

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Dimethyl fumarate for treating moderate to severe chronic plaque psoriasis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dimethyl fumarate (LAS41008) within its marketing authorisation for treating moderate to severe chronic plaque psoriasis.

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 and takes into account the size of the area covered with psoriasis as well as redness, thickness and scaling. In addition, the Dermatology Life Quality Index (DLQI) is a validated tool that can be used to assess the impact of psoriasis on physical, psychological and social wellbeing.

The prevalence of psoriasis in England is estimated to be 1.75%¹, which is about 951,000 people, of whom about 20% have moderate to severe psoriasis (15% moderate, 5% severe)², equating to approximately 190,000 people. About 90% of people with the condition have plaque psoriasis.

There is no cure for psoriasis but there are a wide range of topical and systemic treatments that can manage the condition. Most treatments reduce the severity of psoriasis flares rather than prevent episodes. Psoriasis has to be treated continually and on a long-term basis. 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. Fumaric acid esters have been recommended for treating moderate to severe chronic plaque psoriasis in European guidelines³ and Fumaderm has also been used off-label in in the UK for this population.

NICE technology appraisal guidance 146, 103,180, 350, 419 recommend adalimumab, etanercept, ustekinumab, secukinumab and apremilast respectively as treatment options for adults with severe psoriasis (as defined by a total PASI score of 10 or more and a DLQI score of more than 10) 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 (as defined by a total PASI score of 20 or more and a DLQI score of more than 18) who have not responded to, are intolerant to or are contraindicated to standard systemic therapies. Biosimilar products of the biological therapies are available for use in the NHS.

The technology

Dimethyl fumarate (LAS41008; brand name unknown, Almirall SA) is a methyl ester of fumaric acid anti-inflammatory that inhibits certain functions of skin cells, namely, differentiation, proliferation and migration, as well as affecting the immune system and proliferating cells in general. It is administered orally.

Dimethyl fumarate does not currently have a marketing authorisation in the UK for moderate to severe chronic plaque psoriasis. It is currently being studied in a clinical trial compared with a fumaric acid ester (Fumaderm) or placebo in adults with moderate to severe chronic plaque psoriasis.

Intervention	Dimethyl fumarate (LAS41008)
Population	Adults with moderate to severe chronic plaque psoriasis
Comparators	<ul style="list-style-type: none"> • Fumaric acid esters (does not currently have a marketing authorisation in the UK for this indication) • Systemic non-biological therapies (including acitretin, ciclosporin, methotrexate, phototherapy with or without psoralen, apremilast) • Systemic biological therapies (including etanercept, adalimumab, secukinumab and ustekinumab, ixekizumab [subject to NICE guidance]) • Best supportive care

<p>Outcomes</p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • Severity of psoriasis (including psoriasis areas severity index) • Psoriasis symptoms on the face, scalp, nails and joints • Response rate • Remission rate • Relapse rate • Mortality • Adverse effects of treatment • Health-related quality of life (including dermatology quality of life index).
<p>Economic analysis</p>	<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 of any patient access schemes for the intervention or comparator technologies should be taken into account.</p> <p>For the comparators, the availability and cost of biosimilars should be taken into account.</p>

<p>Other considerations</p>	<p>If the evidence allows, the following subgroups will be considered:</p> <ul style="list-style-type: none"> • previous use of systemic non-biological therapy • previous use of biological therapy • severity of psoriasis (moderate, severe) <p>Where the evidence allows, sequencing of different drugs and the place of dimethyl fumarate in such a sequence will be considered.</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>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Etanercept and efalizumab for the treatment of adults with psoriasis’ (2006) NICE Technology Appraisal 103. Note: guidance for efalizumab has been withdrawn.</p> <p>‘Infliximab for the treatment of adults with psoriasis’ (2008) NICE Technology Appraisal 134. Static list.</p> <p>‘Adalimumab for the treatment of adults with psoriasis’ (2008) NICE Technology Appraisal 146. Static list.</p> <p>‘Ustekinumab for the treatment of adults with moderate to severe psoriasis’ (2009) NICE Technology Appraisal 180. Static list.</p> <p>‘Secukinumab for treating moderate to severe plaque psoriasis’ (2015) NICE Technology Appraisal 350. Review proposal date: July 2018.</p> <p>‘Apremilast for treating moderate to severe psoriasis’ (2016) NICE Technology Appraisal 419. Review proposal date: November 2019.</p> <p>Appraisals in development (including suspended appraisals):</p> <p>‘Briakinumab for the treatment of moderate to severe chronic plaque psoriasis [ID65]. Suspended</p> <p>‘Ixekizumab for treating moderate to severe plaque psoriasis’ NICE technology appraisals guidance [ID904]. Publication expected April 2017.</p> <p>Related Guidelines:</p> <p>‘Psoriasis: The assessment and management of</p>

	<p>psoriasis' (2012) NICE guideline 153 Review date 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/</p>
<p>Related National Policy</p>	<p>NHS England. Manual for Prescribed Specialised Services for 2016/17 Chapter 61 Highly specialist dermatology services (all ages). https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</p> <p>NHS England. 2013/14 NHS standard contracts for specialised dermatology services (all ages). National programmes of care and clinical reference groups Reference: NHS England/A12/S/a. http://www.england.nhs.uk/wp-content/uploads/2013/06/a12-spec-dermatology.pdf</p> <p>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 2–5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf</p>

References

1. NICE (2015) Psoriasis: assessment and management – costing template. Accessed December 2015.
2. Menter A, Korman NJ, Elmets CA et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011; 65:137–74.
3. Pathirana et al. (2010) European S3-Guidelines on the systemic treatment of psoriasis vulgaris. J Eur Acad Dermatol Venereol. 2010 Jan;24(1):117-8.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1468-3083.2009.03389.x/epdf>

Accessed in March 2016.