

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Dimethyl fumarate for treating moderate to severe plaque psoriasis

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of LAS41008 within its marketing authorisation for treating moderate to severe 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 estimated overall UK prevalence of psoriasis is approximately 2% with 1% of people with psoriasis having severe disease¹. Approximately 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. NICE technology appraisal guidance 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. 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.

Biosimilar products of the biological therapies are available for use in the NHS.

The technology

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.

LAS41008 does not currently have a marketing authorisation in the UK for moderate to severe plaque psoriasis. It is currently being studied in a clinical trial compared with LASW1835 (fumaderm) or placebo in adults with moderate to severe psoriasis.

Intervention(s)	Dimethyl fumarate (LAS41008)
Population(s)	Adults with moderate to severe plaque psoriasis
Comparators	<ul style="list-style-type: none"> • Systemic non-biological therapies (including acitretin, ciclosporin, methotrexate, phototherapy with or without psoralen,) • Systemic biological therapies (including etanercept, infliximab, adalimumab, secukinumab and ustekinumab) • Best supportive care (for people in whom biologic therapies are not tolerated or contraindicated).

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • Severity of psoriasis • Other complications of psoriasis (including nail, scalp and joint outcomes) • Response rate • Remission rate • Relapse rate • Mortality • 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 of any patient access schemes for the intervention or comparator technologies should be taken into account.</p> <p>The availability and cost of biosimilars should be taken into account.</p>
Other considerations	<p>Guidance will only be issued in accordance with the marketing authorisation.</p> <p>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 anti-TNF inhibitors.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>‘Apremilast for treating moderate to severe plaque psoriasis’ NICE technology appraisal 368. Review date November 2018</p> <p>‘Secukinumab for treating moderate to severe plaque</p>

	<p>psoriasis' (2015) NICE technology appraisal 350. Review date July 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 efalixumab for the treatment of adults with psoriasis' (2006) NICE Technology Appraisal 103. On static list</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>Related Guidelines:</p> <p>'Psoriasis: The assessment and management of 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>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>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 Department of Health, NHS Outcomes Framework</p>

	2014-2015, Nov 2013. Domains 2-5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf
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Questions for consultation

Have all relevant comparators for dimethyl fumarate (LAS41008) been included in the scope?

- Would infliximab be used as a treatment for the patient population for whom dimethyl fumarate would be a treatment option?

Which treatments are considered to be established clinical practice in the NHS for moderate to severe psoriasis?
'How should best supportive care be defined?'

Are the outcomes listed appropriate?

Are there any subgroups of people in whom dimethyl fumarate (LAS41008) is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider dimethyl fumarate (LAS41008) 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 dimethyl fumarate (LAS41008) 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 dimethyl fumarate (LAS41008) 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 dimethyl fumarate (LAS41008) 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 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 Horizon Scanning briefing note (November 2013)