NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Abrocitinib, tralokinumab and upadacitinib for treating moderate to severe atopic dermatitis

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of abrocitinib, tralokinumab and upadacitinib within their marketing authorisation for treating moderate to severe atopic dermatitis.

Background

Atopic dermatitis (also known as atopic eczema) is a long-term condition that affects the skin. It is characterised by a red blotchy rash, dry, itchy and inflamed skin. The skin can also ooze and weep. Constant scratching can cause the skin to split and bleed, which can cause skin infections. Severe dermatitis can be physically disabling or incapacitating and can cause anxiety or depression.

Estimates of the prevalence of atopic dermatitis vary. It is more common in childhood (affecting 1 in 5 children in the UK) and affects 1 in 12 adults in the UK.[1] Of the people who need treatment for atopic dermatitis, 7% will have moderate to severe disease and around a third of these people (27%) will need a systemic treatment rather than an ointment.[2 3]

Atopic dermatitis is usually managed in primary care. Treatment strategies include advice on the avoidance of factors that can provoke dermatitis, such as soap, and the use of emollients to moisturise and relieve symptoms. For flares, or dermatitis that does not respond to these measures, topical corticosteroids are normally prescribed once or twice daily in conjunction with continued use of emollients (TA81).

Two calcineurin inhibitors (tacrolimus and pimecrolimus) are recommended as second-line treatment options when the disease has not been adequately controlled by the use of topical steroids at the maximum strength and potency or where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy (TA82). Tacrolimus ointment is recommended for treating moderate to severe atopic dermatitis in people aged 2 years and older, while pimecrolimus cream is recommended for treating moderate disease on the face and neck in children aged 2 to 16 years (TA82). Alitretinoin is recommended as a possible treatment for adults with severe chronic hand dermatitis affecting their quality of life and not responding to potent topical corticosteroids (TA177).

People with moderate or severe dermatitis not responding to topical treatments may be referred to secondary care and treated with stronger oral medications such as oral steroids, systemic immunosuppressants (azathioprine, ciclosporin, mycophenolate mofetil and methotrexate).[4] In addition, phototherapy and photochemotherapy (psoralen–ultraviolet A; PUVA) can be used to manage moderate to severe atopic dermatitis in selected adults and older children.[5]

Dupilumab and baricitinib are recommended as options for treating moderate to severe atopic dermatitis in adults whose disease has not responded to at least 1 other systemic therapy, such as ciclosporin, methotrexate, azathioprine and mycophenolate mofetil, or these are contraindicated or not tolerated (TA534 and TA681`). Since the publication of TA534, the marketing authorisation for dupilumab has been extended to include people aged 12 to 17 years, and dupilumab is commissioned by NHS England for this group.

The technologies

Abrocitinib (CIBINQO, Pfizer) is a selective Janus Kinase (JAK) 1 inhibitor. JAKs are enzymes that mediate the transduction of intracellular signals involved in the process of inflammatory disease. Abrocitinib is administered orally. Abrocitinib does not currently have a marketing authorisation in the UK for atopic dermatitis. It has been studied in clinical trials alone or in combination with topical therapy compared with placebo or dupilumab in people with moderate to severe atopic dermatitis that is not adequately controlled with topical medications or for whom topical treatments are not appropriate, or who were candidates for systemic therapy.

Tralokinumab (Adtralza, Leo Pharma UK) is an anti-interleukin (IL)-13 human immunoglobulin- G4 monoclonal antibody. It binds to the type 2 cytokine interleukin-13 IL-13 inhibiting its action. It is administered by subcutaneous injection. Tralokinumab does not currently have a marketing authorisation for treating people with moderate to severe atopic dermatitis and who are candidates for systemic therapy. It has been studied the following in clinical trials:

- In combination with topical corticosteroids compared with placebo in adults with severe atopic dermatitis that is not adequately controlled with cyclosporin A or for whom oral cyclosporin A is contraindicated

- In combination with topical corticosteroids compared with placebo in adults with moderate to severe atopic dermatitis

- As a monotherapy compared with placebo in adults with moderate to severe atopic dermatitis that is not adequately controlled with topical medications or for whom topical treatments are not appropriate.

Upadacitinib (Rinvoq, AbbVie) is a selective and reversible, second generation Janus kinase (JAK) inhibitor. JAK inhibitors are enzymes that mediate the transduction of intracellular signals involved in the process of inflammatory disease. Upadacitinib is administered orally. Upadacitinib does not currently have a marketing authorisation in the UK for atopic dermatitis. It has been studied in the following clinical trials:

- as a monotherapy compared with placebo in people aged 12 years and over with moderate to severe chronic atopic dermatitis. The trials included people whose disease had not previously responded to topical corticosteroids or topical calcineurin inhibitors and in people who had systemic treatment for atopic dermatitis within 6 months.

- as a monotherapy compared with dupilumab in adults with moderate to severe atopic dermatitis. The trial included people who were candidates for systemic therapy or who had recently needed systemic therapy for atopic dermatitis.

- in combination with topical corticosteroids compared with placebo in people aged 12 years and over with moderate to severe chronic atopic dermatitis. The trial included people whose disease had not previously responded to topical corticosteroids or topical calcineurin inhibitors and in people who had systemic treatment for atopic dermatitis within 6 months.

Intervention(s)	Abrocitinib, tralokinumab and upadacitinib
Population(s)	People with moderate to severe atopic dermatitis
Comparators	• Phototherapy including with ultraviolet (UVB) radiation or psoralen-ultraviolet A (PUVA) • Immunosuppressive therapies (azathioprine, ciclosporin, methotrexate and mycophenolate mofetil) • Oral corticosteroids • Alitretinoin (in people with atopic dermatitis affecting the hands) • Dupilumab • Baricitinib • Best supportive care (combination of emollients, low to mid potency topical corticosteroids, and rescue therapy including higher potency topical or oral corticosteroids or topical calcineurin inhibitors)
Outcomes	The outcome measures to be considered include: • measures of disease severity • measures of symptom control • disease free period/maintenance of remission • time to relapse/prevention of relapse • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered: • people with atopic dermatitis affecting the hands; • people for whom systemic therapies have been inadequately effective, not tolerated or contraindicated; • skin colour subgroups. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** 'Baricitinib for treating moderate to severe atopic dermatitis' (2021) NICE Technology Appraisal 681. Review date 2024. Dupilumab for treating moderate to severe atopic dermatitis (2018) NICE Technology Appraisal 534. Review date: 2021. Alitretinoin for the treatment of severe chronic hand eczema (2009) NICE technology appraisal guidance 177. On static list. Tacrolimus and pimecrolimus for atopic eczema (2004) NICE technology appraisal guidance 82. On static list. Frequency of application of topical corticosteroids for atopic eczema (2004) NICE technology appraisal guidance 81. On static list. **Appraisals in development (including suspended**

	appraisals) Tralokinumab for treating moderate to severe atopic dermatitis in people aged 12 and over NICE technology appraisal guidance [ID3823]. Expected publication date to be confirmed. **Related Guidelines:** Atopic eczema in under 12s: diagnosis and management (2007) NICE guideline CG57. **Guidelines in development:** Secondary infection of common skin conditions including eczema: antimicrobial prescribing. Publication expected March 2021. **Related Interventional Procedures:** Grenz rays therapy for inflammatory skin conditions (2007) NICE interventional procedures guidance 236. **Related Quality Standards:** Atopic eczema in under 12s (2013). NICE quality standard 44. **Related NICE Pathways**: Eczema (2021) NICE pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) Manual for prescribed specialised services 2018/19 Chapters 59 and 61 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2,4,5 NHS England (2013) 2013/14 NHS standard contract for specialised allergy services (all ages). Service specification No: B09/S/b NHS England (2013) 2013/14 NHS standard contract for specialised dermatology services (all ages). Service specification No: A12/S/a NHS England (2017) Commissioning medicines for children in specialised services policy

References

1. National Eczema Society. Our skin and eczema. Accessed December 2020.

2. National Institute for Health and Care Excellence (2018) Resource impact report: Dupilumab for treating moderate to severe atopic dermatitis (TA534). Accessed December 2020.

3. National Institute for Health and Care Excellence. Resource impact report: Baricitinib for treating moderate to severe atopic dermatitis (TA681) (2021). Accessed March 2021

4. 4.0British Association of Dermatologists (2020) Atopic eczema. Accessed December 2020.

5. Simpson EL, Bruin-Weller M, Flohr C, Ardern-Jones MR, Barbarot S et al. When does atopic dermatitis warrant systemic therapy? Recommendations from an expert panel of the International Eczema Council. *Journal of the American Academy of Dermatology* 2017; 77(4):623-633.