NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Upadacitinib for treating moderate to severe atopic dermatitis in people aged 12 and over

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of upadacitinib within its marketing authorisation for treating moderate to severe atopic dermatitis in people aged 12 and over.

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 eczema 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 will need a systemic treatment rather than an ointment.[2]

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). Tacrolimus ointment (calcineurin inhibitor) is recommended when moderate to severe atopic dermatitis has not been adequately controlled by 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) Pimecrolimus cream (calcineurin inhibitor) is recommended as an option as a second treatment for moderate atopic eczema on the face and neck in children aged 2 to 16 years that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use particularly skin atrophy (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). In addition, phototherapy and photochemotherapy (psoralen–ultraviolet A; PUVA) can be used to manage chronic severe atopic dermatitis.[3]
Dupilimumab is recommended as an option 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). Since the publication of TA534 the marketing authorisation for dupilumab has been extended to also include people ages 12 to 17 years and dupilumab is commissioned by NHS England for this group.

The technology

Upadacitinib (ABT-494, AbbVie) is a Janus Kinase (JAK)1 inhibitor. JAKs are enzymes that mediate the transduction of intracellular signals involved in the process of inflammatory disease. Upadacitinib is administered orally.

Upadacitinib does not have a marketing authorisation in the UK for atopic dermatitis. It has been studied in 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 in people with moderate to severe chronic atopic dermatitis. 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)	Upadacitinib
Population(s)	People aged 12 years or over 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 • 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.
Other considerations	If the evidence allows the following subgroups will be considered: • people with atopic dermatitis affecting the hands; • people for whom 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:** Dupilumab for treating moderate to severe atopic dermatitis (2018) NICE technology appraisal guidance 534 Alitretinoin for the treatment of severe chronic hand eczema (2009) NICE technology appraisal guidance 177 Tacrolimus and pimecrolimus for atopic eczema (2004) NICE technology appraisal guidance 82 Frequency of application of topical corticosteroids for atopic eczema (2004) NICE technology appraisal guidance 81 **Appraisals in development (including suspended appraisals)**

	Crisaborole for treating mild to moderate atopic dermatitis in people aged 2 years and older (ID1195) NICE technology appraisal guidance. Publication expected June 2020 Baricitinib for treating moderate to severe atopic dermatitis (ID1622). NICE technology appraisal guidance. Expected publication date to be confirmed. **Related Guidelines:** Atopic eczema in under 12s: diagnosis and management (2007) NICE guideline CG57 **Related Interventional Procedures:** Grenz rays therapy for inflammatory skin conditions (2007) NICE interventional procedures guidance 236 **Related NICE Pathways**: Eczema (2018) 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. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 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

Questions for consultation

Treatment pathway

- Is upadacitinib likely to be used in combination with topical corticosteroids or as a monotherapy in clinical practice?

- For a person needing systemic therapy to treat their atopic dermatitis would upadacitinib be used as a first systemic treatment or after immunosuppressive therapies (such as ciclosporin, methotrexate, azathioprine)?
- Would upadacitinib be used after dupilumab and vice versa?
- Would a person who is a 'candidate for systemic therapy' already have had phototherapy?
- Which treatments are considered to be established clinical practice in the NHS for moderate to severe atopic dermatitis in people aged 12-17 who are candidates for systemic therapy? Do these differ to treatments considered to be established clinical practice in the NHS for adults?

Comparators

- Have all relevant comparators for upadacitinib been included in the scope?
- How should best supportive care be defined?

Outcomes

- Are the outcomes listed appropriate?

Subgroups

- Are the subgroups suggested in 'other considerations appropriate?
- Are there any other subgroups of people in whom upadacitinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider upadacitinib will fit into the existing NICE pathway Eczema?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which upadacitinib will beis/are/will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider upadacitinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of upadacitinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 National Eczema Society. What is Eczema? Accessed November 2016. http://www.eczema.org/what-is-eczema. Accessed March 2020

2 Resource impact report: Dupilumab for treating moderate to severe atopic dermatitis (2018). NICE technology appraisal 534

3 British Association of Dermatologists. Atopic Eczema. Accessed March 2020. http://www.bad.org.uk/shared/get-file.ashx?id=69&itemtype=document.