negative impact upon patients who follow a vegan lifestyle or other due to religious or ethical beliefs. Alternative products of a non-biological nature are available for atopic dermatitis. • **Age** – Tralokinumab is only licensed for adult patients – younger patients will not be able to access this treatment under this TA. • **Age** - Abrocitinib and upadacitinib are available/licensed for patients under the age of 18 years (although these patients are commissioned by NHS England).
7	Place in therapy relative to available treatments	• Abrocitinib and upadacitinib do not constitute a new class of treatment, or an additional line of treatment to those already available on the current treatment pathway. These will be an alternative option for patient/clinician choice. • Tralokinumab however, as a new class of treatment, does constitute an additional line of treatment. The current treatment pathway will be amended accordingly.
8	Stakeholder views	• Specialist clinicians who sit in the Surrey Dermatology Network and the wider APC audience have been consulted on this paper. Comments received are incorporated elsewhere.
9	Cost-effectiveness	• NICE considered that the Incremental Cost-effectiveness Ratios (ICERs) for each treatment suggested that abrocitinib, upadacitinib and tralokinumab are likely to be an effective use of NHS resources compared with current treatments.
10	Additional funding required	• Not applicable, budget uplift anticipated as per NICE cost calculations from DOHSC. • Anticipated cost is less than £100k/Place/annum financial threshold for APC decisions.

11	Identified implementation issues	• None identified, prescribing, administration and supply will be the same as for other drugs already used in the treatment pathway. Drugs should be identified as RED (hospital use only), and extra workload will be minimal as patients will already be known to the clinics involved. GPs should continue to ensure patient practice records are kept up to date.

References:

1 Abrocitinib, tralokinumab or upadacitinib for treating moderate to severe atopic dermatitis TA814. Available at https://www.nice.org.uk/guidance/ta814 Accessed 03 August 2022

2 eMC Cibingo 200 mg film-coated tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed 03 August 2022

3 eMC Adtralza 150 mg solution for injection in pre-filled syringe - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed 03 August 2022

4 eMC RINVOQ 30 mg prolonged-release tablets (Great Britain) - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) Accessed 03 August 2022

5 Atopic eczema - NHS (www.nhs.uk) Accessed 03 August 2022

6 NICE Resource impact statement and template. Available at Tools and resources | Abrocitinib, tralokinumab or upadacitinib for treating moderate to severe atopic dermatitis | Guidance | NICE Accessed 03 August 2022

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Declaration of Interest:

None

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Declaration of Interest:

None

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APPENDIX 1

NICE resource template – assumptions made per 100,000 population

	Local assumption current practice (local input)	Local assumption current practice (local input)	Local assumption future practice (year 5) (local input)	Local assumption future practice (year 5) (local input)
Eligible population	% of people	Number of people	% of people	Number of people
Population 18 years or older		78,635		78,635
Population 18 years or older forecast at 2026/27		81,830		81,830
Population aged 12-17 years		6,931		6,931
Population aged 12-17 years forecast at 2026/27		7,212		7,212
Prevalence of atopic dermatitis in adults and receiving treatment	4.30%	3,519	4.30%	3,519
People with moderate to severe atopic dermatitis	7.00%	246	7.00%	246
People with moderate-to-severe AD eligible for systemic therapy	60.00%	148	60.00%	148
People with moderate-to-severe AD with a history of systemic therapy treatment failure	53.00%	78	53.00%	78
Prevalence of atopic dermatitis in young people aged 12-17 years and receiving treatment	6.40%	462	6.40%	462
People with moderate to severe atopic dermatitis	7.00%	32	7.00%	32
People with moderate-to-severe AD eligible for systemic therapy	60.00%	19	60.00%	19
People with moderate-to-severe AD with a history of systemic therapy treatment failure	53.00%	10	53.00%	10
Total eligible population		**89**		**89**

Treatments for adults and young people aged 12-17 years old with moderate-to-severe atopic dermatitis	% of people	Number of people	% of people	Number of people
Number of people receiving standard care	40.00%	35	25.00%	22
Cumulative number of people starting treatment with dupilumab	52.50%	47	40.00%	35
Cumulative number of people starting treatment with baricitinib	7.50%	7	7.50%	7
Cumulative number of people starting treatment with abrocitinib	0.00%	0	10.00%	9
Cumulative number of people starting treatment with upadacitinib	0.00%	0	10.00%	9
Cumulative number of people starting treatment with tralokinumab	0.00%	0	7.50%	7
Total	**100.00%**	**89**	**100.00%**	**89**

Appendix 2 – Blueteq forms

Example of Abrocitinib (1st line form) – these questions are duplicated across all drugs in the proposed pathway

Please indicate whether patient meets the following NICE criteria:

1. I can confirm that this patient is aged 18 years or over

2. Abrocitinib will be used in conjunction with TOPICAL corticosteroids

3. Please provide both the baseline disease activity scores below * baseline scores based on clinical trials and license.

Eczema Area and Severity Index (EASI) score (more than or equal to 16)
Score: Date score taken:

Dermatology Life Quality Index (DLQI) score (more than or equal to 10)
Score: Date score taken:

4. The disease has not responded to the following treatments (unless these are not tolerated or are clinically contraindicated). It is expected that all the treatments below will have been trialled (& optimised) prior to initiation.

Treatment	Start date	Stop date	Details
Topical Corticosteroids (Monotherapy)			
Topical Tacrolimus Or Pimecrolimus (in line with NICE TA82)			
Systemic immunosuppression (at least of the following (ciclosporin, methotrexate, azathioprine OR mycophenolate mofetil)) Please indicate which in the details section.			

Example of Abrocitinib 2nd line form – these questions are duplicated across all drugs in the proposed pathway

Please indicate whether patient meets the following Local policy:	**Please tick**
1. The patient has been previously treated with a high cost cytokine modulator (either a biologic or JAK inhibitor), please enter below: Drug name :	○ Yes ○ No
2. Please check which applies to this patient: ☐ Patient has experienced adverse effects or intolerance to (above drug) ☐ Patient has failed to respond to the initial treatment or has lost response over time Please provide details here::	
3. Please provide patients current (within 3 months) EASI & DLQI scores Eczema Area and Severity Index (EASI) EASI score: Date: **AND** Dermatology Life Quality Index (DLQI) DLQI score: Date:	

Example of Abrocitinib 2nd line form - these questions are duplicated across all drugs in the proposed pathway

Please indicate whether patient meets the following Local policy:	**Please tick**
1. The patient has been previously treated with TWO approved agents and the requested drug has a different mode of action to the previous treatments used **Please provide details of approved treatments received to date?** 1st treatment: 2nd treatment:	○ Yes ○ No
2. Please check which applies to this patient: ☐ Patient has experienced adverse effects to the previous biologic treatment before response can be assessed Please provide details here::: ☐ PRIMARY FAILURE - Patient did not respond to previous treatment in line with NICE criteria at 16 weeks ☐ SECONDARY FAILURE - Patient had an initial response to approved treatment but has now lost response ☐ ADVERSE EFFECTS - Patient has a continuing good response to treatment but is experiencing delayed adverse effects (can occur at any time) Please provide details here:::	
3. Please provide patients current (within 3 months) EASI & DLQI scores Total Eczema Area and Severity Index score (EASI) EASI score: Date: **AND** Dermatology Life Quality Index (DLQI) DLQI score: Date:	