

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Multiple Technology Appraisal

Adalimumab, etanercept and ustekinumab for treating plaque psoriasis in children and young people

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of adalimumab, etanercept and ustekinumab within their marketing authorisations for treating plaque psoriasis in children and young people.

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 young people. 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 young people.

The estimated UK prevalence of psoriasis is approximately 0.55% in children under 10 years and 1.4% in people aged between 10 and 19 years.¹

The NICE clinical guideline 153 on psoriasis for adults, children and young people recommends initial treatment with 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 (narrow band ultraviolet B light). The guideline also recommends psoralen with local ultraviolet A phototherapy (PUVA) for people with palmoplantar pustulosis. It recommends systemic non-biological therapies (such as ciclosporin, methotrexate and acitretin) if psoriasis cannot be controlled with topical therapy and has a significant impact on physical psychological or social wellbeing and when the psoriasis is: extensive; associated with significant functional impairment and distress; or when

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phototherapy has been ineffective or cannot be used. The guideline notes that methotrexate and ciclosporin do not have UK marketing authorisations for treating psoriasis in children and young people. The guideline recommends that acitretin should only be used in exceptional circumstances for children and young people.

There is currently no NICE technology appraisal guidance for treating psoriasis in children and young people. The following NICE technology appraisal (TA) guidance applies to adults:

- TA 146, 103, 180 and 350 recommend adalimumab, etanercept, ustekinumab and secukinumab 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.
- TA 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.
- TA 368 did not recommend apremilast for treating moderate to severe chronic plaque psoriasis.

The technologies

Adalimumab (Humira, AbbVie) is a fully human immunoglobulin G1 monoclonal antibody that inhibits the activity of tumour necrosis factor (TNF). 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 TNF receptor fusion protein that inhibits the activity of TNF. 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.

Ustekinumab (Stelara, Janssen) is a fully human monoclonal antibody that acts as a cytokine inhibitor by targeting interleukin-12 and interleukin-23. It prevents the inflammation associated with psoriasis. It has a marketing authorisation for treating moderate to severe plaque psoriasis in adolescent patients from the age of 12 years and older who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

All 3 of these treatments are administered by subcutaneous injection.

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Intervention(s)	<ul style="list-style-type: none"> • Adalimumab • Etanercept • Ustekinumab
Population(s)	Children and young people with plaque psoriasis
Comparators	<ul style="list-style-type: none"> • Non-biological systemic therapy (including, but not limited to, ciclosporin and methotrexate) • Topical therapy (for people in whom non-biological systemic therapy is not suitable) • Biological treatments used outside of their marketing authorisation (such as infliximab, adalimumab, etanercept or ustekinumab if used outside of the constraints of the relevant marketing authorisation in children and young people) • When appropriate, adalimumab, etanercept and ustekinumab will be compared with each other.
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • severity of psoriasis • response and remission rate • relapse rate • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability and cost of biosimilars should be taken into account.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>

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<p>Other considerations</p>	<p>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.</p> <p>If evidence allows, the appraisal should consider the sequential use of the interventions.</p> <p>If evidence allows, the clinical and cost effectiveness of adalimumab, etanercept and ustekinumab should be considered separately for people receiving these treatments following an inadequate response, intolerance or contraindication to:</p> <ul style="list-style-type: none"> • topical therapies • phototherapies • non-biological systemic therapies • biological therapies <p>The 3 interventions have marketing authorisations covering different age ranges, therefore if evidence allows, the clinical and cost effectiveness of adalimumab, etanercept and ustekinumab should be considered separately for different age groups.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Apremilast for treating moderate to severe plaque psoriasis’ (2015) NICE technology appraisal 368. Review decision expected 2018</p> <p>‘Secukinumab for treating moderate to severe plaque psoriasis’ (2015) NICE technology appraisal 350. Review decision expected 2018</p> <p>‘Ustekinumab for the treatment of adults with moderate to severe psoriasis (2009) NICE Technology Appraisal 180. On static list</p> <p>‘Adalimumab for the treatment of adults with psoriasis’ (2008) NICE Technology Appraisal 146. On static list</p> <p>‘Infliximab for the treatment of adults with psoriasis’ (2008) Technology Appraisal 134. On static list</p> <p>‘Etanercept and efilixumab for the treatment of adults with psoriasis’ (2006) NICE Technology Appraisal 103. On static list</p> <p>Appraisals in development (including suspended</p>

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	<p>appraisals):</p> <p>'Briakinumab for the treatment of moderate to severe chronic plaque psoriasis [ID65]. Suspended</p> <p>Related Guidelines:</p> <p>'Psoriasis: The assessment and management of psoriasis' (2012) NICE guideline 153 Review decision expected December 2016</p> <p>Related Interventional Procedures:</p> <p>'Grenz rays therapy for inflammatory skin conditions' (2007) NICE interventional procedures guidance 236</p> <p>Related Quality Standards:</p> <p>'Psoriasis' (2013) NICE quality standard 40</p> <p>Related NICE Pathways:</p> <p>Psoriasis (2015) NICE pathway http://pathways.nice.org.uk/pathways/psoriasis</p>
Related National Policy	<p>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</p> <p>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</p>

Reference

1. 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.