NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Adalimumab and etanercept for treating severe, chronic plaque psoriasis in children and adolescents

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of adalimumab and etanercept within their marketing authorisations for treating severe chronic plaque psoriasis in children and adolescents.

Background

Plaque psoriasis is an inflammatory skin condition characterised by an accelerated rate of turnover of the upper layer of the skin (epidermis). This leads to an accumulation of skin cells forming raised plaques on the skin. These plaques can be flaky, scaly, itchy and red or a darker colour to the surrounding skin. Plaque psoriasis may affect the scalp, elbows, knees and lower back and sometimes the face, groin, armpits or behind the knees. Although it is a chronic, persistent, severe condition, its course may be unpredictable, with flare-ups and remissions.

Psoriasis is generally graded as mild, moderate or severe and takes into account the location, surface area of skin affected and the impact of the psoriasis on the person. The Psoriasis Area and Severity Index (PASI) is an index of disease severity in adults but has not been validated in children and adolescents. The Children's Dermatology Life Quality index is a validated tool to assess the impact of psoriasis on physical, psychological and social wellbeing in children and adolescents.

The estimated overall UK prevalence of psoriasis is approximately 2% with 1% of people with psoriasis having severe disease. The prevalence is lower in children and adolescents and is 0.55% in children under 10 years and 1.4% in people aged between 10 and 19 years (Gelfand et al. 2005).

NICE clinical guideline 153 on psoriasis recommends that people with psoriasis should be offered topical therapies such as corticosteroids, vitamin D and vitamin D analogues. For people in whom topical therapy does not alleviate symptoms the guideline recommends phototherapy (broad- or narrow band ultraviolet B light), UVA phototherapy with psoralen (PUVA). Systemic non-biological therapies are recommended for people whose psoriasis does not respond to topical therapy and is extensive, associated with significant functional impairment and distress or for people for whom phototherapy has been ineffective or cannot be used to treat their psoriasis. The guideline recommends that systemic treatments used to treat adults such as methotrexate or ciclosporin should be used with caution to treat psoriasis

in children and adolescents because these treatments do not have UK marketing authorisation for psoriasis in this population. Acitretin should only be used in exceptional circumstances for children and adolescents. NICE technology appraisal guidance 146, 103 and 180 recommend adalimumab, etanercept and ustekinumab respectively as treatment options for adults with severe psoriasis who have not responded to, are intolerant to or contraindicated to standard systemic therapies such as ciclosporin, methotrexate or PUVA . Technology appraisal guidance 134 recommends infliximab as a treatment option for adults with very severe psoriasis who have not responded to, are intolerant to or are contraindicated to standard systemic therapies.

The technology

Adalimumab (Humira, AbbVie) inhibits TNF alpha. It is a fully human immunoglobulin G1 monoclonal antibody. It is administered by subcutaneous injection. It has a marketing authorisation in the UK for treating severe chronic plaque psoriasis in children and adolescents from 4 years of age who have an inadequate response to or are inappropriate candidates for topical therapy and phototherapies.

Etanercept (Enbrel, Pfizer) is a recombinant human tumour necrosis factor (TNF) receptor fusion protein that inhibits the activity of TNF. TNF is a cytokine that is released from T lymphocytes; it mediates inflammation and modulates the cellular immune response. It has a marketing authorisation in the UK for treating chronic severe plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

Intervention(s)	• Adalimumab • Etanercept
Population(s)	Children and adolescents with severe, chronic plaque psoriasis who • have had an inadequate response to or for whom topical therapy and/or phototherapy are inappropriate. • have had an inadequate response to or for whom other systemic therapies and/or phototherapy are inappropriate.
Comparators	Non-biological systemic therapy (including, but not limited to, ciclosporin and methotrexate) Where appropriate, adalimumab and etanercept will be compared with each other.

Outcomes	The outcome measures to be considered include: • Severity of psoriasis • remission rate • relapse rate • adverse effects of treatment • health-related quality of life (including the Children's Dermatology Life Quality Index).
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. Biosimilars are not expected to be in established NHS practice at the time of appraisal and are not included as comparators.
Other considerations	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: 'Ustekinumab for the treatment of adults with moderate to severe psoriasis (2009) NICE Technology Appraisal 180. On static list 'Adalimumab for the treatment of adults with psoriasis' (2008) NICE Technology Appraisal 146. On static list 'Infliximab for the treatment of adults with psoriasis' (2008) Technology Appraisal 134. On static list 'Etanercept and efalixumab for the treatment of adults with psoriasis' (2006) NICE Technology Appraisal 103. On static list Appraisals in development (including suspended

	appraisals): 'Secukinumab for treating moderate to severe plaque psoriasis' NICE technology appraisals guidance [ID718] Publication expected July 2015 'Apremilast for treating moderate to severe plaque psoriasis' NICE technology appraisals guidance [ID679]. Publication expected August 2015 'Briakinumab for the treatment of moderate to severe chronic plaque psoriasis [ID65]. Suspended Related Guidelines: 'Psoriasis: The assessment and management of psoriasis' (2012) NICE guideline 153 Review date December 2016 Related Interventional Procedures: 'Grenz rays therapy for inflammatory skin conditions' (2007) NICE interventional procedures guidance 236 Related Quality Standards: 'Psoriasis' (2013) NICE quality standard 40 Related NICE Pathways: Psoriasis (2015) NICE pathway http://pathways.nice.org.uk/
Related National Policy	Manual for Prescribed Specialised Services for 2013/14 Chapter 61 Highly specialist dermatology services (all ages). http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 2-5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

Would adalimumab and etanercept be used at the same position in the treatment pathway for children and adolescents with severe, chronic plaque psoriasis?

Have all relevant comparators for adalimumab and etanercept been included in the scope? Which non-biological treatments are used to treat children and adolescents with severe plaque psoriasis in clinical practice? Would infliximab

or ustekinumab be used outside of their marketing authorisations in a paediatric population in clinical practice in England? Are any biosimilar products for adalimumab, etanercept, infliximab or ustekinumab currently used in clinical practice in England?

Are the listed outcomes relevant and defined appropriately? Are there any additional outcomes that are not currently listed?

Are there any subgroups of people in whom adalimumab or etanercept are expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider adalimumab and etanercept will fit into the existing NICE pathway, psoriasis?

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 adalimumab 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 adalimumab or etanercept to be innovative in their potential to make a significant and substantial impact on health-related benefits and how they might improve the way that current need is met (are they a 'step-change' in the management of the condition)?

Do you consider that the use of adalimumab or etanercept 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.

NICE intends to appraise these technologies through its Multiple Technology Appraisal (MTA) 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

Gelfand J, Weinstein R, Porter S et al. (2005) Prevalence and treatment of psoriasis in the United Kingdom A population based study. JAMA Dermatology 141: 1537-1541.