National Horizon Scanning Centre

Etanercept (Enbrel) for moderate-to-severe plaque psoriasis in children and adolescents

April 2008

This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Etanercept (Enbrel) for moderate-to-severe plaque psoriasis in children and adolescents

Target group
- Plaque psoriasis – in children and adolescents.

Technology description
Etanercept (Enbrel) is a human recombinant tumour necrosis factor (TNF) receptor p75 fusion protein thought to act by competitively inhibiting TNF binding to the cell surface TNF-receptor and thus preventing TNF-mediated cellular responses. Etanercept may also modulate biologic responses controlled by additional downstream molecules that are induced or regulated by TNF. In clinical trials children received 0.8mg/kg up to a maximum dose of 50mg etanercept administered by subcutaneous injection (SC) once a week. Etanercept is intended to be used as an addition to topical therapy.

Etanercept is licensed in the EU for:
- Moderate-to-severe plaque psoriasis in adult patients who have failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or long-wave ultraviolet A with psoralen (PUVA).
- Active polyarticular-course juvenile idiopathic arthritis in children and adolescents aged 4 to 17 years who have had an inadequate response to, or who have proved intolerant of, methotrexate.
- Severe ankylosing spondylitis inadequately responsive to conventional therapy.
- Moderate-to-severe active rheumatoid arthritis either alone or in combination with methotrexate when the response to other disease-modifying antirheumatic drugs is inadequate.
- Active and progressive psoriatic arthritis inadequately responsive to other disease-modifying antirheumatic drugs.

Innovation and/or advantages
There is concern over the safety of currently available systemic treatments in the paediatric population and etanercept would be the first biological therapy licensed in this patient group.

Developer
Wyeth; Amgen.

Availability, launch or marketing dates, and licensing plans:
A type II variation (licence extension) was submitted in December 2007.

NHS or Government priority area:
This topic relates to The Children's National Service Framework (2004).

Relevant guidance
There is no relevant guidance specifically for psoriasis in children and adolescents. Guidance for adults includes:

- NICE technology appraisal in development. Adalimumab for the treatment of psoriasis. Expected date of issue to be confirmed.
• NICE technology appraisal. Etanercept and efalizumab for the treatment of adults with psoriasis. 2006².
• NICE technology appraisal. Infliximab for the treatment of adults with psoriasis. 2008³.
• British Association of Dermatologists. Clinical Guidelines - Psoriasis. 2006⁴.
• British Association of Dermatologists. Guidelines for use of biological interventions in psoriasis. 2005⁵.

Clinical need and burden of disease
Plaque psoriasis is a non-infectious, inflammatory disease of the skin characterised by increased epidermal proliferation which causes raised red patches of skin (plaques). Plaques can occur anywhere on the body but the most common sites are the elbows, knees and scalp. Plaque psoriasis is a chronic-progressive condition but its course may be erratic, with flare-ups and remissions. The disease is disfiguring, stigmatising and associated with a significantly impaired quality of life. Plaque psoriasis has been shown to affect health-related quality of life (HRQoL) to an extent similar to the effects of other chronic diseases such as depression, myocardial infarction, hypertension, congestive heart failure or type 2 diabetes.

It is estimated that plaque psoriasis affects around 1.6% of the UK population. This equates to 859,661 people in England and Wales with the condition. Psoriasis can develop at any age but onset is most common between the ages of 15 and 25⁶. In one study approximately one-third of adults reported onset at or before 16 years of age⁷.

Existing comparators and treatments
First-line therapies
• Emollients, salicyclic acid, topical steroids, vitamin D analogues (for children 6 years and above), coal tar, dithranol and tazarotene (a topical retinoid).

Phototherapy
• UVB or a psoralen/UVA combination.
The use of phototherapy and photochemotherapy is limited in children by concerns over carcinogenicity and premature aging. PUVA is contraindicated in young children, but may be used in adolescents if absolutely necessary.

Systemic treatment (licensed for severe disease resistant to other therapies)
• Acitretin, ciclosporin, methotrexate.

Biological therapies (not licensed in children)
• Adalimumab, alefacept, efalizumab, infliximab.

Efficacy and safety

<table>
<thead>
<tr>
<th>Trial code</th>
<th>NCT00078819⁸</th>
<th>NCT00141921⁹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase</td>
<td>Phase III</td>
<td>Phase III Extension trial.</td>
</tr>
<tr>
<td>Sponsor</td>
<td>Amgen</td>
<td>Amgen</td>
</tr>
<tr>
<td>Status</td>
<td>Completed, published¹⁰</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Location</td>
<td>USA and Canada</td>
<td>USA and Canada</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, double blind</td>
<td>Non-randomised, open-label</td>
</tr>
<tr>
<td>Participants in trial</td>
<td>n=211; 4-17 years; plaque psoriasis. Randomised to etanercept 0.8mg/kg SC (maximum 50mg) weekly or placebo for 12 weeks. Followed by 24 weeks of once-weekly open-label etanercept.</td>
<td>n=182; enrollment on previous study NCT00078819. Etanercept 0.8mg/kg (maximum 50 mg) weekly sub-cutaneously</td>
</tr>
</tbody>
</table>
April 2008

National Horizon Scanning Centre
News on emerging technologies in healthcare

At week 36, 138 patients were re-randomised to etanercept or placebo to investigate the effects of withdrawal and re-treatment. (SC).

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>48 weeks</th>
<th>168 weeks</th>
<th>(SC).</th>
</tr>
</thead>
</table>

Primary outcome

PASI 75\(^a\) response at week 12

Adverse events

Secondary outcomes

PASI 50 at week 12; PASI 90 at week 12; clear or minimal sPGA\(^b\) at week 12; CDLQI\(^c\) at week 12; safety; antibodies to etanercept, and disease rebound.

PASI 50; PASI 75; PASI 90; sPGA; CDLQI; joint pain; PASI score; antibodies

Key results

At week 12, 57% of etanercept group achieved PASI 75 vs. 11% of placebo (P<0.001). At week 12 a significantly higher proportion of etanercept group vs. placebo had PASI 50 (75% vs 23%), PASI 90 (27% vs 7%) and PGA clear or almost clear (53% vs 13%) P<0.001. At week 36, 68% vs. 65% of etanercept and placebo groups reached PASI 75 respectively.

Adverse effects

Rates of non-infectious adverse events (430.5 per 100 patient-years for placebo and 287.6 per 100 patient-years for etanercept) and of infections (308.3 per 100 patient-years for placebo and 229.3 per 100 patient-years for etanercept) were similar in the two groups, and all but 10 events were mild or moderate intensity. There were no serious adverse events during the placebo-controlled period. No deaths, cancers, opportunistic infections, tuberculosis or demyelination events were reported.

Cytokine inhibitors have been associated with infections including tuberculosis and septicaemia. Other adverse effects that have been reported are worsening heart failure and blood disorders\(^1,10\).

**Estimated cost and cost impact**

The median weight of trial patients was 59.8kg. At a dose of 0.8mg/kg this equates to 48mg per dose, at a cost of £178.75 per dose, or £9,295 for a year (assumes continuous dosing for 52 weeks).

---

\(^a\) PASI (Psoriasis area-and-severity index score) is a measure of overall psoriasis severity and coverage which combines assessments of the extent of body-surface involvement in four anatomical regions (head, trunk, arms, and legs), and the severity of desquamation, erythema, and plaque induration. It can be measured as a percentage improvement, where a PASI 75 is a 75% improvement in PASI score.

\(^b\) PGA (Physicians Global Assessment) is a measure of patients’ psoriasis overall relative to baseline. It considers involvement of body-surface area, induration, scaling and erythema. It is scored as 1 (clear), 2 (excellent), 3 (good), 4 (fair), 5 (poor), or 6 (worse).

\(^c\) CDLQI (Children’s Dermatology Life Quality Index) is a 10-item questionnaire completed by the patient, and measures the effect of psoriasis on quality of life.
Potential or intended impact – speculative

Patients

✔ Reduced morbidity
☐ Reduced mortality or increased survival
☐ Quicker, earlier or more accurate diagnosis or identification of disease
✔ Other: Use may be limited by concerns over long-term adverse effects
☐ None identified

Services

✔ Increased use: requires weekly injection and/or monitoring of self-administration
☐ Service reorganisation required
✔ Staff or training required
☐ Decreased use
☐ Other:
☐ None identified

Costs

☐ Increased unit cost compared to alternative
✔ New costs: biologics cost more than conventional treatments.
☐ Increased costs: more patients coming for treatment
☐ Increased costs: capital investment needed
☐ Savings:
☐ Other:

References

1 NICE technology appraisal in development. Adalimumab for the treatment of psoriasis. Issue date to be confirmed.

The National Institute for Health Research National Horizon Scanning Centre Research Programme is funded by the Department of Health. The views expressed in this publication are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health