NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Crisaborole for treating mild to moderate atopic dermatitis in people aged 2 years and older

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of crisaborole within its marketing authorisation for treating mild to moderate atopic dermatitis in people aged 2 years and older.

Background

Atopic dermatitis (atopic eczema) is a long term condition that affects the skin. It may start at any age but the onset is often in childhood. 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. Atopic dermatitis cannot be cured although it can improve significantly, or even clear completely, in some children and as they get older. [1]

Estimates of the prevalence of atopic dermatitis vary. It is more common in childhood and affects 1 in 5 children in the UK.[1] In 2016-17, there were 1,135 admissions with 1,258 finished consultant episodes for atopic dermatitis in England.[2]

Mild to moderate atopic dermatitis is usually managed in primary care. Typical treatment involves emollients and topical corticosteroids (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).

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). Dupilumab is recommended for adults with moderate or severe dermatitis, who have 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).

The technology

Crisaborole (Eucrisa, Pfizer) is a nonsteroidal small molecule that inhibits the enzyme phosphodiesterase 4 (PDE4) and reduces the production of tumour necrosis factor (TNF) -alpha and other cytokines, including IL-12 and IL-23, which are proteins involved in the inflammation process and immune responses. It contains a boron atom that helps penetrate the skin and is essential for its binding activity. It is a topical ointment.

Crisaborole does not have a marketing authorisation in the UK. It has been studied in phase III clinical trials in people aged 2 years and older with atopic dermatitis compared with placebo.

Intervention(s)	Crisaborole
Population(s)	People aged 2 years and older with mild and moderate atopic dermatitis
Comparators	• 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) or current NHS standard treatment
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 for whom therapies have been inadequately effective, not tolerated or contraindicated • people with atopic dermatitis affecting the hands • 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 adults with moderate to severe atopic dermatitis (2018). NICE Technology Appraisal TA534. Review date: August 2021. Alitretinoin for the treatment of severe chronic hand eczema (2009). NICE Technology Appraisal TA177. Guidance on static list. Tacrolimus and pimecrolimus for atopic eczema (2004) NICE Technology Appraisal TA82. Guidance on static list Frequency of application of topical corticosteroids for atopic eczema (2004) NICE Technology Appraisal TA81 Guidance in the static list Proposed NICE technology appraisals: Dupilumab for treating moderate to severe atopic dermatitis in people aged 12 to 17 years [ID1479]. Publication to be confirmed. Related Guidelines: Atopic eczema in under 12s: diagnosis and management (2007) NICE guideline CG57 Atopic eczema in under 12s (2013) NICE quality standard 44 Related Interventional Procedures: Grenz rays therapy for inflammatory skin conditions

	(2007) NICE interventional procedures guidance 236 ImmunoCAP ISAC 112 and Microtest for multiplex allergen testing (2016) NICE diagnostics guidance 24 Related NICE Pathways: Eczema overview (2018) NICE pathway
Related National Policy	NHS England (2017) Manual for prescribed specialised services 2017/18 Chapter 59 - Highly specialist allergy services (adults and children) p.142 See also chapter 61 – Highly specialist dermatology services (adults and children) p.147 NHS England (2013) NHS standard contract for specialised dermatology services (all ages). Reference A12/S/a Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017: Domains 2.

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for treating mild to moderate atopic dermatitis in people aged 2 years and older?

Is best supportive care an appropriate comparator?

How should best supportive care be defined?

Are the outcomes listed appropriate?

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

Where do you consider crisaborole will fit into the existing NICE pathway, Eczema overview ?

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 crisaborole 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 crisaborole 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 crisaborole 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).

References

1. NIHR (2018) Dupilumab for children aged 12 years to 17 years with moderate to severe atopic dermatitis. http://www.io.nihr.ac.uk/wp-content/uploads/2018/06/20586-Dupilumab-for-12-17-years-old-children-with-atopic-dermatitis-V1.0-MAY-2018-NON-CONF.pdf

2. NHS Digital (2017) Hospital Admitted Patient Care Activity, 2016-17: Diagnosis. Accessed September 2018. https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2016-17

3. British Association of Dermatologists. Atopic Eczema. Accessed September 2018. http://www.bad.org.uk/shared/get-file.ashx?id=69&itemtype=document.